CHAPTER I: INTRODUCTION

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OBJECTIVES OF THE STUDY
1.1 Introduction

Coronary Artery Disease (CAD), has the highest share among all Cardiovascular Disease (CVD), and become the leading cause of death worldwide.$^{1,2,3}$ As expected coronary artery disease mortality rates are higher in urban than in rural areas, and CVD is much more prevalent among the upper and middle classes.$^{1-6}$ In 1960, coronary artery disease (CAD) represented 4 % of all CVD deaths, whereas in 1990, the proportion was greater than 50 %. CVD death rates are currently about three times higher than stroke rates. (WHO-2002)

The WHO’s MONICA project found that the majority of individuals who die from myocardial infarction do so within the first hours of the onset of symptoms, i.e. before it is possible to intervene medically. Under such conditions, prevention must be the treatment of choice both on an individual and a population level.$^1$ Survivors of Myocardial Infarction (MI) are at an increased risk of recurrent infarctions and have an annual death rate at least five to six times higher than that of people who do not have CVD. Thus, secondary prevention of major CVD is recognized as a key component of a cost-effective public health strategy to reduce the rising burden of this disease. Although cost-effective treatment is available for the prevention of recurrent vascular attacks, many individuals who have suffered from MI are not receiving adequate preventive treatment even in developed countries.$^{1,2}$ There is a scarcity of data related to the secondary prevention of CVD in lower- and middle-income countries like Iran and India, which currently bear 75% of CVD burden.$^{3,4,5,6,7}$

1.2. Coronary Artery Disease

Definition

Coronary Artery Disease, also called Coronary Heart Disease (CHD), is a condition in which characterized by atherosclerosis in the epicardial coronary arteries. Atherosclerotic plaques, the hallmark of atherosclerosis, progressively narrow the coronary artery lumen and impair antegrade myocardial blood flow. (Figure 1.1) The reduction in coronary artery flow may
be symptomatic or asymptomatic, occur with exertion or at rest, and culminate in a myocardial infarction, depending on obstruction severity and the rapidity of development.\(^8\)

**Figure 1.1.** A) Normal artery with normal blood flow. B) An artery with plaque buildup.

**Prevalence**

According to the American Heart Association and American Stroke Association's 2006 publication on heart disease and stroke statistics, cardiovascular disease (CVD) remains the leading cause of mortality in the United States in men and women of every major ethnic group. It accounts for nearly 1.4 million deaths per year as of 2002 and was responsible for one in almost three deaths in the United States in 2003. Approximately 13 million persons have a history of coronary artery disease and 7.2 million have suffered a myocardial infarction. Almost 2500 Americans die of CVD each day, an average of one death every 35 seconds. CVD claims more lives each year than the next four leading causes of death combined—cancer, chronic lower respiratory diseases, accidents, and diabetes mellitus.\(^9\)
**Pathophysiology**

Coronary artery disease is a chronic process that begins during adolescence and slowly progresses throughout life. Independent risk factors include a family history of premature coronary artery disease, cigarette smoking, diabetes mellitus, hypertension, hyperlipidemia, sedentary lifestyle, and obesity. These risk factors accelerate or modify a complex and chronic inflammatory process that ultimately manifests as fibrous atherosclerotic plaque.

The most widely accepted theory of atherosclerosis states that the process represents an attempt at healing in response to endothelial injury. The first step in the atherosclerotic process is the development of fatty streaks, which contain atherogenic lipoproteins and macrophage foam cells. These streaks form between the endothelium and internal elastic lamina. Over time, an intermediate lesion made up of an extracellular lipid core and layers of smooth muscle and connective tissue matrix eventually forms a fibrous cap. The edge of the fibrous cap (the *shoulder region*) plays a critical role in the development of acute coronary syndromes. The shoulder region is the site where most plaques lose their integrity, or rupture. Plaque rupture exposes the underlying thrombogenic core of lipid and necrotic material to circulating blood. This exposure results in platelet adherence, aggregation, and progressive luminal narrowing, which are associated with acute coronary syndromes.

Inflammation is emerging as a critical component of atherosclerosis genesis, activity, and potential plaque instability. Patients with established coronary artery disease who possess a confluence of risk factors known as the metabolic syndrome remain at particularly high risk for a future vascular event, such as an acute myocardial infarction or cerebrovascular accident. Biochemical markers such as elevated levels of C-reactive protein signal a higher likelihood of vascular inflammation and portend a higher risk of vascular event rates. This marker may also signal more rapidly advancing coronary artery disease and the need for aggressive preventive measures.\(^9\)
Signs and symptoms

Patients with coronary artery disease present with stable angina pectoris, unstable angina pectoris, or a myocardial infarction. They may seek medical attention with their first symptomatic episode of chest discomfort. Many of these patients suffer from unrecognized coronary artery disease and may experience an acute plaque rupture or acute myocardial infarction. Electrical instability can ensue, including potentially lethal cardiac dysrhythmias. Identifying high-risk persons before their first myocardial event is a multifaceted process that involves patient and physician education efforts. Screening for coronary artery disease is not sufficient. Risk factor modification from an early age initiates primary prevention efforts, forestalling the development of symptomatic coronary artery disease. Severe coronary artery disease can be detected before a patient develops symptoms.

Angina pectoris is a perceived symptom resulting from a mismatch of myocardial supply and demand. The compromised myocardial blood flow caused by obstructive coronary artery disease is not able to meet the metabolic demands of the myocardial tissue. The anaerobic threshold is crossed and the patient develops symptomatic angina pectoris. 10

Risk factors of Coronary Artery Disease:

A) Major Risk Factors

Many factors raise the risk of developing CAD. The more risk factors, the greater chance of developing CAD.

- Unhealthy blood cholesterol levels
- High blood pressure
- Smoking
- Insulin resistance
- Diabetes
- Overweight or obesity
- Metabolic syndrome
• **Lack of physical activity**: Lack of activity can worsen other risk factors for CAD. American Heart Association (AHA) in their 1995 statements reported sedentary life style as a new independent risk factor for CAD with a prevalence of at least two times as Hypertension, Dyslipidemia and smoking. Consequently, US Department of Health & Human Services (USHHS) in their 2008 guidelines reported physical activity guidelines for healthy life as 150 minutes of moderate intensity exercise or 75 minutes of vigorous intensity exercise per week. 8, 11, 12

• **Age**: Genetic or lifestyle factors cause plaque to build in arteries as age increases. At middle-aged or older, enough plaque has built up to cause signs or symptoms. In men, the risk for CAD increases after age 45. In women, the risk for CAD risk increases after age 55.

• **Family history of early heart disease**

**B) Emerging Risk Factors**

Debate continues to study other possible risk factors for CAD. High levels of a protein called C-reactive protein (CRP) in the blood may raise the risk for CAD and heart attack. High levels of CRP are proof of inflammation in the body. Inflammation is the body's response to injury or infection. Damage to the arteries' inner walls seems to trigger inflammation and help plaque grow. Research continues to find out whether reducing inflammation and lowering CRP levels also can reduce the risk of developing CAD and having a heart attack. High levels of fats called triglycerides in the blood also may raise the risk of CAD, particularly in women. 13

**Other Factors which Affect Coronary Artery Disease**

**Sleep apnea**: Sleep apnea is a disorder in which breathing stops or gets very shallow while sleeping. Untreated sleep apnea can raise chances of having high blood pressure, diabetes, and even a heart attack or stroke.

**Stress**: Research shows that the most commonly reported "trigger" for a heart attack is an emotionally upsetting event—particularly one involving anger.
Alcohol: Heavy drinking can damage the heart muscle and worsen other risk factors for heart disease. Men should have no more than two drinks containing alcohol a day. Women should have no more than one drink containing alcohol a day.\textsuperscript{13}

1.3 Management of CAD

A) Pharmacologic Therapy

• Antiplatelet Agents

Aspirin is the mainstay of antiplatelet therapy for patients who have known coronary artery disease or symptoms suggestive of coronary artery disease. Aspirin inhibits both cyclooxygenase and the synthesis of thromboxane A\textsubscript{2}. Clopidogrel (Plavix), a thienopyridine derivative, blocks adenosine diphosphate–induced platelet activation. Clopidogrel is indicated as an alternative for patients who cannot take aspirin.\textsuperscript{13}

• Anti-anginal Agents

Beta blockers, calcium channel blockers, and nitrates are the mainstays of antianginal therapy. Unless contraindications exist, all patients who have a history of angina pectoris should carry sublingual nitroglycerin. Beta blockers are recommended as first-line therapy for the management of stable angina in all patients with established coronary artery disease.

Patients who have a history suggestive of vasospastic angina should be treated with a calcium channel blocker or a long-acting nitrate as an initial therapy. Either treatment option can also serve as a substitute for a beta blocker in the presence of traditional angina when intolerable beta blocker effects ensue.

Nitrates improve exercise tolerance and prolong the time to onset of angina in patients with exertional angina. They are contraindicated in patients who have severe aortic stenosis or hypertrophic cardiomyopathy because they can adversely alter hemodynamics and exacerbate symptoms. Ranolazine may be useful for treating refractory angina pectoris.\textsuperscript{13}
B) Surgical Management: Revascularization

The primary revascularization options are PCI and CABG surgery. The most common PCI techniques are percutaneous transluminal coronary angioplasty and coronary stenting. A major limitation of PCI is restenosis at the intervention site. This represents the body's response to local injury with an exaggerated neointimal proliferative response. The use of stents, aspirin, clopidogrel, and glycoprotein IIb/IIIa inhibitors lowers the rate of restenosis to less than 10% at 6 months in optimal circumstances.

The most common conduits for CABG are the saphenous vein and the internal thoracic (mammary) artery. The long-term patency rates of internal thoracic artery grafts are superior to those of venous grafts.\textsuperscript{13}

Percutaneous Coronary Intervention versus Medical Therapy

Percutaneous coronary intervention is more effective than medical therapy in relieving angina, but it confers no greater survival benefit. Aggressive lipid-lowering therapy appears to be as effective as percutaneous coronary intervention plus usual medical care for preventing ischemic events.

Coronary Artery Bypass Grafting Versus Medical Therapy

CABG produces better survival rates compared with medical therapy and is recommended for symptomatic patients with left main coronary artery disease, three-vessel coronary artery disease, or two-vessel coronary artery disease marked by stenosis of the proximal left anterior descending artery. CABG is more effective than medical therapy for the relief of angina, although this benefit narrows after 5 to 10 years.

Percutaneous Coronary Intervention versus Coronary Artery Bypass Grafting

Outcomes following percutaneous coronary intervention and coronary artery bypass grafting have been compared in high-risk patients. The two largest studies in the United States were the Emory Angioplasty versus Surgery Trial (EAST) and the Bypass Angioplasty Revascularization
Investigation (BARI). In both trials, percutaneous coronary intervention was limited solely to angioplasty. Similarly, current CABG techniques, including the more frequent use of arterial conduits, were not included in either trial. EAST results have demonstrated that the long-term survival rates following percutaneous coronary intervention and coronary artery bypass grafting are comparable. BARI results have indicated that coronary artery bypass grafting produces better long-term survival rates than percutaneous coronary intervention. However, the benefit of CABG in BARI was not apparent until 7 years postoperatively, and it was largely attributable to the significantly higher survival rate in the subgroup of patients with diabetes mellitus. Both trials have shown that CABG is superior to PCI in relieving angina and obviating the need for repeat revascularization procedures. With the introduction of drug-eluting stents (DES), coupled with improved catheterization techniques, coronary artery disease treatment is shifting away from bypass surgery toward a percutaneous approach. Restenosis rates have been lowered significantly and acute thrombotic complications are rare given the advances in antiplatelet therapy.

C) Cardiac Rehabilitation & Risk Factor Management

The World Health Organization (1968) definition of cardiac rehabilitation refers to a process by which a person is restored to an optimal physical, medical, psychological, social, emotional, sexual, vocational and economic status.” Over the ensuing years this statement of intent has remained remarkably similar. The WHO’s current definition (1993) addresses the cardiovascular status of the patient before, during, and after the event: “The rehabilitation of cardiac patients is the sum of activities required to influence favorably the underlying cause of the disease, as well as the best possible physical, mental and social conditions, so that they may by their own efforts, preserve or resume when lost, as normal a place as possible in the society. Rehabilitation cannot be regarded as an isolated form of therapy but must be integrated within the entire treatment.
Risk Factor Management

- **Hypertension**

  Management of hypertension in patients with coronary artery disease is exceedingly important. Control of blood pressure reduces myocardial oxygen consumption and thereby reduces angina, and it also lowers the incidence of cardiovascular events.

  Beta blockers devoid of intrinsic sympathomimetic activity represent first-line antihypertensive therapy for patients with a history of myocardial infarction or coronary artery disease with angina. Angiotensin-converting enzyme (ACE) inhibitors are indicated for all patients with diabetes mellitus or a history of myocardial infarction, particularly those with impaired left ventricular systolic function. In the Heart Outcomes Prevention Evaluation (HOPE) study, high-risk patients without a history of a myocardial infarction treated with the ACE inhibitor ramipril experienced a significant reduction in major cardiac events.

  Calcium channel blockers are useful for patients with hypertension and angina despite maximum tolerable administration of beta blockers. The long-acting dihydropyridines are preferred; short-acting preparations should be avoided because they might increase the risk of cardiac events via precipitous blood pressure reduction and induction of the coronary steal phenomenon, diverting coronary arterial blood flow from flow-limited myocardial regions.\(^{13}\)

- **Hyperlipidemia**

  Guidelines of the National Cholesterol Education Program (NCEP) have recommended an LDL level lower than 70 mg/dL for all patients with coronary artery or other atherosclerotic disease. Patients whose LDL levels are higher than 100 mg/dL should start drug therapy. 3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) are the recommended first-line agents for patients who have coronary artery disease and elevated total and LDL cholesterol levels.

  The NCEP also recommends a target HDL level higher than 45 mg/dL for men with coronary artery disease and higher than 55 mg/dL for women. Patients
with the metabolic syndrome (obesity, hypertension, and insulin resistance) often have HDL levels lower than 35 mg/dL. These patients are at especially high risk for arterial vascular disease. Their recommended lifestyle changes include regular exercise and weight loss, which are two of the most effective ways to raise HDL levels. If lifestyle changes fail to increase HDL levels to their target, drug treatment with a fibrate or niacin should be considered, particularly in patients whose triglyceride levels are higher than 200 mg/dL.¹³

- **Diabetes Mellitus**

Diabetics with coronary artery disease have a particularly high risk for recurrent cardiovascular events, and they should be targeted for aggressive risk-factor modification. The American Diabetes Association recommends a hemoglobin A₁c level lower than 7%.¹³

**1.4 Coronary Artery Disease in India**

India and Indian subcontinent (including India, Pakistan, Bangladesh, Sri Lanka and Nepal) is home to 20% of the world’s population and may be one of the regions with the highest burden of CVD in the world. In 2003, the prevalence of CAD in India was estimated to be 3-4 % in rural areas (two fold higher than 40 years ago), and 8-10 % in urban areas (six-fold higher than 40 years ago), with a total of 29.8 million persons affected. In 1990, there were an estimated 1.17 million deaths from CAD in India and at present date the number is expected to almost double to 2.03million.⁴

**1.5 Coronary Artery Disease in Iran**

Iran is a country with a population distribution consisting of large number of young people at the base and middle of the pyramid and a life expectancy that has risen significantly in recent years, probably as a result of the decrease of infant mortality. This situation indicates that this country could suffer a significant increase in the incidence of CAD as these individuals begin to reach later life.¹ Population-based studies confirm that prevalence of coronary artery disease (CAD) is higher among Iranian population even than in western countries; its high mortality rate makes CAD the principal cause of death in recent decades.¹⁴
1.6 Common points in Iran & India with respect to CAD

As a result of economic changes and increased mechanization, physical inactivity and changes in life style as a developing country and other similar cultural risk factors, both countries suffer CAD as leading cause of death and a major health burden. Thus, the health and economic implications of this staggering rise in CAD deaths are profound and warrant prompt attention from governing bodies and policy makers of both countries. 4, 6, 7

1.7 History of Cardiac Rehabilitation; Benefits & Barriers

Fifty years ago, patients who survived from myocardial infarction (MI) were confined to bed for 2 months or longer. The realization that bed rest hindered recovery and contributed to complications radically altered the rehabilitation of cardiac patients.15,16 First revolutionary approach to treatment occurred in 1940s, when Levine and Lown recommended “chair treatment” for post-MI patients.10 Cain in 1961 reported on the use of progressive exercise program for acute MI patients.17 Early efforts had aimed at progressive activity which then gradually coalesced into formal cardiac rehabilitation programs which can promote comprehensive cardiovascular disease risk reduction, decrease in cardiovascular morbidity and mortality, improve in quality of life (QOL) and associated economic benefits. However, these benefits are dependent on program participation and long-term adherence to exercise and other cardiovascular disease risk-reducing behavior.18

Numerous factors contribute to dismal participation rate, including transportation issues, motivation, co-morbidities, misunderstanding of the value of these programs, financial and reimbursement issues and sub-optimal referral rates by physician.19 These barriers make cardiac rehabilitation most underused and poor adherence of patients to this program.20, 21, 22

1.8 Alternatives to standard cardiac rehabilitation

To address common concerns and barriers associated with the traditional protocol for cardiac rehabilitation, a modified protocol could be developed to cost effectively promote independent exercise and other cardiovascular risk reducing behaviors, which will be conducted under limited
supervision. Evidence suggests that alternative approaches (Home-based cardiac rehabilitation) to the delivery of cardiac rehabilitation services, other than traditional supervised group interventions, can be implemented effectively and safely for carefully selected clinically stable patients.\textsuperscript{17} Home-based cardiac rehabilitation approaches have the potential to provide cardiac rehabilitation services to low and moderate-risk patients, with the goal of increasing availability and decreasing costs, while preserving efficacy and safety and it is well established as an alternative method in developed countries.\textsuperscript{24,25,26,27} However, these institution-based and home-based cardiac rehabilitation programs are not popular and routinely practiced in Indian and Iranian population.

1.9. Outcome Measures in CAD & Cardiac Rehabilitation

I. Health Related Quality of Life (HRQOL):

An outcome measure in CR

According to WHO Quality of Life Group (1993), quality of life is defined as a person’s view of life in the context of culture and values and in relation to person’s hopes, dreams, goals, expectations, standards and concerns.\textsuperscript{28} There has been a rapid and significant growth in the measurement of quality of life as an indicator of health outcome in patients with coronary artery disease in recent years. In the clinical course of CAD, there are many aspects where patient’s quality of life may be affected which include symptoms of angina and heart failure, limited exercise capacity, physical debility and psychological stress associated with the chronic stress. Modern treatments focus not only on improving life expectancy, symptoms and functional status, but also quality of life. Thus, an improvement on health-related quality of life (HRQOL) is considered to be important as a primary outcome and in determination of therapeutic benefit. Although there is no consensus on the definition of the concept of HRQOL as yet, but usually it refers to physical, emotional and social well-being. It provides a valid and reliable tool to measure the impact of different treatments across different conditions. It provides an assessment of the
patient’s experience of his or her health problems in areas such as physical function, emotional function, social function, role performance, pain and fatigue. When measuring HRQOL, it is important that the instrument selected measures the health dimensions relevant to that particular set of patients. HRQOL instruments are either generic or disease-specific or another more recent individualized (patient generated) measure. Generic instruments are intended to be broadly applicable across different interventions and patients with different characteristics. Thus, they focus on general issues of health rather than specific features of a particular disease. Disease specific outcomes focus on the complaints that are attributable to a specific diagnosis or patient population. Each type has its own strength and weaknesses. Individualized (patient generated) measures which allow patient from their own perspective to identify the aspects that contribute to their overall quality of life. 

A) Generic Instruments

A number of generic instruments are commonly used in research and clinical evaluation in population with CHD. The two most commonly used ones are the Sickness Impact Profile (SIP) and the Medical outcomes study 36-item Short form Health Survey. 

I) Sickness Impact Profile: it comprises 136 items relating to 12 domains of health (mobility, ambulation, domestic affairs, social interaction, behavior, communication, recreation, eating, work, sleep, emotions and self-care). It is a broadly applicable instrument that measures a variety of health outcomes, including serial changes in well-being over time. Its disadvantage is its relatively long length which is time consuming in clinical practice.

II) SF-36: Medical outcome study 36-item Short Form Health Survey: it comprises 36 items covering 8 domains including physical functioning, social functioning, physical impairment, emotional impairment, emotions, vitality, pain and global health. It is a self-administered instrument which takes about 10 to 15 minutes to complete. It has been used in angina, MI, and heart failure. It has
been shown that in patients with recent MI SF-36 to be a sensitive tool for
detecting improvement of HRQOL after active intervention. Advantages like little needed time to complete it, highly test-retest reliability even in different conditions and in different ethnic groups and good construct validity makes it a superior HRQOL outcome measure compare to other generic instruments.\textsuperscript{29, 30}

**B) Disease Specific Instruments**

A number of instruments have been designed to examine specifically the impact of angina, MI, and heart failure on quality of life as follows: \textsuperscript{29,30}

**I) Seattle Angina Questionnaire (SAQ):** It is a psychometrically solid disease specific instrument designed to assess the functional status of patients with angina. It comprises 19 questions that quantify 5 clinically relevant domains: physical limitation, anginal stability, anginal frequency, treatment satisfaction and disease perception/quality of life. It disadvantages are that it is only sensitive to angina symptom in cardiac patients and not including emotional and social aspects.

**II) Quality of life after myocardial infarction (QLMI / Mac New) questionnaire:** the new version has 27 items in three domains: physical functioning, social functioning and emotional functioning. It is validated and still a good deal of research is being conducted with this instrument.\textsuperscript{29, 31} Compared with SF-36, it is only sensitive in MI patients and despite of good validity, according to some studies there is a need of some modification in some of its items to make it more useful.\textsuperscript{30, 32} It also has a less sensitivity in physical role compared to SF-36 questionnaire.\textsuperscript{30}

**III) Minnesota Living with Heart Failure (MLHF):** it comprises 21 items with a range of responses from no, very little to very much to produce a range of scores from 0 to 105(maximal disability) in relation to signs and symptoms typical of heart failure. The reliability and validity of MLHF are sound and it appears sensitive to changes in treatment and it is used extensively in studies of heart failure. Its disadvantage is it is more sensitive only in heart failure patients.
IV) Myocardial Infarction Dimensional assessment scale (MIDAS): it comprises 35 items covering seven areas of health status including: physical activity, insecurity, emotional reactions, dependency, diet, concerns over medications and side effects. It is only recently developed and further research on its utility is being conducted.\(^{29,30}\)

V) Cardiovascular Limitations and Symptoms Profile (CLASP): it comprises 37 items that yield 4 symptoms subscales including angina, shortness of breath, ankle swelling and tiredness, and functional limitation subscales including mobility, social life and leisure activities, activities within the home, concerns and worries and gender. The CLASP has been validated in patients with chronic stable angina and further research is required before it can be recommended for routine use.\(^{29,30}\)

**Need of SF-36 for present study**

According to our review, a primary disadvantage of generic health-related QOL outcome measures is that they may not be as sensitive to changes as disease specific instruments but, unfortunately the available disease specific QOL instruments rely on the presence of specific symptoms such as angina or dyspnea which are not universally experienced by all cardiopulmonary patient populations such as patients recovering from coronary artery bypass surgery.\(^{33}\)

Quality of Life is an important health-related outcome measure in Cardiac Rehabilitation (CR) programs. Although the primary focus of CR is improving cardiovascular functioning, researchers and practitioners alike now recognize that CR is a multidimensional and multidisciplinary process wherein improved QOL is an important treatment outcome.\(^{28}\)

According to objectives of the present study, the SF-36 was appropriate for this study because it is self-administered and can be completed in 10 minutes. It is broadly used in medical settings and is recommended by American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR-1999) for evaluating QOL in CAD patients.\(^{28}\)
SF-36 originally was standardized on patients with CAD diagnoses. The SF-36 has repeatedly demonstrated considerable test-retest and internal consistency and reliability across different medical settings, conditions, languages, and more recently ethnic backgrounds. The validity of SF-36 by using multi-method approaches also has been well established.\textsuperscript{28,30}

Further, the use of the SF-36 in present study was appropriate because it is shown, among valid generic and disease specific outcomes in cardiac patients; SF-36 physical role has the highest sensitivity which is an important parameter in the present study. \textsuperscript{28, 30} Recent studies still showed it is the most appropriate outcome measure of HRQOL in Ischemic Heart Disease patients. Other disease specific instruments such as Mac New QOL questionnaire, in spite of good validity and reliability needs modifications to provide more useful indications of HRQOL.\textsuperscript{32}

The SF-36 questionnaire consists of 36 questions (items) measuring physical and mental health status in relation to eight health concepts: (Figure 1.2)

- physical functioning
- role limitations due to physical health
- bodily pain
- general health perceptions
- vitality (energy/fatigue)
- social functioning
- role limitations due to emotional health
- general mental health (psychological distress/wellbeing)
Responses to each of the SF-36 items are scored and summed according to a standardized scoring protocol (Ware et al 1993), and expressed as a score on a 0–100 scale for each of the eight health concepts. Higher scores represent better self-perceived health. Five of the scales are unipolar (Physical Functioning, Role Physical, Bodily Pain, Social Functioning, and Role Emotional), meaning that they define health status in terms of the absence of disability. The maximum score of 100 is therefore achieved when no disability is reported. The other scales (General Health, Vitality and Mental Health) are bipolar scales, covering both positive and negative health states. The maximum of 100 on these bipolar scales therefore indicates not just the absence of disability, but the presence of a positive state of health.34

II. Functional Capacity: An outcome in CR

Functional Capacity (Physical capacity) which is an important health and physical fitness outcome in exercise testing and training is commonly measured in terms of Oxygen Consumption (VO₂). Instead of measuring VO₂ in clinical practice which is difficult and expensive due to laboratory needs, metabolic
equivalents (METs), which is a multiple of basal body oxygen requirements is usually used.\textsuperscript{35,36}

**Methods of estimation of MET level:** METs are calculated via estimated oxygen consumption on volitional maximal treadmill stress testing. One MET is equal to 3.5 ml of oxygen per kilogram of body weight per minute.

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1 \text{ MET} = 3.5 \text{ ml O}_2/\text{Kg} \text{ /min}
\]

Thus, Metabolic Equivalents can be used as a physical capacity outcome measure to predict the physical capacity of a person and could be determined by Exercise stress test.\textsuperscript{8} (Figure 1.3)

**Figure 1.3.** Equipment to perform exercise test.

A. ECG Monitor and Recorder
B. Treadmill Machine
C. ECG Electrodes
D. ECG Printer
Before starting exercise test, heart rate and blood pressure are recorded at rest. Sticky electrodes are attached to the chest, shoulders and hips and connected to the EKG portion of the Stress test machine. A 12-lead EKG is recorded on paper.

The treadmill is then started at a relatively slow "warm-up" speed. The treadmill speed and it's slope or inclination are increased every three minutes according to a preprogrammed protocol (Bruce is the commonest protocol in the USA, but several other protocols are perfectly acceptable). The protocol dictates the precise speed and slope. Each three minute interval is known as a Stage (Stage 1, Stage 2, Stage 3, etc. Thus a patient completing Stage 3 has exercised for 3 x 3 = 9 minutes). The patient's blood pressure is usually recorded during the second minute of each Stage. However, it may be recorded more frequently if the readings are too high or too low.

As noted earlier, the EKG is constantly displayed on the monitor. It is also recorded on paper at one minute intervals. The physician pays particular attention to the heart rate, blood pressure, changes in the EKG pattern, irregular heart rhythm, and the patient's appearance and symptoms. The treadmill is stopped when the patient achieves a target heart rate (this is 85% of the maximal heart rate predicted for the patient's age). However, if the patient is doing extremely well at peak exercise, the treadmill test may be continued further. The test may be stopped prior to achievement of the target heart rate if the patient develops significant chest discomfort, shortness of breath, dizziness, unsteady gait, etc., or if the EKG shows alarming changes or serious irregular heart beats. It may also be stopped if the blood pressure (BP) rises or falls beyond acceptable limits. Please note that the systolic BP (upper number) may normally rise to 200 at peak exercise. At the same time, the diastolic BP (lower number) remains unchanged or falls to a slight degree. In contrast, the BP of patients with hypertension or high BP will show a rise of both systolic and diastolic readings. The latter may rise above 90 - 100.

Exercise test may be stopped early if the patient develops significant symptoms (chest pain, extreme shortness of breath, weakness, leg fatigue, dizziness, etc.), serious irregular heart rhythm or marked elevation of blood pressure. It is
emphasized the majority of patient's do not develop these problems. Fatigue, as would be expected after a good workout, is the only residual complaint.

**How safe is a Regular Treadmill Stress Test?** The risk of the stress portion of the test is very small and similar to what one would expect from any strenuous form of exercise (jogging in your neighborhood, running up a flight of stairs, etc.). As noted earlier, experienced medical staff is in attendance to manage the rare complications like sustained irregular heart beats, unrelieved chest pain or even a heart attack.

**What is the reliability of a Regular Stress Test?** If a patient is able to achieve the target heart rate, a regular treadmill stress test is capable of diagnosing important disease in approximately 67% or 2/3 of patients with coronary artery disease. The accuracy is lower (about 50%) when patients have narrowing in a single coronary artery or higher (greater than 80%) when all three major arteries are involved. Approximately 10% of patients may have a "false-positive" test (when the result is falsely abnormal in a patient without coronary artery disease). 8

**III. Left Ventricular Ejection Fraction (LVEF): An outcome in CR**

Cardiac function and its pumping action is usually determined by Cardiac Output(CO), which is the product of heart rate (HR) and stroke volume(SV) which shows the left ventricular contractility. 37,38 It seems the left ventricular stroke volume response to exercise appears to be the primary factor determining the cardiac output response to exercise, and plays an important role in determining exercise tolerance. 39 Contractile state of myocardium can be obtained from ejection fraction (EF) which is the ratio of stroke volume (volume of blood ejected from left ventricle per beat) to end-diastolic volume(volume of blood in left ventricle at the end of diastole,(EDV) or the fraction end-diastolic volume that is ejected as stroke volume. 37,38

\[
EF = \frac{SV}{EDV}
\]
Left Ventricular Ejection Fraction (LVEF) is widely used clinically as an index of contractility of myocardium. It is reduced in patients with dilated heart or other dysfunctions which leads to heart failure; i.e., as a consequence of myocardial infarction. The extent of which EF is depressed is a very good predictor of long-term prognosis. 38

**Methods of measuring EF:** Ejection fraction can be measured with imaging techniques, including:

- **Echocardiogram.** During an echocardiogram, sound waves are used to produce images of your heart and the blood pumping through your heart. It is the simplest clinical method for estimation of ejection fraction and used in current study.

- **Cardiac catheterization.** During cardiac catheterization, a thin, plastic tube (catheter) is inserted into a vein in the arm or leg and then moved to the heart — most likely the left ventricle. Using images taken during the catheterization, your doctor can see how your blood pumps through your heart.

- **Magnetic resonance imaging (MRI).** During an MRI scan, a magnetic field and radio waves are used to create cross-sectional images of specific parts of the body. When an MRI is used to study the heart, it's known as a cardiovascular MRI.

- **Computerized tomography (CT).** During a CT scan, a special X-ray technique is used to create cross-sectional images of specific parts of the body. When a CT scan is used to study the heart, it's known as a cardiac CT.

- **Nuclear medicine scan.** During a nuclear scan, trace amounts of radioactive material — such as thallium — are injected into the bloodstream. Special cameras then detect the radioactive material in your blood as it flows through the heart and lungs.

- **Echocardiography:**

  Echocardiography is a unique noninvasive method for imaging the living heart. It is based on detection of echoes produced by a beam of
ultrasound (very high frequency sound) pulses transmitted into the heart. From its introduction in 1954 to the mid 1970's, most echocardiographic studies employed a technique called M-mode, in which the ultrasound beam is aimed manually at selected cardiac structures to give a graphic recording of their positions and movements. M-mode recordings permit measurement of cardiac dimensions and detailed analysis of complex motion patterns depending on transducer angulation. They also facilitate analysis of time relationships with other physiological variables such as ECG, heart sounds, and pulse tracings, which can be recorded simultaneously. A more recent development uses electromechanical or electronic techniques to scan the ultrasound beam rapidly across the heart to produce two-dimensional tomographic images of selected cardiac sections. This gives more information than M-mode about the shape of the heart and also shows the spatial relationships of its structures during the cardiac cycle.  

A comprehensive echocardiographic examination, utilizing both M-mode and two dimensional recordings, therefore provides a great deal of information about cardiac anatomy and physiology, the clinical value of which has established echocardiography as a major diagnostic tool.
In the M-mode technique, all the ultrasonic pulses are propagated along the same axis and different parts of the heart are studied by changing the direction of the beam manually. An M-mode echocardiogram is not a "picture" of the heart, but rather a diagram that shows how the positions of its structures change during the course of the cardiac cycle. It is an admirable method for studying a structure like a heart valve, but it does not provide information about the spatial relationships of different parts of the heart to each other. However, this can be accomplished by scanning the ultrasound beam rapidly back and forth across a section of the heart.\textsuperscript{40}
Because access to the heart afforded by the ribs and lungs is very limited, almost all cardiac scanners are of the sector type. A mechanical sector scanner can use either an oscillating or rotating scan head. In the rotating type several transducers spin inside a small dome filled with liquid. As each one passes over the heart, it transmits pulses and receives echoes. The next element then takes over, like a succession of beams from a lighthouse scanning over the sea. The echo signals are displayed in B-mode form. Signals from the scan head are used to steer the oscilloscope beam in the same manner as the ultrasound beam. The result is a tomographic image of the heart, showing the structures in the selected scan plane and their motion patterns. (Figure 1.4.)

![Figure 1.5. Basic mechanism of Echocardiography](image)

**Figure 1.5.** Basic mechanism of Echocardiography

**Types of echocardiography:**

There are several different types of echocardiography – all use sound waves to create images of heart. This is the same technology that allows doctors to see an unborn baby inside a pregnant mother. Unlike X-rays and some other tests, echocardiography doesn't involve radiation.
- **Transthoracic echocardiography:**

Transthoracic echocardiography is the most common noninvasive type of echocardiogram test. This type of echocardiography involves placing a device called a transducer on chest that sends special sound waves, called ultrasound, through chest wall to heart. Ultrasound waves can't be heard by the human ear. As the ultrasound waves bounce off the structures of heart, a computer in the echocardiography machine converts them into pictures on a screen.41 (Figure1. 4)

- **Stress echocardiography:**

This is an echocardiography test that's done as part of a cardiac stress test. During a cardiac stress test, patient exercises or takes medicine to make heart pump harder and beat faster. Some heart problems, such as coronary artery disease, are easier to diagnose when the heart is beating fast and pumping hard.41

**What to expect during echocardiography:**

Echocardiography is painless and usually takes less than an hour to perform. For some tests, the doctor will need to inject saline or a special dye into vein that makes heart show up more clearly on the test images. This special dye is different from the dye used during an angiogram test. For most types of echocardiography, clothing should be removed from the waist up. Women will be given a gown to wear during the procedure. Patient should lay on back or left side on an exam table or stretcher. EKG electrodes will be attached to chest to allow an EKG to be done. A doctor or sonographer (a person specially trained to do ultrasounds) will apply a gel to chest that helps the sound waves reach heart. A wand-like device called a transducer will then be moved around on chest.41

The transducer transmits ultrasound waves into chest. Echoes from the sound waves will be converted into pictures of heart on a computer screen. During the test, the lights in the room are dimmed so the computer screen is easier to see. The sonographer will make several recordings of the images to show different
locations in heart. The recordings will be put on a computer disc or videotape for the cardiologist to review.41

- **Transesophageal echocardiography:**

Transesophageal echocardiography (TEE) is used when the doctor needs a more detailed view of the heart. This may be necessary to look for blood clots in the heart or if transthoracic echocardiography doesn't provide a good enough view of certain parts of the heart. A doctor, not a sonographer, performs this type of echocardiography. The test uses the same technology as transthoracic echocardiography, but the transducer is attached to the end of a flexible tube. The tube is guided down throat and into esophagus to get a more detailed image of the heart and major blood vessels leading to and from the heart. For TEE, probably medicine will be given through a needle inserted in one of the veins to help relax during the test. Blood pressure, the oxygen content of blood, and other vital signs will be monitored during the test. The back of mouth is numbed with a gel or a spray to prevent gag when the transducer is put down the throat. The tube with the transducer on the end is gently placed in throat and guided down until it's in place behind the heart. The images of heart are then recorded as the doctor moves the transducer around in esophagus and stomach.41

**Stress echocardiography:**

Stress echocardiography is a transthoracic echocardiogram combined with either an exercise or chemical stress test. For an exercise stress test, patient walks or runs on a treadmill or pedal a stationary bicycle to make heart beat fast and pump hard. For a chemical stress test, medicine will be given to make heart beat fast and pump hard. The structures of the heart will appear as white objects, while any fluid or blood will appear black on the screen. Doppler ultrasound techniques are often used during echocardiography tests. Doppler ultrasound is a special ultrasound that shows how blood is flowing through the blood vessels. This allows the sonographer to see the blood flowing in different speeds and directions. The speeds and directions appear as different colors moving within the black and white images.41
1.10 Importance of Ejection Fraction & Functional Capacity in Cardiac Rehabilitation programs

Recent studies have reported that endurance exercise training of sufficient intensity can improve left ventricular systolic performance and consequently improve myocardial perfusion in patients with coronary artery disease. Thus, exercise training of appropriate intensity may improve both exercise capacity and cardiac function of patient with CAD. Therefore LVEF & Functional Capacity, both can be used as important physiologic outcomes to evaluate therapeutic protocols.

1.11. Need of Alternative methods for CR

Exercise training in supervised environments has been shown to provide benefit in terms of functional physical capacity, coronary artery disease risk factors profiles, and mortality from CAD at the levels of both primary and secondary prevention. Despite these benefits, supervised exercise training which is the one of the elements of cardiac rehabilitation, is not available to the majority of patients with CAD. Evidence suggests that only 25-30% of eligible patients are enrolled in institution based cardiac rehabilitation programs after CABG. Clearly, large proportion of patients who stand to benefit from the exercise training component of cardiac rehabilitation are not being served.

1.12 Statement of Problem

Large number of patients who stand to benefit from the exercise training component of cardiac rehabilitation (CR) are not being served due to access issues, practical problems and economic restraint. Cardiac rehabilitation and exercise training may be a potentially useful alternative in cardiac care for Indian and Iranian population reducing morbidity and mortality in coronary artery disease (CAD) patients and improving their quality of life and well-being.
1.13 Recent trends in scientific study of the importance of the cardiac rehabilitation in clinical practice

International status:

Developed countries with their modern "know how" are progressing rapidly in exploring the possibilities of exercise training in the management of coronary artery disease. In US & Canada& UK, researchers well established the problems of standard cardiac rehabilitation programs in their population and focusing on new alternatives and making effective use of available technologic advances like computer technology, computerized cardiac care service, World Wide Web links and Tele-cardiac rehabilitation, lessons from computerized link projects, TV cables and other options.

National status:

Cardiac rehabilitation is not routinely practiced to treat patients with coronary artery disease in India and Iran. We need to emphasis more on developing structured and appropriate technique, bearing in mind the socio-economic problems, which are hurdles to delivery of health care at the doorstep of the common man in Indian and Iranian population. So, development of a more functional, and cost effective remedy in cardiac rehabilitation in clinical practice is paramount. The wealth of knowledge that has been passed on by our researchers regarding the cardiac rehabilitation has to be collaborated with a detailed well organized study. Such a scientific study facilitates clinicians to practice and incorporate exercise training in the management of cardiac patients. With reference to Indian and Iranian scenario there is a paucity of studies on the efficacy of cardiac rehabilitation on quality of life for coronary artery disease patients.
1.14 Significance of the study in the context of current status

Recognizing need to improved access to exercise training, early studies investigated unsupervised home based training as an option for patients after CABG surgery. The results have been mixed and non-conclusive. Some investigators have reported no difference in exercise performance between institution and home based groups\textsuperscript{54, 55} whereas others reported greater improvement in the supervised, institution based group.\textsuperscript{56} These studies were suffered from small sample size and lack of standardized protocol for patients in home based exercise groups and no controlled group.\textsuperscript{24}

A recent retrospective review\textsuperscript{35} has reported improvement in peak VO\textsubscript{2}, peak work rate and peak MET levels in both supervised and unsupervised home based groups. The review of literature clearly indicates that even in all recent clinical trials, patients were not directly randomized to home versus institution based cardiac rehabilitation with control groups. Published evidence on the effect of home-based cardiac rehabilitation on quality of life in coronary heart disease patients have mixed results and are not generalizable to other communities due to lack of standard protocols and standard study designs, ethnic, cultural and environmental differences.\textsuperscript{24-27, 31,35,36}

None of the above mentioned studies assessed nonphysical outcomes such as health related quality of life or social support and other objective measurements like ejection fraction & functional capacity in a single randomized controlled trial.

Since there is also no acceptable, available published evidence particularly in Indian and Iranian population, this study was proposed to give Hospital versus Home-based cardiac rehabilitation and to assess the Quality of Life, Functional Capacity and Ejection Fraction of coronary heart disease patients in Indian and Iranian population. Even though cardiac rehabilitation in both forms i.e. supervised and home-based programs had proven benefits in reducing morbidity and mortality, this has been very poorly studied and addressed for our population. As evidence has shown that now coronary artery disease is on rise in developing countries and particularly in Indian and Iranian population\textsuperscript{1-6, 44, 45},
this study intended to address the benefits which can be achieved by cardiac rehabilitation.

Therefore, the purpose of the present study was to determine the effect of Hospital versus Home-based monitored Cardiac Rehabilitation programs in Acute coronary artery disease patients treated either conservatively or surgically. It aimed to determine which program conferred the greatest benefits in terms of improvements in Quality of Life, Functional Capacity, and Left Ventricular Ejection Fraction.
OBJECTIVES OF THE STUDY

- To find out the effect of Hospital versus Home-based cardiac rehabilitation on Quality of Life in low and moderate risk coronary artery disease patients in Indo-Iranian population
- To find out the effect of Hospital versus Home-based cardiac rehabilitation on Left Ventricular Ejection Fraction in low and moderate risk coronary artery disease patients in Indo-Iranian population
- To find out the effect of Hospital versus Home-based cardiac rehabilitation on Functional Capacity by means of symptom-limited exercise testing using Bruce protocol in low and moderate risk coronary artery disease patients in Indo-Iranian population