Research Article

Effect of Cardiac Rehabilitation Program on Heart Rate Recovery in Diabetic Patients Post Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention

Hazem R. Khorshid*, Yasser A. Adelhady, Nour El-Deen M. Elgarhy** and Hesham B. Mahmoud****
* Department Cardiology, Faculty of Medicine, Ain Shams University.
**Department Cardiology department, Faculty of Medicine, Bani-Suef University.

Abstract

Introduction: Diabetes Mellitus is associated with increased mortality from coronary artery disease. Cardiac rehabilitation (CR) is an evidence-based form of secondary prevention and is well-established in the effective management of patients with acute coronary syndrome (ACS). The heart rate is an important prognostic factor of cardiovascular diseases. Heart rate recovery (HRR) is a strong independent mortality predictor in patients with previous myocardial infarction (MI). **Aim:** To study the effect of exercise based cardiac rehabilitation program on HRR in diabetic patients with ST segment elevation myocardial infarction (STEMI) post successful primary percutaneous coronary intervention (1ry PCI). **Methods:** Fifty diabetic patients, who presented with STEMI started CR program at Ain Shams cardiac rehabilitation unit 30 days post successful primary PCI after myocardial infarction. Before CR program they were subjected to a symptom limited exercise test (modified Bruce protocol) to exclude any remaining ischemia and calculate enrollment resting heart rate (HR), maximum HR, HR reserve, baseline HR recovery in 1st minute (HRR1) and 2nd minute (HRR2) into recovery. Another symptom limited exercise test was done after completion of the CR program. In order not to affect the results of the study, patients on beta blockers or other rate-reducing drugs, anti-hypertensive drugs, lipid lowering drugs and anti-diabetic drugs continued using the same doses during the study period. **Results:** There was statistically significant increase in HR reserve from 53.7±10.5 bpm to 64.1 ±11.8 bpm as well as significant increase in HRR1 and HRR2 from 12.3 ±2.8 bpm & 23.1± 6.45 bpm to 24.4 ±4.3 bpm & 39.1±4.7 bpm respectively after completion of the CR program (P-value<0.01). **Conclusions:** We conclude that in post MI diabetic patients treated by 1ry PCI, exercise based CR program improves the HR recovery which may have a positive prognostic effect on morbidity and mortality

Keywords: Cardiac rehabilitation; Diabetes; Myocardial infarction; Heart rate recovery; Exercise.

Introduction

Coronary heart disease (CAD) is the main cause of death worldwide. The development of CAD is multi-factorial and is related to several risk factors such as diabetes, smoking, diet, exercise, hypertension and hypercholesterolemia[1]

CAD in patients with Diabetes Mellitus (DM) is the major cause of mortality and morbidity in western countries. These patients have 2 to 4 times higher risk of cardiovascular diseases as compared with individuals without DM.[2]

DM in patients with acute ST-elevation myocardial infarction (STEMI) is a well-established risk factor for death and heart complications such as cardiogenic shock .[3]

Modification of these modifiable risk factors can reduce the burden of CAD by approximately 90%. These risk factors also have a strong impact on the prognosis of established CAD patients. In addition to well-established pharmacological management of CAD patients, it is therefore recommended that behavioral changes to modify these lifestyle factors in affected individuals form the basis of all CAD secondary prevention strategies.[4]

Cardiac rehabilitation goals include improving aerobic endurance and muscular strength, and modifying cardiovascular risk factors, including losing weight, controlling blood pressure, lowering cholesterol, improving blood glucose and cessation of smoking .[5]

Training in aerobic and resistance exercise improves the action of insulin, lipids, blood pressure and cardiovascular risk. For continued benefit, regular exercise is necessary.[6]

A comprehensive outpatient cardiovascular rehabilitation program should be provided to all eligible patients with acute coronary syndrome or whose status is immediately post-coronary artery bypass surgery or post-PCI prior to hospital discharge or during the first follow-up visit .[7]

Changes in heart rate associated with physical activity are the result of ongoing cooperation between parts of the autonomous nervous system. During exercise, the increase in heart rate is due to sympathetic activation and withdrawal of parasympathetic. Rapid decline in post-exercise heart rate is believed primarily due to parasympathetic reactivation. Disorders in the autonomic regulation of the circulatory system result in less pronounced decrease in heart rate after exercise cessation and are associated with total and cardiovascular mortality and morbidity in apparently healthy subjects, in patients with coronary artery disease or in patients with diabetes.[8]

HR recovery was found to be predictive of mortality regardless of severity of CAD. One plausible explanation for the increase in HR recovery may be the healing after acute event such as MI, CABG, or coronary stent placement rather than training effect. [9]

Patients and Methods

This study was conducted on fifty diabetic patients who started CR program at Ain Shams cardiac rehabilitation unit 30 days post successful primary PCI after myocardial infarction between December 2017 to December 2018. Approval of Beni-Suef university ethical committee was obtained and informed consent was obtained from all patients before enrollment in the study.

All the patients were on optimal doses of guideline directed medical therapy for treatment of STEMI patients.[10]

In order not to affect the results of the study, patients on beta blockers or other rate-reducing drugs, anti-hypertensive drugs, lipid lowering drugs and anti-diabetic drugs continued using the same doses during the study period.

Exclusion Criteria:

- Patients with Decompensated HF.
- Hemodynamicaly unstable arrhythmia (frequent extra systoles, atrial fibrillation, ventricular arrhythmia).
- Chronic obstructive pulmonary disease.
- Patients with uncontrolled hypertension.
- Musculoskeletal disease that prevent the patient from exercise.
- Patients with co morbidities (severe renal failure, severe liver failure, malignancy).
- Patients with incomplete cardiac revascularization with residual ischemic symptoms.
- Patients refusal to participate in the study.

Symptoms of cardiovascular disease were assessed before beginning of the rehabilitation program. Dyspnea was evaluated according to NYHA classification. Chest pain was evaluated according to CCS (Canadian Cardiovascular Society) classification .[11]

The patients were divided into three groups according to smoking status. Current smokers were defined as those who smoked within 1 month before registration. Ex-smokers were defined as those who quitted for at least 1 month. Non-smokers were defined as those who never smoked.[12]

Patients were considered hypertensive if they were on antihypertensive drugs or their BP > 140/90 mmHg .[13]

Patients were considered diabetic if RBS >200mg/dl, FBS>126mg/dl or were on antidiabetic medications.[14]

BMI was calculated as weight in kilogram divided by height in meter square.[15]

- Overweight was defined by a BMI>25kg/m^2.
- Obesity was defined by a BMI>30kg/m^2.

All patients were requested to have an echo-cardiogram done to assess the systolic function by calculating the Ejection fraction (EF%), by 2D echo, Simpson's method and to assess the segmental wall motion abnormality before and after the enrollment program.
Laboratory tests done before and after completion of the program included:

- Complete blood counts.
- Complete lipid profile.
- Renal function.
- Liver enzyme.
- HBA1c.
- Thyroid profile.

All patients were advised adopt Mediterranean diet regimen.[(16)]
All patients were in sinus rhythm and free of significant arrhythmias. Before CR program they were subjected to a symptom limited exercise test (modified Bruce protocol) to exclude any remaining ischemia and calculate enrollment resting heart rate (RHR), peak HR (PHR), HR reserve, baseline heart rate recovery in 1st minute (HRR1) and 2nd minute (HRR2). Another symptom limited exercise test was done after the completion of the CR program.

In order to calculate HR recovery, the PHR during the exercise test was recorded. Then HRR1 and HRR2 was calculated as explained below:
***HRR1=PHR-HR** at **first** minute from stopping the exercise test.
***HRR2=PHR-HR** at the **second** minutes from stopping the exercise test.
The cardiac rehabilitation team determined the PHR and RHR, then the training HR range was calculated from the formula based percentage of heart rate reserve as suggested by the Karvonen formula.[(17)]

The Karvonen formula is used to calculate exercise HR at a given percentage training intensity. The given percentage of heart rate reserve was added to the resting heart rate. During CR program CR team increased the intensity of training every month as training heart rate (THR) was calculated as (40% - 60% X HR reserve) + RHR.

Moderate intensity exercise training 2 times a week for 12 weeks was prescribed achieving target heart rate of 40–60% of HR reserve calculated from pre-exercise symptom limited stress test by modified Bruce protocol. Each session was 30 min in duration. The exercise sessions were initiated with 5 min of warm-up exercise such as walking and stretching, followed by treadmill walking supervised by a nurse and one of our study team.

The Borg scale 6-20 of rate of perceived exertion (RPE) was used to follow up the progression of exercise intensity in every rehabilitation session where the patients were exercised at an RPE of 11–13 [(18).]
Patients were monitored by continuous ECG monitoring, recording of heart rate, blood pressure and symptoms pre and post activity.

The program also included smoking cessation and nutrition education as well as advising the patients to maintain moderate exercise outside the hospital.

Statistical methodology

Analysis of data was performed using SPSS v. 22 (Statistical Package for Social science) for Windows.
Description of variables was presented as follows:
● Description of quantitative variables was in the form of mean, standard deviation (SD), median and range.
● Description of qualitative variables was in the form of numbers (No.) and percent’s (%).
Data was explored for normality using Shapiro/ Kolomogrov tests of normality.
Assessment of the effect of cardiac rehabilitation program was carried out by paired t-test for parametric data and Wilcoxon test for non-parametric data.
The significance of the results was assessed in the form of P-value that was differentiated into:

- Non-significant when P-value > 0.05.
- Significant when P-value ≤ 0.05.
- Highly significant when P-value ≤ 0.01.

Results

Fifty diabetic patients, who were presented to with STEMI (28 anterior STEMI and 22 inferior STEMI) and were managed by successful coronary revascularization.

Table (1): Baseline characteristics of patients in the study.

characteristics	Values
Age (years)	
Mean ± SD	49.4±9.3
Range(min-max)	(30-68)
Gender n (%)	
Females	9(18)
Males	41(82)

Scale data was presented as mean±SD and categorical data was presented as number and percent.

Table (1): illustrates that mean age of patients included in the study was 49.4±9.3 years and ranged from 30 to 68 years with median 52 years. The study included 9 (18%) females and 41 (82%) males.

Table (2): Special habits and comorbidities of patients in the study

Characteristics	Values
Smoking n (%)	
No	16(32)
Ex-smokers	13(26)
Smokers	21(42)
HTN n (%)	
No	9(18)
Yes	41(82)
Dyslipidemia n (%)	
No	8(16)
Yes	42(84)

HTN: Hypertension

Table (2) illustrates that there were 16(32%) non-smokers, 13(26%) ex-smokers and 21(42%) smokers in the present study. Most of patients under the study were hypertensive 41(82%) where only 9(18%) were non hypertensive. 42 patients (84%) were dyslipidemic.

Table (3): Effect of the CR program on clinical, laboratory and exercise parameters.

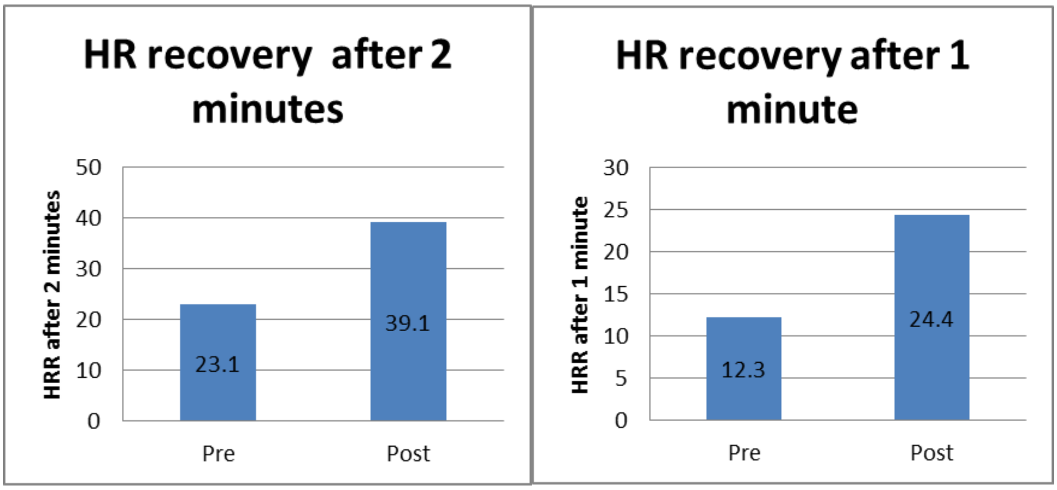
Parameters	Before	After	P-value
Duration of exercise (min) Mean ±SD Range (min-max)	 7.5±1.7 8-3	 14.6 ±2.9 9.2-15.3	 <0.01**
METS Mean ±SD Range (min-max)	 3.4±1.1 2.7-7.1	 7.2±2.4 6.4-12.0	 <0.01**
Resting HR (bpm) Mean ± SD Range (min-max)	 80.6±8.9 62-100	 69.1 ±6.8 60-85	<0.01**
HR reserve Mean ± SD Range (min-max)	 53.7 ±10.5 37-75	 64.1 ±11.8 43-81	<0.01**
HR recovery 1 minute Mean ± SD Range (min-max)	 12.3 ±2.8 8-19	 24.4 ±4.3 13-34	<0.01**
HR recovery 2 minutes Mean ± SD Range (min-max)	 23.1± 6.45 18-29	 39.1±4.7 31-56	<0.01**
Blood pressure Systolic Diastolic	 135.30 ± 8.33 84.90 ± 11.54	 134.90 ± 6.80 78.40 ± 9.87	 0.893 0.003
Lipid profile LDL HDL TG	 135.16±17.8 36.2±9.8 153.9±18	 99.7±5.7 55.2±6.0 115±5.9	 <0.001** <0.001** <0.001**
BMI (Kg/m2)	26±1.4	24.5±1.2	<0.001**

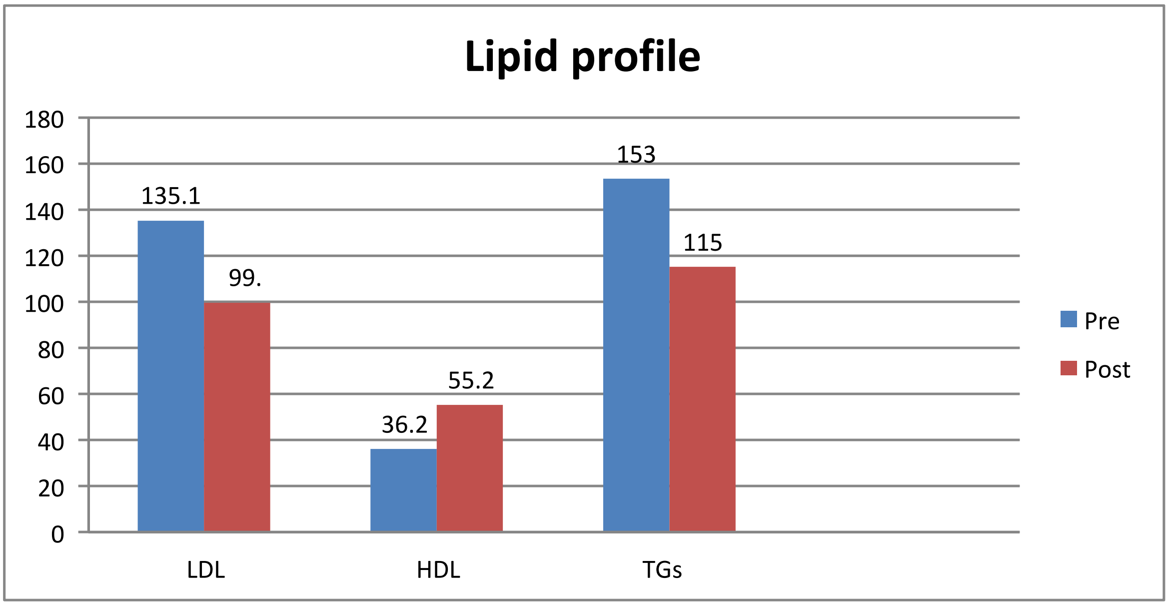
P-value >0.05 (Non-significant). P-value ≤0.05 (Significant). P-value ≤0.01 (Highly significant) METs: Metabolic equivalent of task, HR: Heart rate, LDL: Low density lipoproteins, HDL: High density lipoproteins, TG: Triglycerides.

Table (3) & figure (1) show a statistically significant increase in the duration of exercise from 7.5±1.7 minutes to 14.6 ±2.9 minutes and METS from 5.3±1.1 to 9.3±2.4 after completion of the rehabilitation program (P-value<0.01). There was also a significant decrease in resting HR from 80.6±8.9 bpm to 69.1 ±6.8 bpm (P-value<0.01) and there was also a statistically significant increase of HR reserve from 53.7±10.5 bpm to 64.1±11.8 bpm and HR recovery after 1 and 2 minutes which significantly increased from 12.3 ±2.8 bpm & 23.1±6.45 bpm to 24.4±4.3 bpm& 39.1±4.7 bpm respectively (P-value<0.01). Resting systolic and diastolic blood pressures showed no statistically significant changes (134 ± 19.83 to 131.84 ± 16.42, p-value 0.316), (113±13.98 to 112.90±13.67, p-value 0.955) and (70.30±10.22 to 70.80±8.83, p-value 0.765) respectively. Regarding lipid profile, there was a statistically significant decrease in the LDL, TG with a statistically significant increase in HDL (P-value<0.001).

The patients also showed a statistically significant decrease in the BMI after the completion of CR program (P-value<0.001).

Figure (1): Effect of the CR program on Lipid profile and HRR1 and HRR2





.
HRR: Heart rate recovery, LDL: Low density lipoproteins,
HDL: High density lipoproteins, TGs: Triglycerides

Table (4): Effect of the CR program on HBA1C

Parameter	Before	After	P-value
HBA1C. **Mean±SD** **Range (min-max)**	7.3±1.95 5-12.6	6.5 ±1 5-9.2	<0.01*

Scale data was presented as mean±SD *P-value is considered significant at <0.05
****P-value is considered significant at <0.01**

Table (4) & figure (2) shows that there was a statistically significant decrease in HBA1c from 7.3±1.95% to 6.5±1% after completion of the cardiac rehabilitation program (P-value<0.01).

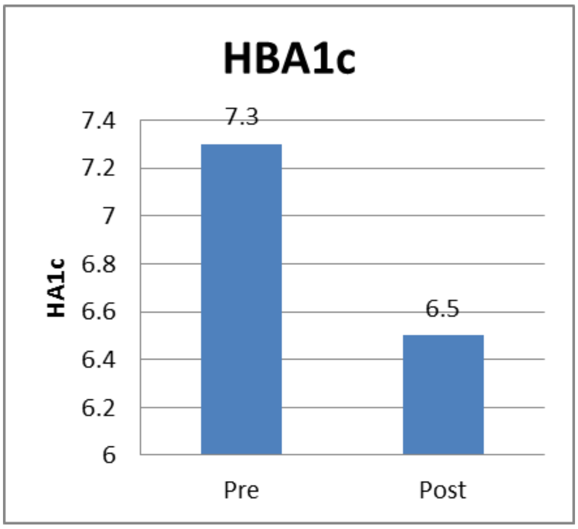


Figure (9): HBA1c pre and post CR.

Table (5): Effect of the CR program on EF .

Parameter	Before	After	P-value
EF (%) Mean ±SD Range(min-max)	 48 ±9.9 30-68	 51.6 ±7.7 40-65 52	 **<0.01***

Scale data was presented as mean±SD, *P-value is considered significant at <0.05, **P-value is considered significant at <0.01, EF: Ejection fraction

Table (5) & figure (3) demonstrate that there was a statistically significant increase in EF from 48±9.9% to 51.6±7.7% after completion of the cardiac rehabilitation program (P-value<0.01).

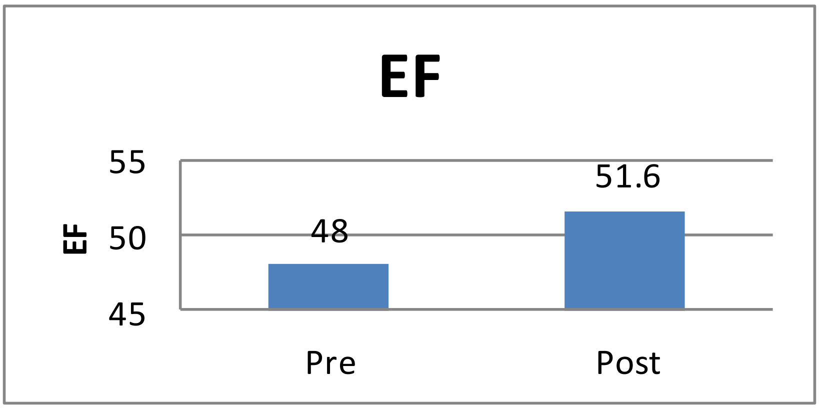


Figure (10): EF(%) pre and post CR.

Discussion

The present study showed that HR recovery improved significantly after first and second minutes, from 12.3±2.8 bpm and 23.1±6.45 bpm to 24.4±4.3 bpm and 39.1±4.7 bpm after completion of the cardiac rehabilitation program respectively. Our results are supported by Michael A, who underwent his study on 1070 consecutive patients (including 458 diabetic patients) who underwent exercise stress testing before and after completion of the 12-week Phase 2 cardiac rehabilitation program under physician supervision, typically involving 3 visits per week. The study showed that heart rate recovery significantly improved after phase 2 CR exercise training.[19]

Another study by Francesco et al., that studied the effect of endurance exercise based on HR recovery 1st min in elderly patients after MI agreed with our results. This was a prospective observational study, including 268 older patients after MI, subdivided into two groups. Group A enrolled in an exercise training program and Group B discharged generic instructions to continue physical activity. All group A and group B patients underwent an exercise test at baseline and 3 months of follow-up. An improvement in HR recovery was observed in group A (13.5±3.7 to 18.7±3.5 bpm, p-value < 0.001) after completion of the exercise training program, whereas no changes in HR recovery were observed in group B patients .[20]

The present study showed significant decrease in resting HR after the exercise training program from 80.6±8.9 to 69.1 ±6.8 bpm (P-value<0.01). Tsai et al.,, who investigated the effects of CR on HR recovery and resting HR after exercise in patients receiving coronary artery bypass graft surgery, supports our results. A CR program was randomly assigned to thirty patients who received bypass graft surgery (study group n= 15; control group n= 15). In the study group, HR resting was significantly lower (77.46±9.49 vs.92.31±10.18 p-value < 0.001).[21]

The significant improvement in HR recovery and decrease in resting heart rate appears to be related to the positive effect of exercise training on the autonomic nervous system as the heart rate is regulated and predominantly determined by the autonomous nervous system function with regular exercise training increases the parasympathetic tone as changes in HR during exercise and recovery phases are functional .[22]

Decreasing HR resting and improving HR recovery can also be caused by an increase in venous return and systolic volume leading to an increase in systolic volume and, according to Frank-Starling law, when blood volume increases in its cavities, heart contractility increases.[23]

There was a significant moderate negative correlation between patient age and HR reserve before and after the program in our study (R=-.335, P-value=.017) and (R=-.441, P-value= .001) respectively. Yiling et al., who evaluated 459 healthy men, age 20–59 years, who completed a maximal treadmill exercise test to delineate heart rate reserve as a predictor of cardiovascular and all-cause mortality in men, found that there was decrease in maximal exercise heart rate and heart rate reserve with increasing age.[24]

Aging is associated with changes in pacemaker tissue, a decrease in the responsiveness of autonomic cardiovascular reflexes, a decline in the intrinsic heart rate, and decreased adrenergic receptor sensitivity. Decreased responsiveness of the sinus node to catecholamines may also explain the lower maximal heart rate and heart rate reserve of older subjects despite increased plasma norepinephrine.[25]

The significant increase in functional capacity in the present study was reflected by the statistically significant increase in duration of exercise from 7.5±1.7 minutes to 14.6 ±2.9 minutes and METS from 5.3±1.1 to 9.3±2.4 after completion of the rehabilitation program (P-value<0.01). Our results are similar to the significant improvement in exercise capacity found by Rebecca et al.,, who retrospectively reviewed data from 458 patients enrolled in CR programs following acute coronary syndrome with cardiac rehabilitation and exercise training.[26]

Another study agreed with our results was carried out by Parvand et al., who underwent his study on 40 patients and used the METS scale to examine the functional capacity variable. A significant increase in METS value from secondary post-test to primary (P<0.05).[27]

Our study showed that there was a statistically significant increase in EF from 48±9.9% to 51.6 ±7.7% after completion of the rehabilitation program (P-value<0.01) and there was a significantly higher EF after the program among patients with inferior infarction than patients with anterior infarction (P-value<0.001). Our results are supported by Masoumeh et al., who evaluated 140 patients with MI (88 anterior STEMI and 52 inferior STEMI) enrolled in the cardiac rehabilitation program in his study, 84 of whom had EF between 30% and 50%. The LVEF increased from 45.14± 5.77% to 50.44±8.70% (P<0.001) at the end of the rehabilitation period with significant improving among patients with inferior infarction (p>0.05).[28]

Another study supports the findings from *Kurosh et al.,* who evaluated 146 CAD patients in a single case group (CR undertaking after PCI), and control group (no rehabilitation after PCI) of improving left-ventricular systolic function. Echocardiography (Pre-CR and Post-CR LV diastolic dysfunction) in the CR group only substantially changed following the CR program of exercise (p value= 0.043). There was a significant increase in the ejection fraction in the CR group (p value < 0.05).[29]

Improving the systolic function in our study seems to be related to the effect of early registration by patients with CR after primary PCI, which could prevent ventricular restructuring after acute myocardial infarction.[30]

Our study showed that after the rehabilitation program, there had been statistically significant decline from 7,3±1,95% to 6,5±1% in HBA1c (P-value<0,01). The study of 80 chronically stable coronary artery disease patients shows reduction of the glycated hemoglobin (7.13± 1.34g/dl to 6.65±0.9g/dl, (P<0.001)) after enrolment of CR program has supported our results.[31]

Another study conducted by Salameh et al., aimed to compare the effects of 10-week exercise on the glycemic index level in adults with type 2 diabetes before and immediately after the exercise. Twenty subjects with type 2 diabetes enrolled in the study. The mean HbA1c reading before and after training in both groups has been significantly improved (p < 0.001).[32]

The improvement of HBA1C in our study can be caused primarily through diffusion using glucose carrier proteins (GLUT) as a combined effect of anti-diabetic medical treatment optimization, dietary control and the positive effect of exercise for glucose metabolism. GLUT4 levels are considered an important determiner for the sensitivity of insulin and both aerobics and resistance exercises are used to increase the GLUT4 abundance and translocation and thus to absorb blood glucose by means of a way that does not regulate the transportation of glucose, especially by translocating the GLUT4 Isoform from the intracellular compartment to the plasma membrane and transverse tubular. Therefore, even in the presence of type 2 diabetes, glucose uptake is normal in the contracting muscle. The glucose uptake remains high following exercise, while the contractional trajectory remains active for several hours.[33]

Exercise training was expected to result in significant decrease in resting systolic and diastolic blood pressures; however, in our study there were no statistically significant changes (134±19.83 to 131.84±16.42, p-value 0.316), (113±13.98 to 112.90±13.67, p-value 0.955) and (70.30±10.22 to 70.80±8.83, p-value 0.765) respectively, this may attributed to the small number of patient included in this study. The meta-analysis on endurance training involved 72 trials and 105 study groups. Training induced significant net reductions in resting and day time ambulatory blood pressure of, respectively, 3.0/2.4 mmHg (P<0.001) and 3.3/3.5 mmHg (P<0.01). Systemic vascular resistance decreased by 7.1% (P<0.05). Endu-rance training decreases blood pressure through a reduction in systemic vascular resistance, and favorably affects concomitant cardiovascular risk factors. The Exercise is a cornerstone therapy for the prevention, treatment and control of hypertension.[34]

The present study showed significant decrease in of the LDL, TG and significant increase of HDL. Our results are supported by Sarrazadegan et al., who evaluated 547 patients with documented CAD before and after a 24 session CR program between 1998 to 2003. All parameters of lipid profile improved significantly (p-value <0.001).[35]

Also our results were also supported by Viviane et al., who studied 200 CAD patients referred to supervised 12 week CR program of three weekly sessions. After the program the total cholesterol, LDL, TGDs and HDL improved.[1]

The improvement in lipid profile was mostly due to greater effect of exercise and healthy life style education on rehabilitation program.

The present study showed a statistically highly significant reduction in the BMI and weight (BMI was decreased from 26.8±1.4kg/m^2 to 24.7±1.2kg/m^2, and weight 68.2±9.0kg to 76.0± 4.2kg, with p-value<0.001). This positive effect has also been demonstrated by Sarrafzadegan et al., study that showed reduction in BMI from mean 27.2 to 26.6 kg/m2and waist circumference from 99.3 to 96.3 (p-value = 0.001).[(35)]

Lifestyle changes, exercise is important for the overall reduction of body weight and subsequent decrease BMI. Exercise consumes a lot of energy, exercise is the most effective way to consume fat as a fuel, and that exercise will stimulate energy expenditure for hours after completing exercise.[(36)]

Conclusion and Recommendations

The present study showed that 2 sessions of exercise training/week for 12weeks is sufficient to obtain improvement in HR recovery, resting HR and HR reserve; in diabetic patients after primary PCI for STEMI which may have a positive prognostic effect in morbidity and mortality.

CR program should have an important and integral role in contemporary management of diabetic patients with ST segment elevation myocardial infarction post primary PCI as it causes significant improvement of cardiovascular risk factors as diabetes and should be implemented in routine management of these patients and supported by the government and health insurance institutes.

Limitations

1. Small number of patients.
2. Shorter duration of follow up (longer follow up for cardiac events will give strength to the present research).
3. Single center study**.**

References

1. Viviane C, Nele P, Catherine De, et al., Aerobic interval training and training equally improve exercise capacity in the patient with CAD: the SANTEX-CAD study. International journal of cardiology, 2015; 179; 203-210.
2. Hu G., Jousilahti P, Katoch S, et al., sex differences in cardiovascular and total mortality among diabetic and non-diabetic individuals with or without history of myocardial infarction. Diabetologia 2005: 48: 856-861.
3. Zeller M, Cottin Y, Brindisi MC, et al., The RICO survey working group. Impaired fasting glucose and cardiogenic shock in patients with acute myocardial infarction. European Heart J 2004; 25:308-12.
4. Falk M, Charlotte M, Katharine D, et al., an effectiveness of non-pharmacological secondary of coronary heart disease. European journal of cardiovascular prevention & rehabilitation EJCPR, 2010; 17:688-700.
5. Christensen K and Jordan M. pumping up cardiac rehabilitation, exercise guidelines for post-heart surgery clients. American Fitness, 2008; 26:58-63.
6. Vanhees L, Arena R, Fletcher G, et al., European Association for Cardiovascular Prevention & Rehabilitation; American Heart Association. Circulation. 2012; 126: 2261-74.
7. Smith S, Benjamin E, Bonow R, et al., AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease. Circulation, 2011; 124:2458-2473.
8. Gayda M, Bourassa M, Tardif J, et al., Heart rate recovery after exercise and long-term prognosis in patients with coronary artery disease. Canadian Journal of Cardiology, 2012; 28:201-7.
9. Gibbons R. Abnormal heart rate recovery after exercise lancet. 2012; 359:1536:1537.
10. Borja I, Stefan J, Stefan A, et al., Guidelines for the management of acute myocardial infarction in patients imparting with ST-segement elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Heart Journal, 2018:39:119–177.
11. Cannon C, Brindis R, Chaitman B, et al., Elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes and coronary artery disease.Circulation 2013; 127:1052–89.
12. James P, Oparil S, Carter B, et al., Evidence-based guideline for the manage-

ment of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee 2014; 311:507-20.

13. American Diabetes Association. Physical activity/exercise and diabetes. Diabetes Care. 2004; 27:s58-s62.
14. Hamm L, Sanderson B, Ades P, et al., Core competencies for cardiac rehabilitation/ secondary prevention professionals: 2010 update: position statement of the American Association of Cardiovascular and Pulmonary Rehabilitation. Journal of Cardiopulmonary Rehabilitation and Prevention. 2010; 31:2-10.
15. Schwingshackl L and Hoffmann G: Mediterranean dietary pattern, inflammation and endothelial function: A systematic review and meta-analysis of intervention trials. Nutrition, Metabolism and Cardiovascular Diseases, 2014; 24: 929-9.
16. Tanaka H, Monahan K, Seals D. Age-predicted maximal heart rate revisited. J Am Colleague Cardiology. 2001;37:153–6.
17. Casillas J, Besson D, Hannequin A, et al., Effects of an eccentric training personalized by a low rate of perceived exertion on the maximal capacities in chronic heart failure. European Journal of Physical Rehabilitation Medicine 2015.
18. Michael A. Jolly, Danielle M. Brennan, Leslie Cho. Impact of Exercise on Heart Rate Recovery, Circulation 2011; 124: 1520-1526.
19. Francesco Giallauria, Rosa Lucci, Marco Pietrosante, et al., Exercise-Based Cardiac Rehabilitation Improves Heart Rate Recovery in Elderly Patients After Acute Myocardial Infarction, Journal of Gerontology: medical sciences 2006;61:713–717.
20. Tsai S, Lin Y and Wu SK. The effect of cardiac rehabilitation on recovery of heart rate over one minute after exercise in patients with coronary artery bypasses graft surgery. Clinical Rehabilitation. 2005; 19:843–849.
21. Borresen J and Lambert M. Autonomic control of heart rate during and after exercise: measurements and implications for monitoring training status. Sports Medicine 2008; 38: 633-646.
22. Bonaduce D, Petretta M, Cavallaro V, et al., Intensive training and cardiac autonomic control in high level athletes. Medical Society of Sports and Exercise. 1998; 30:691-6.
23. Cheng Y, Macera T, Church S, et al., Heart rate reserve as a predictor of cardiovascular and all-cause mortality in men. Med. Sci. Sports and Exercise, 2002; 34: 1873–1878.
24. Tanaka H. Age-predicted maximal heart rate revisited Journal of the American College of Cardiology; 2001; 37: 153-156.
25. Rebecca J. Norton, Sarah G, Hayes Dalal, et al., Home-based cardiac rehabilitation for people with heart failure: A systematic review and meta-analysis, 2016; 221: 963–969.
26. Parvand M, Goosheh B and Sarmadi A. Effect of Cardiac Rehabilitation on Heart Rate and Functional Capacity in Patients After Myocardial Infarction. Iranian Rehabilitation Journal. 2016; 14:157-162.
27. Masoumeh S, Mohammad G, Mohsen K, et al., Cardiology Research and Practice 2013; 9:302:309.
28. Kourosh S, , Younos N, , Alireza A, et al .J Tehran Heart Cent. 2014; 9: 54–58.
29. Gill JM. Physical activity, cardio-respiratory fitness and insulin resistance: a short update. Curr Opin Lipidol. 2007; 18:47-52.
30. Haitham G , Adel Shabana and Hazem K. Effect of exercise training on heart rate recovery in patients post anterior myocardial infarction 2018; 70: 77-82.
31. Salameh B,Muhammed A, Abdul Majeed A, et al., Diabetology & Metabolic Syndrome 20091:27.
32. Colberg S, Sigal R, Fernhall B, et al., American College of Sports Medicine, American Diabetes Association Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. Diabetes Care. 2010; 33:2692–2696.
33. Cornelissen V and Fagard R. Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. Hypertension. 2005; 46:667–675.
34. Sarrafzadegan N, Rabiei K, Kair A, et al., changes in lipid profile of patients referred to cardiac rehabilitation program. Eur J Rehali, 2008;15:467-72.
35. Zelasko C. Exercise for Weight Loss: What Are the Facts? Journal of American dietetic Association 1995: 12; 1414-7.