MJMR, Vol. 34, No. 1, 2023, pages (319-328).

Open Access
ISSN: 2682-4558

Research Article

The impact of high-intensity interval training on ventricular remodeling in patients with a recent Non ST Segment Elevation Acute Myocardial Infarction

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DOI: 10.21608/MJMR.2022.148101.1108

Abstract
Introduction : Exercise-based secondary prevention programs have confirmed improvements in mortality and morbidity in patients with stable coronary heart disease (CHD) and after AMI, respectively. High intensity interval training (HIIT) is more effective at improving V-O2 peak and can be performed safely . our study aimed to determine the impact of HIIT o ventricular remodeling in patients with recent non ST segment myocardial infarction (NSTEMI). **Methods:** sixty-five patients who were suffered from a recent STEMI were randomized to four groups : Group I : re-vascularized and perform HIIT program ,Group II : re-vascularized and not perform HIIT program ,Group III : not re-vascularized and perform HIIT program and Group IV : not re-vascularized and not perform HIIT . Baseline clinical assessment (ie , medical history, physical examination and anthropometric measurements) , transthoracic echocardiography, and cardiopulmonary exercise test (CPET) available parameter were performed at baseline and after three months (duration of HIIT program). **Result:** there was significant improvement in CPET parameters in groups that perform HIIT program while no significant changes were obtained according to echocardiographic parameters. **Conclusion** : HIIT program leads to significant improvement in CPET parameters.

Keywords: HIIT, NSTEMI & coronary heart disease .

Introduction
Acute myocardial infarction (AMI) can induce changes in left ventricular (LV) topography (i.e ventricular remodeling) and is a major contributor in the development of heart failure despite advances in coronary revascularization and optimal medical therapy.[1]Exercise-based secondary prevention programs had confirmed improvements in mortality and morbidity in patients with stable coronary heart disease (CHD) and after AMI, respectively.[2,3] The importance of starting aerobic exercise training early post-AMI and the beneficial effects on LV remodeling had been emphasized .[4] High intensity interval training (HIIT) was more effective at improving maximal oxygen uptake (VO_2 max) and can be performed safely compared to the more established moderate-intensity continuous exercise training (MICET) in stable CHD patients.[5,6]

Aim of The Work : to evaluate the short term effect of HIIT on cardiopulmonary exercise test (CPET) variables and left ventricular remodeling in CHD patients who recently suffered non ST segment myocardial infarction (NSTEMI) .

Patients and Methods
This is a prospective non randomized longitudinal study included consecutive 65 patients with recent NSTEMI within the preceding 6 weeks, whom referred for cardiac rehabilitation in our department at the period from January 2019 to April 2021.

Patient with any of the following criteria would be excluded : Patients recently diagnosed as ST Segment Elevation Acute Myocardial Infarction (STEMI) , history of coronary bypass surgery, incomplete revascularization , NYHA class III: IV symptoms, Severe left ventricular dysfuncion (ejection fraction ≤30%) & actively decompensated heart failure with orthopnea or paroxysmal nocturnal dyspnea.

Clinical assessment : medical history including age, sex, smoking ,hypertension, diabetes mellitus, history of previous coronary artery disease and NYHA class.[7] were obtained . physical examination including arterial blood pressure, general examination, cardiac examination and electrocardiogram (ECG) were obtained .

Transthoracic echocardiography : Standard transthoracic 2D echocardiography was performed by (ACUSON SC2000 siemens) cardiac ultrasound system with a 6-MHz transducer. All echocardiographic images were obtained by two cardiology specialists using standard tomographic views . All data were stored on an external hard-drive and analyzed offline on a commercially available work station. Echocardiographic parameters of LV dimension, systolic and diastolic functions were assessed. 2D speckle-tracking strain analysis: Global longitudinal strain (GLS) was assessed using standard 2D apical four-chamber, two-chamber, and three-chamber view using speckle-tracking analysis.

All images were recorded using high frame rate loops (50-80 Hz) for reliable analysis by the software (velocity Vector imaging VVI , Siemens). Manual tracing of the endocardial borders on an end-systolic frame (aortic valve closure) was performed and the myocardial region of interest was adjusted to include all the endocardium and epicardium, excluding the pericardium. Automatically tracing was then applied on subsequent frames. Adequate tracing for each segment was verified and manually corrected, if necessary. If tracing was still judged incorrect, the specific segment was excluded from the global strain measurement. If more than two segments were discarded, GLS and strain rates were not reported for that patient. The GLS was determined by averaging all values of the 18 segments of the three views[8,9].

Maximal CPET available parameter: such as resting heart rate , heart rate reserve , peak systolic and diastolic blood pressure were recorded while aerobic exercise was performed to reach 85 % : 95 % of maximal heart rate (HIIT)[10].

VO_2 max. parameter was calculated by the following equation:
15.3 X (maximal heart rate /resting heart rate).[11]

Exercise training intervention (High Intensity Interval Training):
All trainings were center-based under supervision of an experienced rhuematologist. The HIIT training protocol was recently described. Following a 5-minute warm-up, patients performed two to three sets of 6 to 8 minutes with repeated bouts of 15 to 30 seconds at 85:95% of maximal heart rate alternated by 15 to 30 seconds of passive recovery . The targeted Borg rating of perceived exertion (RPE) was set at 15 during the HIIT bouts. The sets were separated by a 5-minute active recovery phase. The training session was terminated by a 5-minute cool-down phase[10].

Follow up: after six month (duration of the HIIT program),clinical assessment (ie , medical history and physical examination), transthoracic echocardiography, and CPET were performed

Statistical analysis:
The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 25 **.** Descriptive statistics were done for parametric quantitative data by mean, standard deviation and minimum and maximum of range, and for non-parametric quantitative data by median and interquartile range (IQR), while they were done for categorical data by number and percentage. Distribution of the data was done by Shapiro Wilk test. Analyses were done for non-parametric quantitative data between the two groups using Mann Whitney test. The level of significance was taken at (P value < 0.05) .

Result

Our study included 65 patients, they were classified according to revascularization and performing HIIT program into four groups:

Group I (n =18): re-vascularized and perform HIIT program.

Group II (n =22): re-vascularized and not perform HIIT program.

Group III (n =12): not re-vascularized and perform HIIT program.

Group IV (n =13) : not re-vascularized and not perform HIIT.

Table1: comparison between group I & group II as regard their clinical characteristics

	Group I n =18	Group II n =22	P value
Age (years)	50.5 ± 6.2	51.8 ± 6.1	0.23
Male n (%)	13 (72 %)	13 (59 %)	0.86
DM n (%)	12 (66 %)	12 (54 %)	0.1
HTN n (%)	10 (55 %)	14 (63 %)	0.23
Smoking n (%)	13 (72 %)	13 (59 %)	0.7
Family history n (%)	5 (27 %)	9 (40 %)	0.8
NYHA class I n (%)	10 (55 %)	10 (45 %)	0.1
NYHA class II n (%)	8 (45 %)	12 (55 %)	0.1

There was no statistical significant difference between group I & group II as regard their clinical characteristics. Table (1)

Table 2: Comparison between group III & group IV as regard their clinical characteristics

	Group III n =12	Group IV n =13	P value
Age (years)	49.8± 10.2	50.1 ± 10.3	0.1
Male n (%)	8 (66 %)	9 (69 %)	0.8
DM n (%)	7 (58 %)	9 (69 %)	0.2
HTN n (%)	10 (83 %)	11 (84 %)	0.2
Smoking n (%)	8 (66 %)	9 (69 %)	0.8
Family history n (%)	4 (33 %)	4 (30 %)	0.7
NYHA class I n (%)	5 (41 %)	4 (30 %)	0.14
NYHA class II n (%)	7 (59 %)	9 (70 %)	0.2

There was no statistical significant difference between group III ad group IV as regard their clinical characteristics . Table (2)

Table 3: Comparison between group I & group II as regard their baseline echocardiographic parameters

	Group I n =18	Group II n =22	P value
LVEF %	60 ± 5	57± 7	0.22
LVEDD cm	5.3 ± 0.4	5.4 ± 0.4	0.4
E wave	56.2 ± 17.9	60.9 ± 19.5	0.44
A wave	66.7 ± 12.1	63.4 ± 13.8	0.45
E/A ratio	0.9 ± 0.5	1.1 ± 0.5	0.26
TDI- é septal	9.7 ± 11.5	7.3 ± 2.3	0.75
TDI - é lateral	10.8 ± 2.3	10.9 ± 2.7	0.72
E/e	8.2 ± 3.9	9. ± 4.9	0.39
GLS	-17.2 ± 1.5	-17.6 ± 1.1	0.25

There was no statistical significant difference between group I & group II as regard their echocardiographic parameters (LVEF, LVEED, E wave, A wave, E / A ratio, TDI - é septal (Cm/S), TDI- é lateral (cm/s), E/é and GLS) before rehabilitation . Table (3)

Table 4 : Comparison between group III & group IV as regard their baseline echocardiographic parameters

	Group III n =12	Group IV n =13	P value
LVEF %	54.8 ± 7.7	57.6 ± 7.1	0.31
LVEDD cm	5.3 ± 0.4	5.5 ± 0.4	0.35
E wave	51.6 ± 22.1	61.1 ± 24.8	0.41
A wave	62.9 ± 10.9	68.1 ± 4.3	0.31
E/A ratio	0.8 ± 0.5	0.9 ± 0.3	0.98
TDI- é septal	7.9 ± 2.4	7.4 ± 2.1	0.54
TDI - é lateral	11.8 ± 2.5	10.5 ± 2.8	0.13
E/e	7.9 ± 5.7	9.7 ± 5.7	0.39
GLS	-16.9 ± 0.9	-17.2 ± 0.6	0.62

There was no statistical significant difference between group III & group IV as regard their echocardiographic parameters (LVEF, LVEED , E wave, A wave, E / A ratio , TDI - é septal (Cm/S), TDI- é lateral (cm/s), E/é and GLS) before rehabilitation . Table (4)

Table 5: Comparison between group I & group II as regard their baseline cardio-pulmonary parameters

	Group I n =18	Group II n =22	P value
Heart rate rest BPM	86 ± 16	80 ± 7	0.12
Heart rate max BPM	155 ± 11	149 ± 10	0.16
Heart rate reserve BPM	65 ± 15	59 ±11	0.13
vo2 max mL/kg/min	26 ± 3	26 ± 2	0.99

There was no statistical significant difference between group I & group II as regard baseline heart rate, heart rate max., heart rate reserve and vo_2 max. Table (5)

Table 6: Comparison between group III & group IV as regard their baseline cardio-pulmonary parameters

	Group III n =12	Group IV n =13	P value
Heart rate rest BPM	83 ± 6	79 ± 4	0.38
Heart rate max BPM	155 ± 11	146 ± 17	0.17
Heart rate reserve BPM	73 ± 12	67 ±16	0.08
vo2 max mL/kg/min	28 ± 2	28 ± 3	0.91

There was no statistical significant difference between group III & group IV as regard baseline heart rate, heart rate max., heart rate reserve and vo_2 max. Table (6)

Table 7: Comparison between group I & group II as regard their echocardiographic parameters at six month follow up

	Group I n =18	Group II n =22	P value
LVEF	60 ± 5	57 ± 7	0.22
LVEDD cm	5.3 ± 0.3	5.4 ± 0.4	0.40
E wave	56.2 ± 17.8	60.9 ± 19.5	0.44
A wave	66.7 ± 12.14	63.3 ± 13.8	0.45
E/A ratio	0.9 ± 0.4	1.1 ± 0.5	0.26
TDI- é septal	9.7 ± 11.4	7.2 ± 2.3	0.75
TDI - é lateral	10.8 ± 2.3	10.9 ± 2.7	0.72
E/ é	8.1 ± 3.8	9.6 ± 4.9	0.39
GLS	-17.2 ± 1.5	-17.6 ± 1.1	0.25

There was no statistical significant difference between group I & group II as regard echocardiographic parameters (LVEF, LVEED, E wave, A wave, E / A ratio, TDI - é septal (Cm/S), TDI- é lateral (cm/s), E/é and GLS) at six month follow up . Table (7) .

Table 8: Comparison between group III & group IV as regard their echocardiographic parameters at six month follow up

	Group III n =12	Group IV n =13	P value
LVEF	54 ± 7	57 ± 7	**0.3**
LVEDD cm	5.3 ± 0.4	5.6 ± 0.5	**0.3**
E wave	52.1 ± 19.4	58.1 ± 22.2	**0.62**
A wave	63.3 ± 13.7	66.9 ± 5.9	**0.62**
E/A ratio	0.9 ± 0.5	0.8 ± 0.3	**0.89**
TDI- é septal	7.3 ± 2.2	6.9 ± 1.9	**0.7**
TDI - é lateral	11.3 ± 2.7	10. ± 2.8	**0.37**
E/ é	8.5 ± 5.7	9.5 ± 5.4	**0.7**
GLS	-16.4 ± 1.1	-17 ± 0.9	**0.15**

There was no statistical significant difference between group III & group IV as regard echocardiographic parameters (LVEF, LVEED, E wave, A wave, E / A ratio, TDI - é septal (Cm/S), TDI- é lateral (cm/s), E/é and GLS) at six month follow up. Table (8).

Table 9: Comparison between group I & group II as regard their cardio-pulmonary parameters at six month follow up, NYHA class, event &survival rates

	Group I n =18	Group II n =22	P value
Heart rate rest BPM	77 ± 6	77 ± 5	0.24
Heart rate max BPM	155 ± 13	131 ± 9	**<0.0001**
Heart rate reserve BPM	78 ± 14	53 ±10	**<0.0001**
vo_2 max mL/kg/min	30 ± 3	26 ± 2	**<0.0001**
NYHA class I n (%)	14 (77 %)	10 (45%)	**0.02**
NYHA class II n (%)	4(33%)	12 (55%)	**0.0001**
Event rate (%)	2 (11%)	4 (18%)	0.2
Survival rate (%)	16(88%)	18(81%)	0.1

Group I had achieved statistically significant higher heart rate max. as compared to group II (155 ± 13 BPM Vs 131 ± 9 BPM , P < 0.0001) , heart rate reserve (78. ± 14 BPM Vs 53 ±10 BPM , p <0.0001) and Vo2 max (30 ± 3 ml/kg/min Vs 26 ± 2 ml/kg/min , P <0.0001) at six month follow up. Group I had achieved statistically significant higher number of patients with NYHA class I as compared to group II (14(77%) Vs 10 (45%) , p 0.02) and lower number of patients with NYHA class II as compared to group II (4 (33%) Vs 12 (55%), p 0.0001) at six month follow up but there was no

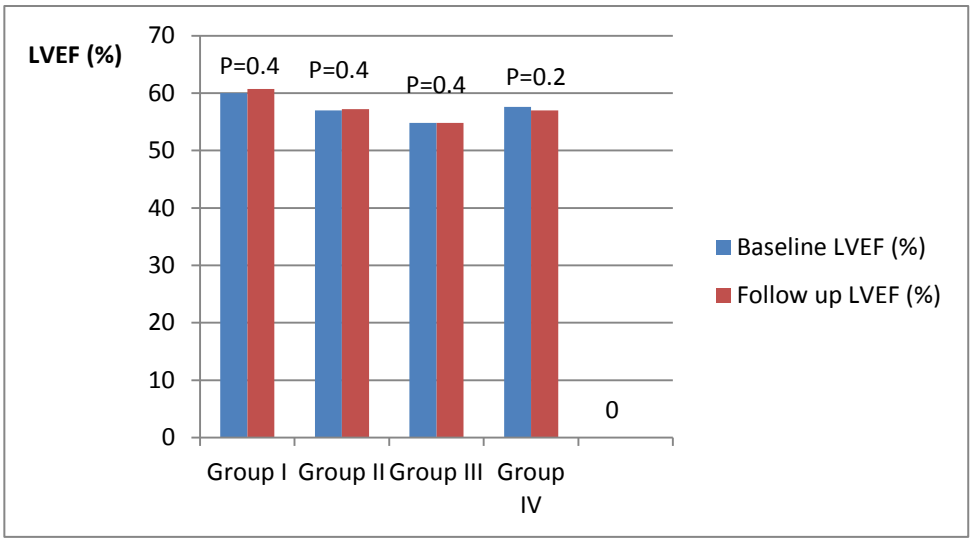
statistical significant difference between group I & group II as regard heart rate rest , event rates and survival rates at six month follow up. (Table 9)

Table 10: Comparison between group III & group IV as regard their cardio-pulmonary parameters at six month follow up , NYHA class , event &survival rates

	Group III n =12	Group IV n =13	P value
Heart rate rest BPM	77 ± 5	76 ± 3	0.24
Heart rate max BPM	149 ± 13	136 ± 14	**0.004**
Heart rate reserve BPM	71 ± 12	59 ±14	**0.04**
vo_2 max mL/kg/min	29 ± 2	27 ± 3	0.25
NYHA class I n (%)	9 (75 %)	5 (38%)	**0.001**
NYHA class II n (%)	3 (25%)	8 (61%)	**0.001**
Event rate (%)	4 (33%)	6 (46%)	0.5
Survival rate (%)	8 (66%)	7 (53%)	0.8

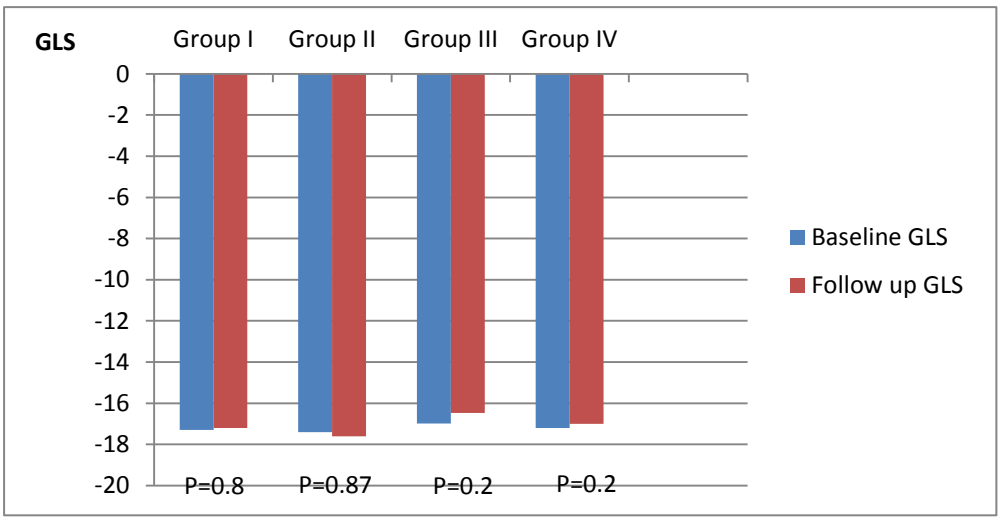
Group III had achieved statistically significant higher heart rate max. as compared to group IV (149 ± 13BPM Vs 136 ± 14 BPM , P 0.004) , heart rate reserve (71 ± 12 BPM Vs 59 ±14 BPM , p 0.04) at six month follow up. Group III had achieved statistically significant higher number of patients with NYHA class I as compared to group IV (9 (75 %) Vs 5 (38%) , p 0.001) and lower number of patients with NYHA class II as compared to group IV (3 (25 %) Vs 8 (61%) , p 0.001) at six month follow up but there was no statistical significant difference between group III & group IV as regard heart rate rest , Vo2 max. , event rates and survival rates at six month follow up. (Table 10)

Figure 1: Comparison between groups regarding their baseline LVEF and follow up LVEF after six month



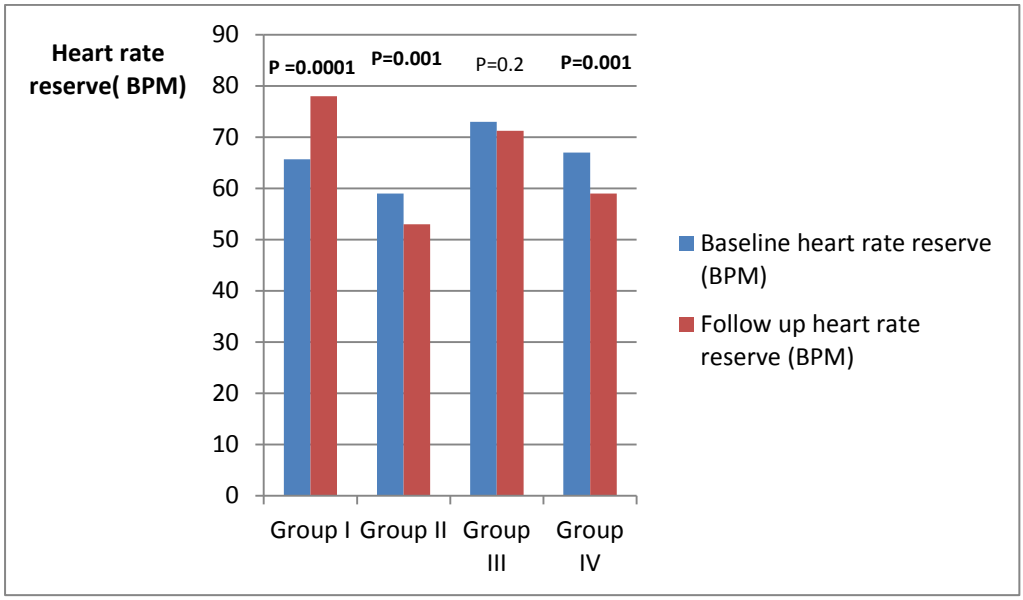
There was no statistical significance difference in baseline LVEF and follow up LVEF after six month among cases of each group . (fig. 1)

Figure 2 : Comparison between groups regarding their baseline GLS and follow up GLS after six month



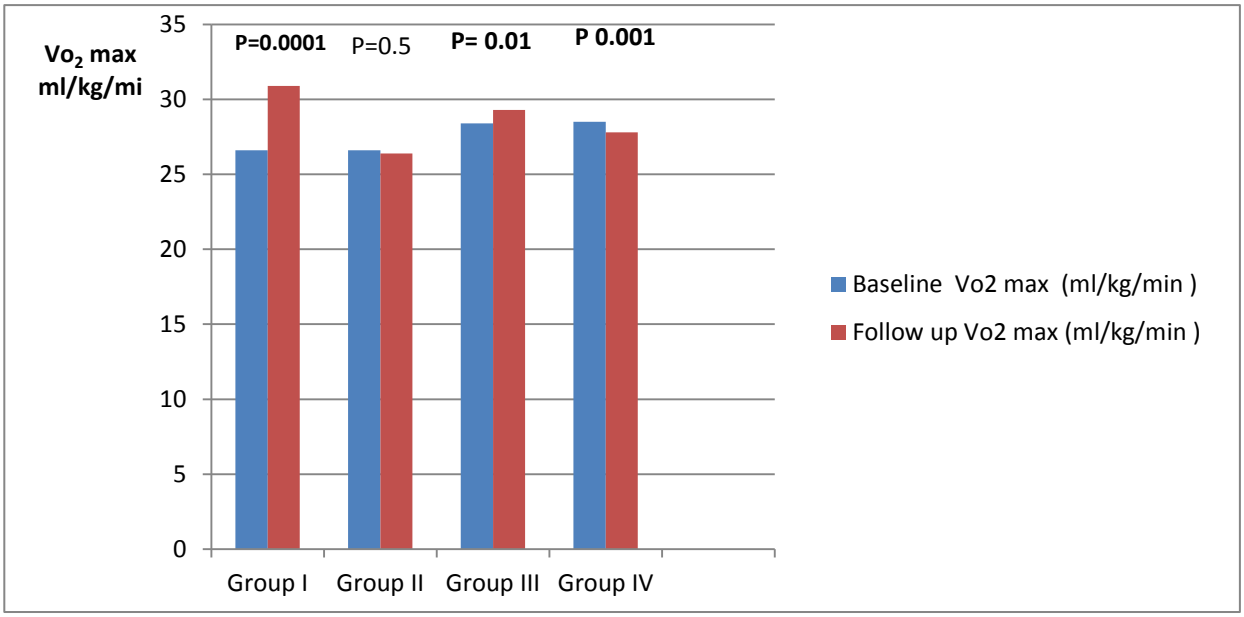
There was no statistical significance difference between baseline GLS and follow up GLS after six month among cases of each group .(fig.2)

Figure 3: Comparison between groups regarding their baseline heart rate reserve and follow up heart rate reserve after six month



Group I had achieved statistically significant higher follow up heart rate reserve as compared to their baseline heart rate reserve (65 BPM Vs, 78 BPM, P value = 0.0001). Group II had achieved statistically significant lower follow up heart rate reserve as compared to their baseline heart rate reserve (59 BPM Vs 53 BPM, P value = 0.001). Group IV had achieved statistically significant lower follow up heart rate reserve as compared to their baseline heart rate reserve (67 BPM Vs 59 BPM , P value = 0.001).There was no statistical significance difference between baseline heart rate reserve and follow up heart rate reserve after six month among cases of group III . (fig.3)

Figure 4: Comparison between groups regarding their baseline Vo_2 max and follow up Vo_2 max after six month



Group I had achieved statistically significant higher follow up Vo_2max. as compared to their baseline Vo_2max. (30 ml/kg/min Vs 26 ml/kg/min , P value 0.0001). Group III had achieved statistically significant higher follow up Vo_2 max. as compared to their baseline Vo_2max. (29.3 ml/kg/min Vs 28 ml/kg/min , P value 0.01). Group IV had achieved statistically significant lower follow up Vo_2 max. as compared to their baseline Vo_2max. (28,8 ml/kg/min Vs 28 ml/kg/min , P value 0.01). There was no statistical significance difference between baseline Vo_2 max and follow up Vo_2 max after six month among cases of group II . (fig.4)

Discussion

Exercise-based secondary prevention programs had confirmed improvements in mortality and morbidity in patients with stable coronary heart disease (CHD) and after AMI, respectively. The importance of starting aerobic exercise training early post-AMI and the beneficial effects on LV remodeling had been emphasized in meta-analysis [12].

Our prospective longitudinal study revealed that patients in rehabilitation groups had achieved statistically significant higher VO_2 max than non-rehabilitation groups. The significant increase in VO_2 max., found in our study , was in accordance with a study that was by lund et al.,[13], 28 patients with a recent AMI performed high-intensity interval training twice a week for 12 weeks then a cardiopulmonary exercise test was performed to determine Vo_2 max. the result showed that there was a significant increase in VO_2max. (35.2 vs. 38.9 ml/kg/min, P < .001).

Also this is in agreement with study by Trachsel et al.,[14] , 19 post-AMI patients were randomized to either HIIT (n=9) or usual care (n=10). CPET, transthoracic echocardiography, and cardiac biomarker assessment (ie, N-terminal pro B-type natriuretic peptide levels and G protein-coupled receptor kinase 2 expression) were performed before and after a 12-week training intervention . There was a significant improvement in VO_2 max. with exercise training in the HIIT group but not in the usual care group ((27 Vs 30 mL/Kg/min , P < 0.001) in the HIIT and (29.2 Vs 29.3 mL/Kg/min, P 0.8) in the usual care group, respectively). There was a significant improvement in predicted VO_2 max. with exercise training in the HIIT group but not in the usual care group (93 Vs 101 mL/Kg/min , P < 0.008 in the HIIT and (90.9 Vs 90 mL/Kg/min, P 0.7) in the usual care group, respectively).

Our prospective longitudinal study revealed that patients in rehabilitation groups had achieved statistically significant higher heart rate max. & heart rate reserve than non-rehabilitation groups. This contrasts with study that was performed by Dun et al[15] , 29 MI patients after percutaneous coronary intervention who began CR within 2 weeks after hospital discharge. Eleven patients (seven men; four women; age: 61 ± 11 yrs) who completed ≥24 supervised HIIT sessions with metabolic gas exchange measured during HIIT once weekly for 8 weeks and performed pre- and post- CR cardiopulmonary exercise tests were included. The result showed no statistically significant difference was found for HR. However the small number of studied patients can explain this non statistically significant result .

Our prospective longitudinal study showed no statistically significant differences between rehabilitation groups & non-rehabilitation groups according to heart rate rest. This contrasts with study that was performed by Songsorn et al.,[16]. In this study, 21 low physical activity young adults were randomly assigned into two groups: whole-body HIIT (n = 10, females = 2/males = 8, age 22 ± 0.8 years, BMI 19.5 ± 1.0 kg/m2) and control (n = 11, females = 4/males = 7, age 21.7 ± 0.8 years, BMI 19.8 ± 0.9 kg/m2). A 6-week exercise program (3 days per week) consisting of 10 min of whole-body HIIT. Baseline and post-training resting heart rate (HR rest) were recorded. The result showed HR rest decreased significantly following training (73.94 ± 13.2 vs. 66.1 ± 10.8 bpm, $p < 0.05$). Our study seems to be more valuable as this study had short duration of exercise , small number of patient and this decrease may be due to response to medical treatment

According to event rates, survival rates and echocardiographic parameters as regards (EF, LVEED, E and A waves TDI septal and lateral and GLS) there were no statistically significant differences between rehabilitation groups & non-rehabilitation groups . This contrasts with study by Nottin et al.,[17] , 23 triathletes underwent conventional and speckle tracking imaging echocardiography at rest before and immediately after an ultralong distance triathlon. The result showed LV systolic dysfunction was characterized by a decrease in LV longitudinal strain (-19 Vs -16 , P 0.01) . However, these findings in healthy subjects and athletes seem to be transient and particularly after prolonged and strenuous exercise in addition to small number of individuals included and are discussed controversial.

Conclusion :

Short term HIIT programs leads to significant improvement in vo_2 max , heart rate max and heart rate reserve without statistically significant difference in resting heart rate and echocardiographic parameters .

Study limitations :

Our findings have to be interpreted in the context of numerous limitations. First of all, the sample size in the present study was small with inclusion of predominantly male patients at a single institution and the difficulties to convince the patients to perform a rehabilitation program.

Conflict of interest statement: the authors declare no potential conflict of interests

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