

Evaluation of the Effect of Different Forms of Training on Autonomic Nervous System Activity in Patients with Acute Myocardial Infarction

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Abstract

Introduction: training alone or as a part of a cardiac rehabilitation programs can be beneficial for patients with acute coronary artery disease. However, due to diversity of proposed programs, various studies have yielded different results in this area. The objective of this research is to evaluate the various forms of training as a rehabilitation method after acute myocardial infarction on the autonomic system activity. **Methodology:** In this prospective and case-control study, a total of 60 patients with the first acute myocardial infarction were randomly selected. Trainings controlled by treadmill for 15 to 20 minutes, three days per week for three weeks and then 5 weeks of training at home, including 30-minute walking 3 times per week based on the heart rate were used in two groups (each contained 20 subjects). The control group performed 8 weeks of training at home. HRV parameters including SDNN, LF, HF, TP, pNN50, and SDNN index, SDANN and LF / HF were measured at baseline and one week after the completion of the rehabilitation programmed in all patients. **Results:** in three groups of A, B, and control, the mean SDNN variations (28.30, 29.28 and 15.40, respectively), the mean LF variations (57.10, 198.8, and -47.70, respectively), the mean HF variations (-11.70, 120.60 and -58.10, respectively), the mean TP variations (192.80, 1251.20 and -225.00, respectively), the mean NN50 variations (0.80, 4.60 and -0.40, respectively), the mean variations in SDNN index (90.20, 13.4 and -0.20, respectively), and the mean SDANN variations (80.80, 22.24 and 16.20, respectively) were significantly higher in intervention groups. However, no significant difference was observed between two intervention groups and the mean variations in LF / HF were not significant among three groups. **Conclusion:** The present study revealed that rehabilitation based on planned training at hospital compared to training at home had more favorable impact on autonomic nervous system activity after acute myocardial infarction. For this reason, the establishment of rehabilitation centers in hospitals seems to be necessary, since uncontrolled rehabilitation at home may have less impact due to different reasons such as inadequate patient compliance.

Keywords: Rehabilitation, Training, Acute Myocardial Infarction, Autonomic Nervous System Activity, Heart Rate Variability

Introduction

Cardiovascular diseases are the major cause of death in the world in people aged over 30 years, and acute myocardial infarction accounts for about 10% of these deaths (Winter et al., 2018). It has been proven that routine life style and lack of physical activity are risk factors for cardiovascular disease. Accordingly, physical activity and training both at workplace and during leisure time are recommended (Physical, 2015; Wang et al., 2016). Changes (increase or reduction) in cardiac biomarker values, along with at least one of the cases of ischemic symptoms, typical ECG changes, or disorder in the structure or movement of the cardiac wall detected by imaging techniques are considered as criteria required for the diagnosis of acute myocardial infarction in one clinical area (Cabello et al., 2016).

According to results of some studies, an increase in sympathetic activity occurs in the autonomic nervous system in patients with acute myocardial infarction makes them predisposed to fatal ventricular arrhythmias and sudden death (Kleiger et al., 2005). Heart rate variability (HRV) is a relatively simple, non-invasive, repeatable, and low-cost method to determine the status of cardiac autonomic regulation. Heart rate variability (HRV) analyzes the variations in intervals between normal heart rates or R wave peaks (RR or NN interval) (Cabiddu et al., 2015). The study of heart rate variability and the R-R interval are used in evaluating the sympathetic and parasympathetic variations on the sinus group and diagnosing of patients who are at risk for cardiovascular events associated with death. Improvement of these unpleasant variations in patients after cardiac rehabilitation can be achieved (Kleiger et al., 2005; Brateanu, 2015;

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Compostella et al., 2017).

Time domain indices include the standard deviation of all NN intervals (SDNN), the standard deviation of the average NN interval calculated from the 5-minute segments (SDNN), and the percentage of NN consecutive intervals with a difference of more than 50 millisecond (pNN50). Frequency domain indices include low frequency (LF) peak and high frequency (HF) peak expressed in squares of millisecond or normalized units (nu) (Kleiger et al., 2005; Heart rate variability, 1996). It has been shown that time domain variables are usually associated with each other and are affected by parasympathetic blocks in varying levels. Accordingly, these indices are parasympathetic cardiac regulation markers. However, HF peak is considered as the most important HRV index for vague cardiac activity (heart rate vague regulation). Although there is no complete agreement on the interpretation of the LF component, this parameter is generally considered as sympathetic and parasympathetic regulation marker (Iellamo et al., 2000; Duru et al., 2000; Barboza et al., 2012).

One of the most important results of physical activity after myocardial infarction is reduction in the activity of the sympathetic nervous system, which leads to change in the sympathetic to parasympathetic balance and increase in the activity of the parasympathetic system due to reduced sympathetic system overcome. Diastolic dysfunction is an important factor in complications caused by myocardial infarction, and unlike systolic function, no treatment or intervention has significantly proven improvement in the diastolic function. Data related to animal studies and patients with diastolic heart failure suggest that training can have a positive impact on diastolic function parameters (Fontes-Carvalho et al., 2015). Other factors (other than HRV) predicting the occurrence of arrhythmia after myocardial infarction and increased mortality include heart rate turbulence, change in QT size, T wave alternance, and sensitivity of baroreceptors' reflex (Fujimoto et al., 1999; Średniawa et al., 2016; Arisha et al., 2013). Limited number of papers has been published so far on the effects of different forms of training on autonomic nervous system activity in patients with acute myocardial infarction. The objective of this research was to evaluate the effect of different forms of training on the activity of the autonomic nervous system in patients with acute myocardial infarction by examining HRV.

Methodology

In this case-control and prospective study, patients with acute ST elevation, diagnosed based on American Heart Association's guidelines, underwent initial examinations after initial improvement and walking ability 10 days after the onset of myocardial infarction. Having normal sinus rhythm, willingness to participate in the study, left ventricular ejection fraction (LVEF) from 30 to 40 percent, and tolerating the training in the initial test were considered as research inclusion criteria. Exclusion criteria of study included age over 75 years systolic blood pressure above 200, or diastolic blood pressure above 100 mm Hg, ventricular atrial block / acute systemic disease, unstable angina / peripheral neuropathy (based on hospital records), chest pain during training, valve disease required surgery, severe kidney failure (serum creatinine over 2.5 mg / dL), and diabetes and thyroid diseases. Assessments before the study (first visit) included examining the heart murmurs, lead ECG 12, Eco Doppler, CBC and serum Na, K, BUN, and CR levels measurement. Information such as age, gender, location of myocardial infarction, drugs used, and medical history were also recorded.

Patients underwent 24-hour holter and HRV indices were recorded. Then, patients were divided into two groups (contained 20 subjects and 40 subjects) based on their willingness to attend the hospital and perform the trainings or willingness to perform these trainings at home. The group contained 40 subjects were randomly divided into two groups of A and B (20 subjects in each group). In the studied group, the movements included 5 to 10 minutes of warm-up and 5 to 10 minutes of cooling and endurance trainings with treadmill, which involved the full control of the heart rate for 15 to 20 minutes, three days per week, for 3 weeks, based on the Carvenon formula. Then, training of walking was performed at home for 5 weeks, and 30 minutes each time 3 times per week. These patients were divided into two groups A, including 40 to 50 percent of the maximum heart rate, and group B, including 60 to 80 percent of the maximum heart rate, based on the maximum heart rate during training. All patients were referred for re-examination 1 week after performing the trainings underwent 24-hour holter and HRV indices were re-recorded. Finally, the data were compared in pair among 3 groups.

Results

A total of 60 patients with acute myocardial infarction examined in 3 groups (each contained 20 subjects). Patients' characteristics and baseline variables are summarized in Table 1.

Table 1: Patients' characteristics and baseline variables in three groups

Variable	A (n=20)	B (n=20)	Control (n=20)
gender			
male	(80%) 16	(80%) 16	(90%)18

female	(20%) 4	(20%)4	(10%)2
Age (year)	(29-73) 54.60±13.39	(46-59) 53.70±4.52	(48-63) 54.3±6
Previous history			
High blood pressure	(30%)6	(10%)2	(0%)0
Hyperlipidemia	(0%)0	(20%)4	(0%)0
Smoking	(40%)8	(30%)6	(50%)10
High blood pressure And smoking	(10%)2	(10%)2	(10%)2
Smoking and drug abuse	(20%)4	(0%)0	(10%)2
High blood pressure, hyperlipidemia and cigarette smoking	(%0)0	(0%)0	(20%)4
The location of myocardial infarction			
Anterior - Septal	(50%)10	(40%)8	(30%)6
Lateral	(10%)2	(0%)0	(0%)0
lower	(20%)4	(30%)6	(20%)4
Wide	(10%)2	(0%)0	(10%)2
Anterior - septal and lower	(0%)0	(0%)0	(20%)4
Posterior and lower	(10%)2	(0%)0	(0%)0
Right and lower ventricles	(0%)0	(10%)2	(20%)4
Lateral and lower	(0%)0	(10%)2	(0%)0
Posterior, lateral and lower	(0%)0	(10%)2	(0%)0
Type of intervention			
Streptokinase	(50%)10	(10%)2	(60%)12
PCI	(50%)10	(90%)18	(40%)8
Type of medication			
ACET inhibitor, beta blocker, statins and aspirin	(40%)8	(20%)4	(20%)4
Inhibitors, ACE, beta blockers, statins, aspirin and Aldactone	(60%)12	(80%)16	(80%)16

The mean baseline and end of study HRV parameters in the three groups are summarized in Table 2.

Table 2: Base and end of study HRV parameters in three groups

variable	Investigation time	A (n=20)	B (n=20)	Control (n=20)
SDNN(ms)	before	(49-125) 94.30±21.40	(38-140) 80.10±28.34	82.10±23.93 (43-112)
	after	(80-194) 122.60±33.50	(48-161) 109.50±33.93	97.50±30.15 (50-144)
LF(ms ²)	before	(59-1059) 388.10±308.24	(68-664) 252.90±188.56	(31-865) 337.10±258.50
		(60-969) 445.20±75.19	(23-1826) 451.70±527.54	(50-648) 289.40±239.28
HF		(10-528) 126.60±151.88	(17-185) 85.90±64.26	(26-512) 144±142.43
		(12-204) 114.90±73.58	(23-1130) 206.50±326.93	85.90±57.43 (24-185)
TP	after	(400-3714) 2036.60±1169.99	(289-2557) 1356.10±813.56	(203-4492) 1791.40±1168.97
		(323-5272) 2229.40±1316.24	(126-10029) 2607.30±2789.50	(200-3171) 1566.40±1169.07
PNN50	before	(0-12) 4.50±4.48	(0-7) 3.40±2.60	(0-6) 2.30±2
		(0-19)	(0-37)	(0-7)

		5.30±6.04 (18-63)	8±11.38 (19-49)	1.90±2.31 (15-67)
SDNN index		42.80±14.40 (20-74)	35.20±11.12 (26 -104)	40.50±13.81 (25-59)
		47±15.18 (44-130)	49.10 ±21.67 (27-137)	40.3±10.63 (30-99)
SDANN	after	83.80 ±22.62 (64-175)	68.70±28.94 (39-138)	68.90±21.45 (35-125)
		108.6±34.70 (2/01-7/80)	91.50±35.91 (0.47-9.72)	
LF/HF	before	4.44±2.05 (2.18 -7.84)	3.99±2.47 (0.50 -7.61)	4.29±2.71 (0.06-7.52) 4.51±3.11 (0.27-8.64)
		4.41±1.73	3.20±2.10	

The mean variations in HRV parameters in the three groups are summarized in Table 3 (Table 3).

Table 3: variations in baseline and end of study HRV parameters in three groups

Variable	A (n=20)	B (n=20)	Control (n=20)	P. value
SDNN(ms)	28.30±28.02	29.40±5.53	15.40±34.13	0.03
LF(ms ²)	57.10±165.45	198.80±5.53	-47.70±235.63	0.03
HF	-11.70±129.56	120.60±5.53	-58.10±111.94	0.02
TP	192.80±1319.78	1251.20±234.16	225±1253.3	0.03
PNN50	0.80±3.61	4.60±10.86	-0.40±2.56	0.05
SDNN index	4.20±14.02	13.90±17.94	-0.20±14.32	0.02
SDANN	24.80±23.33	22.80±33.37	16.20±33.26	0.04
LF/HF	-0.03±1.65	-0.79±2.08	0.21±2.98	0.36

Based on the results of one-way ANOVA test, in all cases, except for LF / HF, significant difference was found among three groups. The results of the pairwise comparison of the groups based on Tukey post hoc test showed that there was a significant difference between two groups A and control (P = 0.03) and between the two groups B and control (P = 0.04) in the case of SDNN. In the case of LF, the only significant difference was seen between the two groups B and control (P = 0.02). There was no significant difference between the two groups A and control (P = 0.46). With regard to HF, only significant difference was observed between the two groups B and the control (P = 0.02). No significant difference was found between the two groups A and Control (P = 0.75).

With regard to TP, the only significant difference was observed between the two groups B and control (P = 0.02). There was no significant difference between the two groups A and control (P = 0.72). With regard to pNN50, the only significant difference was observed between the two groups B and control (p <0.001). There was no significant difference between the two groups A and control (p = 0.84). In SDNN index, the only significant difference was observed in between two groups B and control (p = 0.02). There was no significant difference between the two groups A and control (P = 0.65). There was a significant difference between two groups A and control (p = 0.02) and group B and control (p = 0.02) with regard to SDNN. No significant difference was found between the two groups A and B (p = 0.99, 0.25, 0.10, 0.13, 0.19, 0.13 and 0.98, respectively) in any of the cases.

Discussion and Conclusion

Heart rate variability (HRV) refers to continuous variations in heart rate, which depends on the continuous modulation of sympathetic and parasympathetic branches of the autonomic nervous system. HRV is an effective predictor of myocardial infarction and early warning signs of diabetic neuropathy disease. It is now used as a useful tool in cardiology for risk classification after admission and after discharge. Recent evidence suggests that HRV analysis might predict complications even in patients undergoing cardiac surgery (Nenna et al., 2017; Princip et al., 2016). In the current study, the effect of different forms of training on autonomic nervous system activity in patients with acute myocardial infarction was investigated based on HRV indices. HF peak is the most important index of HRV for vague heart activity (heart rate vague regulation). Although there is no complete agreement on the interpretation of the LF component, this parameter is generally considered as sympathetic and parasympathetic regulation marker. In this research, we showed that both

protocol A (in terms of SDNN and SDANN variables) and protocol B (in terms of all protocols examined except for (LF / HF)) for rehabilitation of patients compared to control group (training at home) had more favorable results. In some studies conducted in this regard, the effect of training-based rehabilitation on disrupted autonomic function in coronary artery disease and myocardial infarction was examined. Kleiger et al showed that the prognosis of these patients in cases with SDNN was less than 50 ms (Kleiger et al., 2005). However, in another study, La Rovere et al reported that cut off point of 70 seconds as predictor of 1 and 2-year mortality after the heart attack (La et al., 1998). As stated, it was proven that physical activity can have a positive impact on patients with myocardial infarction. In a research carried out by Kasargod Prabhakar and Stewart, mortality rate in cardiovascular diseases were lower among people with regular or moderate physical activity than those who had less physical activity or did not have any physical activity. The relationship between mortality and severe training is relatively lower and may even lead to an increased risk of mortality. The meta-analysis of rehabilitation tests in the study conducted by Kasargod Prabhakar and Stewart revealed that people who have physical activity experience less mortality, which its results were closely associated with those of our study (Kasargod Prabhakar & Stewart, 2018).

In line with results of our study, some studies have shown that trainings significantly improve the HRV parameters in patients with myocardial infarction. In one of these studies conducted by Fujimoto et al, the results were similar to those of our study in terms of significant increase in SDNN, SDANN, and HF after physical activity (Fujimoto et al., 1999). In the study conducted by (Iellamo et al., 2000; Stahle et al., 1999; Tsai et al., 2006; Malfatto et al., 1998), the results were almost similar to ours, and moderate increase in Sdnn, Sdann And Hf after physical activity was seen. In some of the parameters, the results of the mentioned studies were different from results of our research (especially in comparison with the protocol group B and control group).

Various reasons can be proposed in justifying the differences in the results of studies in this regard, such as low sample size, different inclusion and exclusion criteria for different groups in terms of cardiac status, different examination times in terms of myocardial infarction and trainings interval, lack of information on the size of the infarct and its location, and lack of information on other potential intervening factors, such as diet and other concurrent physical activities. In addition, the use of different training protocols and different ways of recording HRV parameters might also be effective in this regard. These different results between two groups A and B compared with the control group indicated that the parameters involved in regulating exercise activities are one of the most important factors in obtaining different results in various studies. In this research, based on the capacity of physical activities, patients were divided into two groups. In one group of activities were applied up to 40-50% of the maximum heart rate, and in the other group, they were applied up to 60-80% of their heart rate. Although no significant difference was found between the two groups, improvement in HRV indices was more in the second group. Based on the results obtained; it seems that the establishment of rehabilitation centers at hospitals in patients after acute myocardial infarction is essential since it has positive effect on the autonomic system.

Conclusion

The present research showed that rehabilitation based on planned training at hospital compared to training at home could have a more favorable effect on autonomic nervous system activity after acute myocardial infarction. For this reason, the establishment of rehabilitation centers at hospitals seems to be an essential, since rehabilitation at home in uncontrolled way is less effective due to various reasons, such as inappropriate patient care.

Recommendations

It seems that conducting future studies with higher sample sizes to be helpful in achieving more conclusive results in this regard. In addition to the sample size, this study suffers some other limitations, such as lack of use of using non-training group at home. In the case of using non-training group at home, more complete and comprehensive results might be achieved.

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