

The Effect of Rehabilitation Training and Total Checkup as a Noninvasive Method on Hemodynamic Parameters in Patients who Candidate for Heart Transplantation

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Abstract

Aims: Heart transplantation is a valuable technique but the side effects of this surgery should be considered. The purpose of this study was to investigate the effect of rehabilitation training in patients who candidate for heart transplantation. **Materials and Methods:** This study was done by semi-experimental clinical trial method. Participants were selected from people who refer to the clinic (2010–2018). The information of the patients who candidate for heart transplantation (4 women, 14 men) were obtained (age: 60 ± 13 , body mass index: 26.7 ± 3.7). Hemodynamic parameters were measured before and after the treatments. Training setting was at least 3 months and based on the exercise test of patients. Pharmacological and nutritional control and lifestyle education were also carried out. **Results:** The hemodynamic parameters were improved significantly ($P \leq 0.05$). In some cases improvement in Pro Brain natriuretic peptide and homocysteine were observed. **Conclusion:** Along with other surgical techniques, it was possible to change the lifestyle as much as possible and encourage patients to noninvasive treatment. Patients should follow strict discipline, nutritional and drug policies. Patients should continue this lifestyle and positive thinking regularly. Probably the most important reason for patients undergoing heart transplant is sarcomeropathy. For this reason, regular exercise with effects on genetic signaling pathways can improve this condition if diagnosed early. Despite all the medical controls, it is likely that the most important point that improves patient's reliance is the patient's trust in the treatment method and the existence of a human relationship between the patients and the physician.

Keywords: Cardiac function, exercises rehabilitation, heart transplantation, noninvasive treatment, total checkup

INTRODUCTION

Cardiovascular disease in one of the major threatening risks for health.^[1] Based on publications reports in 2006, more than 81,000,000 individuals have suffered cardiovascular diseases in US that 831,000 persons have died among these events. These surgeries has been reported about 1,763,200 cases, which about 2200 cases from them have been cardiac transplantation surgery. Moreover, the expenses for treatment of cardiovascular diseases have been estimated more than 503 billion dollars in the US in 2010.^[1,2] Therefore, finding a wonderful way for prevent or even low price and noninvasive treatment is required.

Heart transplantation surgery is a very valuable technique but the high side effects of this surgery should be considered.^[3-7]

The diagnosis of cardiac transplantation for the patient will cause psychological and economical stresses. In addition, the patient should use the immunosuppressive drugs permanent after transplantation, which is an important point in cure the procedure. However, the death of patients resulting from cardiac transplantation is possible due to the rejection that is great and early complication.^[3-6] In addition, the problems

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in related to the weak of cardiac muscle have various etiology.^[8] Moreover, in many cases, applied treatment techniques including of cardiac transplantation depends to the quality of information about cardiac diseases and prevention from their happening and progression.^[6]

The most important causes about suffering cardiovascular diseases include sedentary lifestyle, diabetes, twin pregnancy, alcohol consumption, smoking, Multiple sclerosis (MS), low socioeconomic class and education level.^[9,10] It has been shown that regular physical activity and nutrition control with pharmacotherapy have been caused improved ejection fraction, stroke volume (SV), cardiac output (CO) and improvement of cardiac function.^[11-20] The previous studies have endorsed that the regular exercises have been caused the improvement of hemodynamics parameters, aerobic capacity and even stimulation of immunity and genetic signaling pathways.^[18,19,21-23] In addition, the other studies have reported the improvement of Pro brain natriuretic peptide (ProBNP) indices that related to homocysteine levels.^[24] Exercise function (VO_2 peak) should be considered seriously in addition to all instructions and introduced indices in order to diagnosis of each group of cardiac diseases. The result of exercise test and investigation of hemodynamics parameters especially EF and SV to be one of the factors, which determines the policy of treatment.^[3,8,25-27]

The various articles have shown the positive effects of regular physical activity on the patients in groups A, B and even C based on New York Heart Association (NYHA). Nevertheless, for treatment of group D, just serious medical and surgery have been used until now. Based on above discussions about complication of heart transplantation^[1,5,6,8] and experiences in our rehab clinic, the aim of this study was better understanding the effect of non-invasive treatment (total checkup, new drug, supplement trophy, and scientific exercise training) in the patients who candidate for heart transplantation. Probably if this procedure will use in the future it does not need for heart transplantation. It will save the patients from heavy controls of medicine after heart transplantation. The patients will back to their family and society by this method and do his/her own social roles more than the past and with more self-confidence. Therefore, the healthy, economic, social, and psychological great aims have been concealed in this method.

MATERIALS AND METHODS

Participants

Participants were selected from people who refer to the clinic (2010–2018). In the present study, based on the NYHA classification, only some patients who were located in C and D groups and signed the consent form of the intervention were reported. The data about 18 persons of cardiovascular patients who candidate for heart transplantation were obtained (4 women, 14 men) (age: 60 ± 13 , body mass index [BMI]: 26.7 ± 3.7). The reports presented in this study do not result

in participation in the same period. Instead, participants at different periods have referred to the clinic as a case. However, the conditions of treatments are the same for all courses.

All patients were diagnosed as candidate for heart transplant before referring to rehabilitation clinic. Many patients have associated diseases such as diabetes, kidney failure, orthopedic problems, multiple sclerosis, Parkinson diseases, osteopenia, hypertension, sarcopenia etc., In addition, some patients had done some surgery such as angioplasty before beginning exercises training. Hemodynamics parameters of the patients were measured regularly. The patient's database, imaginary and videos interviews exist in rehabilitation clinic.

Total checkup

The first stage of total checkup consisted of primary investigations, biography, life style, measurement of blood pressure, biochemical assays (hematological and lipid profile, ProBNP, homocysteine level, fasting blood sugar etc.), BMI, drug consumption, family history due to autosomal dominant or autosomal recessive inheritance disorder.

The second stage was investigation of thought, culture and lifestyle of patients, which performed by physician and through psychological questionnaire with 20 questions. In this stage what is the best treatment for the patients? Surgery or noninvasive treatment.

The third stage consists of investigating of hemodynamics parameters of patients by impedance cardiography (cardio screen, Medis, Nicomo, Germany).

The fourth stage consisted of pulmonary function study (Mini spir. Roma-Italy).

The fifth stage included of diagnosis of vascular age and stress index (Angioscan, CKaH-01M).

The sixth stage was the most important, which was diagnosis for the VO_2 peak of the patient by modified BUROS test. The test performed under supervision specialist physician and with monitoring of electrocardiogram and vital signs.

Prescription of exercises and interventions

The beginning of exercise training was planned with frequency of 3 sessions in a week (at least 3 months regular and controlled exercises) based on intensity, speed, gradient, and tolerance in exercise test. The main aim was that the patient should reach about 400 k/Cal daily in each session finally. Muscle resistance training were performed with the intensity of 40%–50% 1-RM due to ACSM's.^[28] Just drug and trace parenteral nutrition (hyperalimentation) were used for some of very weak patients at the beginning of the period with life style education (without any exercises). In addition the supplement were used for some of very weak patients including of Cardio Health (forever living product RG CO), erythropoietin, TA65 (telomere elongation)^[21] (TA sciences Co), L-Arginine, amino fugene, lipofundin, RED Q10 etc., The B complex vitamins as well as folic acid were used in the patients who used Metformin in order to controlling

homocysteine. Decreasing medicines for dyslipidemia were controlled in order to avoidance from myalgia especially in the patients who reported muscle soreness.

Statistical analysis

All data were presented based on mean and standard deviation. Kolmogorov–Smirnov test was applied for evaluation of distribution normality. Paired sample *t*-test performed between the pre- and post-test. A meaningful level was considered for all tests as $P \leq 0.05$. All analysis were performed by SPSS 18 software (SPSS Inc., Chicago, Illinois, USA).

RESULTS

The information of the patients who referred to the Rehabilitation Clinic (4 women, 14 men) were obtained (age: 60 ± 13 , BMI: 26.7 ± 3.7). Hemodynamics parameters of patients in the present report improved significantly [Table 1]. Hemodynamics changes of several patients have been

presented in Figures 1-3. In addition, the changes in related to blood parameters have been presented in Figure 3. Some results have been presented, as a case due to participants of this study were candidate for heart transplant.

DISCUSSION

The aim of this study was to investigate the effect of rehabilitation training in patients who's candidate for heart transplant. The healthy, economic, social and psychological porpus have been concealed in the total checkup method. In the present study, patients undergoing cardiac transplantation were improved by at least 3 months of regular and fully controlled exercise and were excluded from surgical procedures. Hemodynamics parameters in the present study improved significantly [Table 1 and Figures 1-3].

Family history due to autosomal dominant or autosomal recessive inheritance disorder have importance role in cardiomyopathy. In addition to the poor life style, the major

HR.....84 1/min	LCWI.....1.6 kg m/m ²	HR.....88 1/min	LCWI.....2.4 kg m/m ²
HPD.....713 ms	VI.....12 1/1000/s	HPD.....680 ms	VI.....43 1/1000/s
BP.....96/57 (68) mmHg	ACI.....41 1/100/s ²	BP.....96/55 (66) mmHg	ACI.....71 1/100/s ²
PP.....39 mmHg	HI.....1.2 Ohm/s ²	PP.....41 mmHg	HI.....6.8 Ohm/s ²
SV.....44 ml	PEP.....207 ms	SV.....67 ml	PEP.....144 ms
SI.....23 ml/m ²	LVET.....225 ms	SI.....33 ml/m ²	LVET.....235 ms
CO.....3.7 l/min	STR.....0.92 (207/225)	CO.....5.9 l/min	STR.....0.61 (144/235)
CI.....1.9 l/min/m ²	ETR.....32 %	CI.....2.9 l/min/m ²	ETR.....35 %
DO ₂ l.....ml/min/m ²	Z ₀26.4 Ohm	DO ₂ l.....ml/min/m ²	Z ₀26.6 Ohm
SVR.....1329 dyn s cm ⁻⁵	TFC.....37.8 1/kOhm	SVR.....816 dyn s cm ⁻⁵	TFC.....37.7 1/kOhm
SVRI.....2556 dyn s cm ⁻⁵ m ²	TFCl.....19.7 1/kOhm/m ²	SVRI.....1635 dyn s cm ⁻⁵ m ²	TFCl.....18.8 1/kOhm/m ²
TAC.....1.1 ml/mmHg	SpO ₂%	TAC.....1.6 ml/mmHg	SpO ₂%
TACl.....0.59 ml/m ² /mmHg		TACl.....0.81 ml/m ² /mmHg	
LCW.....3.1 kg m		LCW.....4.7 kg m	
(a1)		(a2)	

Figure 1: Hemodynamic parameters of the patients (a: from men, age: 50), candidate for heart transplant, before (a1) and after (a2) of noninvasive treatment

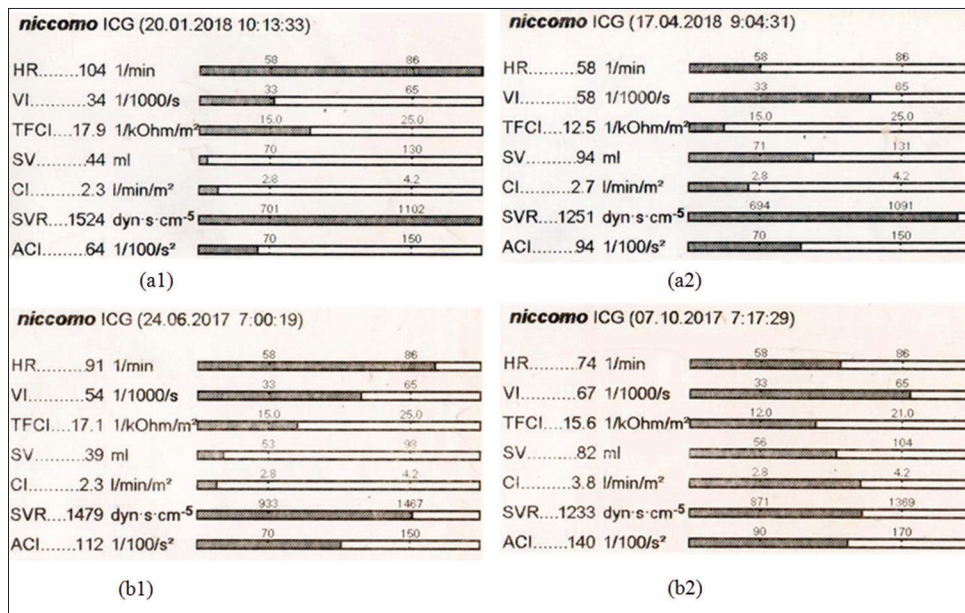


Figure 2: Hemodynamics parameters of two patients, who's were candidate for heart transplant (a: male, age: 43), (b: female, age: 44) were recorded before (a1 and b1) and after (a2 and b2) of noninvasive treatment

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Hormone					Sampling : 1396/06/19
Test	Result	Unit	Method	Reference value	
Pro BNP	↑ 1170	pg/ml		up to 125	
Special Biochemistry					Sampling : 1396/06/19
Test	Result	Unit	Method	Reference value	
Homocystein	↑ 17.0	μmol/L	CLIA	5 - 15	
d1					
Hormone					Sampling : 1396/10/09
Test	Result	Unit	Method	Reference value	
Pro BNP	↑ 435	pg/ml	ECLIA	up to 125	
Special Biochemistry					Sampling : 1396/10/09
Test	Result	Unit	Method	Reference value	
Homocystein	6	μmol/L	CLIA	5 - 15	
d2					
Hormone					Sampling : 1397/03/10
Test	Result	Unit	Method	Reference value	
Pro BNP	↑ 319	pg/ml	ECLIA	up to 125	
Special Biochemistry					Sampling : 1397/03/10
Test	Result	Unit	Method	Reference value	
Homocystein	13	μmol/L	CLIA	5 - 15	

Figure 3: Pro brain natriuretic peptide and homocysteine of patient (d: male, age: 54), during noninvasive treatment (d1, d2, d3)

Table 1: The differences of measured parameters before and after noninvasive treatments based on mean and standard deviation

	Pre	After	t	df	Significance (two-tailed)
HR	77.44±12.21	71.44±13.69	2.076	17	0.053
VI	35.89±13.31	46±12.45	-4.219	17	0.001
TFCI	15.61±3.37	16.34±3.56	-1.133	17	0.273
SV	53.44±15.62	70.94±18.68	-5.971	17	0.000
CI	2.25±0.43	2.73±0.51	-3.913	17	0.001
SVR	1619.11±375.28	1364.5±296.39	3.811	17	0.001
SVRI	2876.33±623.73	2395.44±496.60	4.069	17	0.001
ACI	59.61±26.42	77.67±34.96	-2.844	17	0.011
CO	3.97±0.83	5.06±1.09	-5.375	17	0.000
Systolic time ratio	0.48±0.14	0.41±0.12	2.780	17	0.013
VO ₂ peak	11.19±6.3	29.44±9.52	-7.731	17	0.000

HR: Heart rate, VI: Velocity index, TFCI: Thoracic fluid content index, SV: Stroke volume, CI: Cardiac index, SVR: Systemic vascular resistance, SVRI: SVR index, ACI: Accelerated cardiac index, CO: Cardiac output

etiology of cardiomyopathy is sarcomeropathy (cardiac dropsy). It is mean that the actin and myosin chain is not work correctly, which produce severe pump failure. Exercise training can improved cardiomyopathy by two major pathways: The FNDC5 gene and Tissue plasminogen activator (TPA). The FNDC5 gene is related to irisin.^[29] The TPA release Pro BDNF, which induces neuromuscular pathways, and open the canals for effect of Ca⁺⁺ on heart muscle and better function of the sarcomere.^[30] The effect of exercises training (adaptation) on BMI can decrease many inflammation factors after a while, through decreasing of adipose tissue as well as decreasing of inflammation cytokines secretions. This is separated from improved in anti-oxidant system after exercises adaptations. While regular exercises improved immune system and anti-inflammatory agent of the patient heart transplant needs

to immunosuppressive drugs.^[31] In addition, it is one of the effective factors in cardiovascular disease with diabetics and increasing of leptin secretion and tumor necrosis factor-α from adipose tissue which reduce glucose uptake by muscles. While decreasing of adipose tissue reduce the secretion of inflammation cytokines and increase the secretion of adiponectin after adaptation. One of the main routs of these alterations is conversion of white adipose tissue to brown through stimulation of airisin and proliferator-activated receptor gamma coactivator 1-alpha.^[22,23]

In the present study, the patients who's candidate for heart transplant improved under the effect of at least 3 months noninvasive treatment. Various causes including of changing in lifestyle, improvement of hemodynamics parameters, the

changes of blood indices, improvement of BMI, genetic changes probably, decreasing of inflammation factors and apoptosis and more important than others, humanistic relation between physician and patients may cause such changes. In addition, serious decision of patient will be accounted as an important factor for changing in lifestyle. Because health has physiological, psychological and sociological dimensions from the point of WHO view. As the present evaluation has been done based on hemodynamics parameters, physiological discussions and its possible factors of this improvement will be indicated shortly.

The development of aerobic power of patients had been reported in various studies especially in response to combinational aerobic and resistance exercises,^[11-14,16] that the mentioned matter was one of the factors for decreasing of fatigue, decreasing of skeleton weakness as well as increasing of power and motivation in the patients in their own exercises controlling. moreover the improvement of parameters in the diastolic function of left ventricle,^[15] avoidance from ventricle function drowning in the patients who suffered infarction,^[18] improvement of pulmonary capacities, improvement of left ventricle systolic volume, stopping of disease advancement,^[17] decreasing of RHR in the patients in response to regular exercises have been observed. The decreasing of observed RHR in the present study can be resulting from medicine controlling. Beside of the other hemodynamics and neuronal factors can state the role of exercises in the present study.^[20,32]

In addition, the alterations of lipid profile is one of the most important factors, which can control atherosclerosis. Physical activity can cause to increase HDL-C and paroxonase-1 activity (PON-1). PON-1 had been an enzyme linked to HDL-C and inhibit LDL-C oxidation. Decreasing of PON-1 activity has relation with diabetics, cardiovascular diseases. In contrast, increasing PON-1 activity plays a major role in the improvement of function and metabolism of homocysteine, lipoproteins, hemoglobin etc., The interaction of PON-1 and homocysteine plays a major role in controlling of much diseases including of atherosclerosis, diabetes, kidney failure and Alzheimer.^[33]

Cardiac structural alterations are discussable in response to the kinds of resistance and endurance exercises. Endurance exercises increasing of pre-load and following to that is physiological eccentric hypertrophy. In response to exercises training, these alterations will be performed through GH/IGF-I axis. While in the pathologic conditions (such as hypertension or Systemic Vascular Resistance), renin-angiotensin mechanism will be caused pathological concentric hypertrophy.^[2]

In response to exercises training (adaptation), hypoxia will be made depends on the intensity of exercise, which causes angiogenesis signaling pathways and increasing of vascular compliance. It has been shown that the exercise training had been caused temporary ischemia without the signs of angina and declining of ST segment.^[34] In the normal conditions, ANP will be secreted from vestibular cells in response to traction

of vestibule's wall. However, BNP will be secreted from ventricle's wall in the pathologic conditions.^[35] One of the most important causes for increasing of ANP and BNP hormones in response to physical activity, is increasing of diameter of heart's wall,^[36-38] which has an important role in increasing of gene state of this hormone as the placement of ANP and BNP synthesis possibly. The most possibility of the mechanism is more increasing of ANP and BNP in response to endurance exercises with increasing cardiac pre-load and increasing of end diastolic volume and its following, the traction of cardiac wall.^[36-38]

CONCLUSION

The results of this study show that we can be hopeful to changing lifestyle and promotion of patients for controlled exercises training and non-invasive therapy besides of the other valuable techniques of surgery. The patients should follow exercises nutrition and medicine rules during this period. In addition, the accurate and fast diagnosis is very important. The patients should continue this lifestyle and positive thought forever. However, there are all-modern and scientific medical controls, the most important point that indicates to the improvement of patient is possible the confidence of patient to the physician and the existence of humanistic relation between patient and physician. In spite of all medical controls in the present study, patients were not fully treated in clinic or Hospitalization condition. It is suggested that patients be fully controlled and fully trained in the clinic (CBR or RBR Admit) to use this plan.

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Conflicts of interest

There are no conflicts of interest.

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