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The effect of concurrent endurance and resistance training on echocardiographic and electrocardiographic variables in patients with beta-thalassemia major

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ABSTRACT

Introduction: Patients with beta-thalassemia major require lifelong blood transfusions, leading to iron overload and toxicity, which can result in cardiomyopathy, arrhythmias, and heart failure—major causes of mortality in this population. This study aimed to evaluate the effect of a concurrent endurance-strength training program on cardiovascular parameters in individuals with beta-thalassemia major.

Material & Methods: This semi-experimental study involved 40 patients (male and female) aged 16-40 years diagnosed with beta-thalassemia major. Participants were randomly assigned to a control group (CG) or an experimental group (EG). The EG underwent an 8-week concurrent endurance and strength training program that included low-intensity treadmill running for 10-20 minutes and resistance exercises such as squats, barbell chest presses, barbell overhead presses, dumbbell lateral raises, leg presses, and modified sit-ups at 40-50% of one-repetition maximum (1RM). Echocardiographic data, blood pressure, and heart rate were collected, and statistical analysis, SPSS software version 22 was utilized, employing covariance tests and both dependent and independent t-tests at a significance level of ($p < 0.05$).

Results: The EG exhibited statistically significant reductions in resting heart rate and systolic blood pressure compared to the CG ($p<0.05$). Significant end-systolic and end-diastolic volumes were also noted in the EG ($p<0.05$).

Conclusion: Improvements in heart rate, blood pressure, and heart volume suggest that concurrent endurance and strength training may positively affect cardiovascular function in patients with beta-thalassemia major.

Keywords: Endurance and strength training, Eechocardiography of the heart, Beta thalassemia major.

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1. Introduction

Thalassemia syndrome is a genetic disorder that affects the production of globin chains. In patients with β-thalassemia, there can be a complete absence of the β-globin chain (major thalassemia) or a reduced production (minor thalassemia). The signs of this disease typically manifest from the early years of life. Patients require regular blood transfusions to sustain their lives. Blood transfusions help prevent complications such as anemia due to ineffective erythropoiesis, but they also lead to the accumulation of toxic iron in the endocrine glands, liver, and heart. Iron chelation therapy can reduce iron overload-related complications in these patients and contribute to the continuation of life However, the most significant causes of mortality in these patients include cardiomyopathy and arrhythmic events, including QTc interval prolongation, which is recognized as a marker of ventricular repolarization in high-risk individuals (1). The prevalence of complications associated with thalassemia varies across different regions of the world, influenced by factors such as access to blood transfusion services, regular chelation therapy, genetic differences, and the effectiveness of iron chelation treatments. According to estimates, the prevalence of cardiac complications in Iran reaches 76.4%, while this figure is reported to be 5% and 10% in North America and China, respectively (2). Exercise can be beneficial for patients with major thalassemia, particularly in improving quality of life and certain blood parameters, such as iron levels. However, current research primarily focuses on low-impact exercises and monitoring iron levels and quality of life, while less attention has been given to other key clinical parameters, such as endocrine status, cardiac function, and immune system performance. The existing evidence regarding personalized exercise programs designed based on comprehensive clinical monitoring for patients with β-thalassemia major is limited, making this an essential area for future research (3). In a study conducted by Farahani et al. (2012), the QTc interval and several other cardiac variables showed significant changes after performing an exercise test compared to the control group. In this research, the levels of ferritin and blood pressure in patients also exhibited meaningful changes. These variables are closely associated with the occurrence of left ventricular myocardial infarction, which is common in patients with major thalassemia (4). Ventricular repolarization was evident as an increase in QT dispersion and T peak-to-end/QT ratios. Additionally, patients with major thalassemia experienced a decrease in heart rate variability indices. Improvement in heart rate after exercise was significantly observed compared to the control group; however, some studies indicate that patients with major thalassemia may still experience subclinical cardiac dysfunction despite regular physical activity. This highlights the need for continuous monitoring and appropriate rehabilitation programs (5-6). Arab Golnazi et al. (2016) reported that an eight-week exercise program consisting of a combination of resistance and endurance training in patients with beta-thalassemia major led to a reduction in ferritin levels, improved cardiac function, and decreased cardiac workload (7). A limited number of studies have examined the interaction between physical activity and cardiovascular function in patients with major thalassemia. In the past two decades, research has shown that combined exercises (resistance and endurance) can have positive effects on physical responses and adaptations. However, the impact of this type of exercise on patients with major thalassemia has only recently gained more attention (8). In the present study, an attempt has been made to investigate the effects of endurance-strength exercises on changes in cardiac data of these individuals, such as end-systolic and end-diastolic volumes, ejection fraction, and cardiac waves. It seems that the combination of echocardiographic findings and electrocardiograms provides a comprehensive view of heart health in patients with major thalassemia. Monitoring these variables is crucial for the early detection and management of potential cardiac complications, which are the leading cause of mortality in this population.

2. Methodology

2.1. Materials and methods

The present study was designed as a semi-experimental, applied, quantitative, and field research.

2.2. Participants

In this study, 40 patients (both male and female) diagnosed with major thalassemia who visited the thalassemia department in Langroud County and were not suffering from acute or severe illness at the time of the research were randomly divided into two groups: an experimental group (20 participants) and a control group (20 participants). The experimental group participated in endurance and resistance training sessions for 8 weeks, three times a week, with each session lasting one hour. One week prior to the commencement of the training program, three introductory sessions were held to familiarize participants with the research considerations, including weight training techniques and proper hydration during exercise. Pre-tests were conducted to measure anthropometric variables (including age, height, weight, and body mass index) while participants were fasting and after using the restroom. To assess maximum muscular strength, participants warmed up by selecting very light weights and then chose weights they estimated they could lift for 12 to 15 repetitions with proper form. The amount of weight and the number of repetitions they could perform until fatigue were measured and recorded. These values were then used in the Brzycki formula to calculate one-repetition maximum (1RM) for various exercises, such as bench press and bicep curls (9).

$$1RM = weight / (1.0278 - 0.0278 \times reps)$$

2.3. Measurements

After eight weeks, echocardiography was performed using the My Lab ultrasound device, brand Esaote, manufactured in Italy, with product ID MCT_1. This non-invasive ultrasound scanning system was utilized for imaging the heart and examining the vascular system, with the procedure lasting between 45 minutes to one hour. Patients were required to remove their upper clothing, and a gel was applied to the chest to facilitate the transmission of sound waves. Patients were instructed to lie in various positions and, at times, hold their breath. High-frequency ultrasound waves were transmitted through the probe, and the received data were displayed on a monitor. ECG was recorded using a 12-lead single-channel ECG device from KENZ, Japan, model ECG110, under standard conditions (removal of metals, use of gel, speed of 25 mm/s). Cardiac parameters were analyzed in lead II. To measure the resting heart rate of participants in both groups, readings were taken 24 hours after the last session while seated, using a digital Omron model 1120 blood pressure monitor, manufactured in Japan. Additionally, heart rate during treadmill exercise and 5-15 seconds post-exercise was measured using a Bluetooth chest strap, Polar H10, manufactured in Germany, along with the Elite HRV software.

2.4. Intervention

Training Protocol: As shown in Table 1, 50% of the predetermined weight for exercise was established for two weeks. After this period, a new weight was calculated biweekly using the initial method. If a participant was unable to lift the new weight, the previous weight was retained. During the first four weeks, the exercise program consisted of three days of activity, including warm-up, walking on a treadmill, followed by one set of weight training, and concluding with a cool-down. In the second four weeks, the exercise program included two days of activity, comprising warm-up, and treadmill walking, followed by two sets of weight training, and a cool-down. The endurance training protocol is detailed in Table 2. The exercises included gentle movements, stretching, warm-up, and light jogging on the treadmill. Throughout the treadmill exercise, whenever a participant felt fatigued, they would rest and then continue exercising. Both groups utilized iron-reducing medications over the eight weeks, while the experimental group engaged in endurance-resistance training (10). After eight weeks, echocardiography was performed as a non-invasive ultrasound scanning system for imaging the heart and examining the vascular system. Following the eight weeks of training and the completion of all sessions by the participants, all patients underwent a post-test, which included all pre-test assessments under similar conditions.

Table 1. *Strength Training Program*

	Type of Exercise	**Muscle Group**	**Intensity**	**Training Phase**		**Repetition Intensity**	**Number of Training Sessions per Week (days)**	
1	Squat	Quadriceps femoris, Hamstrings, Gluteus maximus	50% 1RM	Weeks 1-4	Weeks2-8	15-Dec	3	2
2	chest press	Pectorals (chest), deltoids (shoulders), and triceps (arms).	50% 1RM	Weeks 1-4	Weeks2-8	15-Dec	3	2
3	Forearm Barbell	Biceps brachii muscle	50% 1RM	Weeks 1-4	Weeks2-8	15-Dec	3	2
4	Lateral Raise	deltoid	50% 1RM	Weeks 1-4	Weeks2-8	15-Dec	3	2
5	Barbell Calf Raise	Gastrocnemius, soleus	50% 1RM	Weeks 1-4	Weeks2-8	15-Dec	3	2
6	Modified Sit-Up	Rectus abdominis	50% 1RM	Weeks 1-4	Weeks2-8	15-Dec	3	2

Table 2. *Endurance Training Program*

Week	Warm-up time(min)	Walking time(min)	velocity (m/s)
1	5	10	4-Mar
2	5	12	3.4-5.5
3	8	15	3.4-5.5
4	8	15	5-Apr
5	10	15	5-Apr
6	10	20	5-Apr
7	12	20	6-May
8	12	20	6-May

***They could rest each 10 minutes intervals of 20 minutes.**

2.5. Statistical Methods

Statistical analysis, SPSS software version 22 was utilized, employing covariance tests and both dependent and independent t-tests at a significance level of ($p < 0.05$).

3. Results

Table 3 shown presents the descriptive characteristics, blood pressure, electrocardiography, and echocardiography data of the study participants.

Table3. *Descriptive characteristics, blood pressure, electrocardiography, and echocardiography data of the study participants*

Variables	Sport	Control
Gender		
Male	48.5	**52.6**
Female	51.5	**47.4**
Age (Year)	25.7±31	**25.4±5.9**
Single	71	**76**
Married	29	**24**
Wight Kg	52.91±6.30	**51.83±5.2**
Pre Test	53.27±4.2	**51.93±6.4**
Post Test		
BMI Kg/M^2	19.89±2.1	
Pre Test	20.28±3.1	**19.67±7.3**
Post Test		**19.72±1.1**
FFMI Kg		
Pre Test	34.5	**33.5**
Post Test	35.2	**33.6**
BFP%		
Pre Test	19.4±7.4	**18.4±4.3**
Post Test	19.2±6.2	**18.7±8.1**
Average age of thalassemia	16.28±11.07	**14.42±13.34**
Diagnosis month		
Desferal history	22.22±2.4	**21.36±1.6**
SBP MmHg		
Pre Test	115.5±2	**18.9±9.7**
Post Test	93.9±12.3	**119.8±2.3**
MmHg DBP	72.29±6.6	**75.43±14.1**
Pre Test	69.3±7.4	**77.03±8.7**
HR R/Min	79.65±15.1	**78.58±3.9**
Pre Test	74.71±9.6	**79.22±14.2**
S QTc Pre Test	401.6±30.2	**403.7±16.4**
Post Test	422.7±31	**402.91±11.4**
ESV ml	60.2±36.2	**60.5±23**
Pre Test	62.6±18.4	**60.01±12.1**
EDV ml	126.4±14.5	**127.8±23.4**
Pre Test	132.7±26.3	**126.37±21.5**
EF%	55.5±11.7	**55.7±31.2**
Pre Test	60.32±12.3	**55.1±16.7**

The student t-test for comparing the variables of the groups at pre- and post-test stages is shown in the table .Considering that the values of the electrocardiography and echocardiography variables in the experimental group demonstrated a statistically significant difference ($p < 0.05$), it can be concluded that the intervention was effective.

Table 4. *The results of student t-test in interventions*

Factors	sport		control	
	$M_1 - M_2$	P	$M_1 - M_2$	P
HR	-0.380	0.014	-0.203	0.641
QTC	-0.329	0.015	-0.247	0.620
ESV	-0.318	0.014	-0.127	0.425
EDV	-0.448	0.016	-0.126	0.581

Investigating the relationship of variables shown in table5. The value of $p < 0.05$ indicates that the endurance-strength training program has a significant effect on the electrocardiographic and echocardiographic variables in patients with beta-thalassemia major.

Table 5. *Investigating the relationship of variables*

Factors	R^2	P
HR	0.668	0.002
QTC	0.538	0.002
ESV	0.231	0.001
EDV	0.138	0.003

4. Discussion

In this study, the factors related to heart rate, blood pressure, and echocardiographic and electrocardiographic data were examined. By analyzing the cardiac waves and the results recorded in the control group, a favorable trend in post-test results compared to pre-test results was observed and documented.

According to the findings of this research, heart rate and echocardiographic data showed significant improvement after eight weeks of combined training, while the QTc wave increased. The effects of combined training on heart rate and blood pressure can lead to a strong coordination of neuro-hormonal activity, including a decrease in heart rate post-exercise, improved cardiovascular performance, increased parasympathetic activity, reduced cardiovascular risk factors, and physiological adaptations. Ultimately, these changes result in better cardiovascular health. These adaptations in response to regular exercise enable the heart to pump blood more efficiently (11). In general, exercise may have a positive impact on electrocardiographic parameters, including heart rate, although specific data in patients with major thalassemia is limited. The study by Barbero et al. (2012) also reported that combined exercise could provide numerous benefits for patients with major thalassemia; however, its effects on heart rate can be complex and depend on the individual's clinical condition. Close monitoring, regular assessments, and adherence to medical recommendations are essential to ensure the safety and effectiveness of the exercise program. In examining the effects of eight weeks of combined training on electrocardiographic variables, a significant increase in the QTc interval was observed. The reason for the elevated QT interval may indicate abnormal myocardial repolarization, which can be detected even before the onset of overt cardiomyopathy (4).

The QT interval measured on the electrocardiogram (ECG) indicates the time required for the heart's electrical system to reset after each heartbeat. A prolonged QT interval can increase the risk of serious heart rhythm problems known as arrhythmias. A study showed that patients with higher myocardial iron burden had longer QT intervals. This means that as the amount of iron in the heart increases, the time required for the heart to reset after each heartbeat also increases. This relationship is significant because it indicates that iron overload can directly affect the electrical activity and performance of the heart (12). Exercise, especially concurrent resistance-endurance training, can lead to an increase in the percentage of iron autolysis from tissues Changes in the cell membrane, in turn, release tissue iron and increase serum ferritin and iron levels. However, Desferal helps to eliminate iron as long as iron is present in the blood (13). And significantly reduces serum ferritin levels in patients with major thalassemia (7)

However, the increase in QTc interval in the Kolios study (2021) was also reported in the assessment of electrocardiographic (ECG) status and arrhythmia burden in patients with major thalassemia with a mean age of 36 years in 12-lead ECG and 24-hour Holter monitoring. The results overall indicate that patients with beta major thalassemia, even in the absence of systolic dysfunction, experience changes in their heart and autonomic nervous system that may predispose them to dangerous arrhythmias. Although dangerous markers such as atrial fibrillation and recurrent episodes of it were observed, these abnormalities do not show significant changes in short-term assessments. This is because beta major thalassemia is a chronic genetic disease and is usually managed with supportive treatments (such as blood transfusions and therapies to remove excess iron). However, the disease itself and its effects on the heart progress gradually over the years. The cardiac complications of this disease, such as myocardial damage, fibrosis, and rhythm disorders, are gradual processes that require a long time to develop and exacerbate and may change slowly over time. Significant changes in certain indicators (such as the onset of heart failure or the development of serious arrhythmias) may require more time to observe. These studies can provide important information about the course of the disease, the progression of complications, and the effectiveness of treatments (6).

Also, in the study of the effects of eight weeks of concurrent training, significant increases were observed in echocardiographic variables. In the study by Razaghi et al. (2020), the effect of combined aerobic and resistance training also reported significant improvements in left ventricle measurements, including left ventricular end-diastolic dimension, final systolic volume, and ejection fraction. These improvements are associated with increased strength and muscle mass, reduced oxidative stress, and decreased inflammation, which contribute to heart health. The changes indicate a healthier and more efficient heart structure. It has also been reported that combined training, compared to aerobic training alone, leads to greater improvements in systolic function (14). While the results from exercise are promising, some research highlights the need for specific interventions. This is because not all patients may respond similarly, and it depends on varying degrees of disease severity and individual health status (15). In the study by Amiri Pour et al. (2023), which addressed the cardiac performance of patients after surgery, initial cardiac function level, exercise continuity, and the components of the resistance training program were important factors that affected the outcomes. Overall, patients who initially have lower cardiac function may benefit more from these exercise programs, which is a reason for the significant improvement in echocardiographic variables in this research. The authors suggest that these programs should be continuous and preferably last more than six months to maximize their benefits. This point highlights the importance of continuity and proper planning in improving the cardiac health of patients (14).

5. Conclusion

Adherence to necessary precautions and regular follow-up via echocardiography or electrocardiography, patients may benefit from incorporating low-impact exercise modalities into their routine to improve their cardio-physical performance. Future studies should explore the effects of various exercise interventions across different age groups and activity levels to determine the optimal exercise prescription for individuals with thalassemia major.

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