

Ege Journal of Medicine / Ege Tip Dergisi 2024; 63 (2): 261-270

# Effects of cardiac rehabilitation on functional capacity, psychological symptoms and quality of life in patients with left ventricular assist device

Sol ventrikül destek cihazı takılmış kalp yetmezlikli hastalarda kardiyak rehabilitasyonun fonksiyonel kapasite, psikolojik semptomlar ve yaşam kalitesi üzerine etkisi

Ece Cinar<sup>1</sup>

Tahir Yaŭdı<sup>2</sup>

Mustafa Özbaran<sup>2</sup>

Hale Üzümcügil<sup>1</sup>

Kazım Capacı<sup>1</sup> Mehdi Zoahi<sup>3</sup>

Cağatay Engin<sup>2</sup> Sanem Nalbantgil<sup>4</sup>

<sup>1</sup> Ege University School of Medicine, Department of Phsyical Medicine and Rehabilitation, Izmir, Türkiye

<sup>2</sup> Ege University School of Medicine, Department of Cardiovascular Surgery, Izmir, Türkiye

<sup>3</sup> Ege University School of Medicine, Department of Cardiology, Izmir, Türkiye

# ABSTRACT

Aim: In this prospective randomized trial, we aimed to study the effects of cardiac rehabilitation on functional capacity, depression, and quality of life, in patients undergoing left ventricular assist device (LVAD) implantation for the treatment of heart failure. We also aimed to compare the effectiveness of home and hospital-based exercise programs.

Materials and Methods: 42 patients who had received LVAD implants in our university hospital were included in the study. After the subjects were randomized into a hospital exercise group (n=20) and a home exercise group (n=22). They were enrolled in a cardiac rehabilitation program for 8 weeks, which lasted for one hour, three times per week in the hospital and at home respectively. All subjects were assessed at baseline and at the end of 8th week. They were assessed using a cardiopulmonary exercise test (CPET) for peak oxygen consumption (VO2), pulmonary function tests, 6-minute walk test (6MWT) in addition to Short form 36 (SF-36), Minnesota Living with Heart Failure Questionnaire (MLHFQ), State Trait Anxiety Inventory (STAI) and Beck Depression Index for depression (BDI) before and after intervention

Results: In our study, we detected a significant improvement in peak VO2 6MWT values, MLHFQ, STAI state anxiety sub-score in the hospital exercise group (p<0.05). The home exercise group did not improve significantly in any of the parameters except in the pain sub-score of SF-36 (p<0.05).

Comparison of the changes seen in the parameters over time, the hospital group showed significantly more improvement than the home exercise group in peak VO2. 6MWT, MLHFQ and trait anxiety subscore of STAI (p<0.05).

Age correlated with better gains in FEV1 (r=-0.35, p<0.05) and 6MWT (r=-0.39, p<0.01). Gains in 6MWT correlated with the gains in peak VO2 (r=0.54\*\*, p<0.01). Duration of HF correlated with a poorer response in the FEV1 (r=0.19, p<0.05) and 6MWT (r=-0.25, p<0.01) gains.

**Conclusion:** In this study, we detected a positive effect of supervised hospital exercise program on functional capacity, quality of life and anxiety in patients with implanted LVADs.

Keywords: Heart transplantation, heart failure, cardiac rehabilitation.

Corresponding author: Ece Cinar Ege University School of Medicine, Department of Phsyical Medicine and Rehabilitation, Izmir, Türkiye E-mail: ececinar1@gmail.com Application date: 03.08.2023 Accepted: 18.12.2023

**Amaç**: Bu randomize, prospektif, tek-kör çalışmanın amacı, sol ventrikül destek cihazı (SVDC) takılmış olan kalp yetmezliği hastalarında, kardiyak rehabilitasyonun yaşam kalitesi, depresyon ve fonksiyonel kapasite üzerine olan etkisinin araştırılmasıdır. Aynı zamanda, ev egzersiz programının etkinliğinin hastanede gözetimli egzersiz ile kıyaslanması amaçlanmıştır.

**Gereç ve Yöntem:** Üniversitemizde SVDC implantasyonu yapılmış olan 42 hasta çalışmaya dahil edildi. Hastalar ev egzersiz grubu (n=22) ve hastane grubu (n=20) olmak üzere iki gruba ayrıldıktan sonra, 8 hafta süren, haftada üç gün, günde bir saat olmak üzere kardiyak rehabilitasyon programına alındı. Hastalar başlangıçta ve 8. hafta sonunda değerlendirildi. Hastaların değerlendirilmesinde kardiyopulmoner egzersiz testi (KPET), pik oksijen tüketimi (VO2) değeri, solunum fonksiyon testleri, 6 dakika yürüme testi (6DYT), kısa form 36 (KF-36), Minnesota Kalp yetersziliği ile yaşam anketi (MKYYA), State Trait anskiyete ölçeği (STAÖ), ve Beck depresyon envanteri (BDE) kullanılmıştır.

**Bulgular**: Çalışmamızda hastane grubunda zaman ile pik VO2, 6DYT, MKYYA, STAÖ trait alt skorunda anlamlı iyileşme saptanmıştır (p<0,05). Ev egzersiz grubunda ise sadece AF-36 anketinin ağrı alt skorunda anlamlı iyileşme elde edilmiştir (p<0,05).

İncelenen parametrelerin zaman içindeki değişimleri incelendiğinde, pik VO2, 6DYT, MKYYA, STAÖ'nün state anksiyete alt skorundaki iyileşmeler, hastane grubunda ev egzersiz grubuna göre anlamlı yüksek saptanmıştır (p<0,05).

Yaş ile 6DYT değişimi arasında (r: -0,39, p<0,01) ayrıca yaş ile FEV1'deki değişim arasında (r: -0,35, p<0,05) anlamlı korelasyon elde edilmiştir. Kalp yetmezliği süresi ile de 6DYT değişimi (r: -0,25, p<0,01) ve FEV1 değerindeki değişim (r: -0,19, p<0,05) arasında anlamlı korelasyon saptanmıştır.

**Sonuç**: Çalışmamızda hastane ortamında gözetimli kardiyak rehabilitasyon programının SVDC takılmış hastalarda pik VO2, altı dakika yürüme mesafesi, Minnesota kalp yetmezliği ile yaşam anketi, State-Trait anksiyete ölçeğinde olumlu değişime yol açtığı görülmüştür.

Anahtar Sözcükler: Kalp nakli, kalp yetersizliği, kardiyak rehabilitasyon.

#### INTRODUCTION

Heart failure is a major health condition that results in high mortality and morbidity (1, 2). While there are many advances in the management of conditions that might contribute to heart failure such as hypertension or coronary heart disease. there seems to be little improvement in the incidence of heart failure (2). While patients with heart failure have symptoms attributable to congestion in both systemic and pulmonary circulation, they also have problems such as decreased exercise capacity, lower quality of life, and higher incidence of depression and anxiety (3). Heart transplantation is still the gold standard in the management of heart failure (2, 4). Since the number of donors is insufficient and pharmacological interventions that are used after transplantation have many side effects and are even contraindicated in some patients, only a portion of heart failure patients achieve a successful transplantation. Heart failure patients without a chance of successful transplantation or who are on waiting lists benefit from another form of therapy, namely left ventricular assist device (LVAD) implantation (5).

Cardiac rehabilitation (CR) is a supervised rehabilitation program that aims to improve

cardiac functions as well as symptoms related to heart failure (6). It is proven that CR has beneficial effects on ameliorating the symptoms of heart failure, promoting quality of life and alleviating depression in patients with cardiovascular disease (6). Despite the empirical evidence, few studies evaluate the effects of personalized exercise programs in patients with LVADs. While some of the past studies enroll LVAD patients in an early stage after surgery, usually in inpatient clinics, fewer studies enroll patients in outpatient rehabilitation programs (7-9).

This study aimed to investigate the effects of a supervised, hospital-based outpatient cardiac rehabilitation program for patients with LVADs, on quality of life, functional state and depression, compared with an analogous home exercise program, especially in the chronic stage. For ethical reasons, we could not enroll a control group with no exercise therapy.

## **MATERIALS and METHODS**

This study was approved by ethics committee of Ege University School of Medicine on 26.09.2014

## ÖΖ

with the approval number 14-4.1/10. Sample size was calculated using a priori power analysis with the Gpower software for Windows. With an effect size of 0.9 and alpha value of 0.05, the minimum required number of patients for each group was calculated to be 19. Patients were informed about the study and consent forms were obtained.

#### Inclusion criteria

Being implanted with an LVAD was the main inclusion criterion. To differentiate from the acute increase of exercise capacity as a result of the LVAD implantation, 6 months after surgery was chosen as the cutoff time point to include patients in the study. Those patients who were able to walk independently and were able to complete the submaximal exercise test, namely the 6minute walk test (6MWT) were invited to join the study.

#### Exclusion criteria

Patients without independent functional ambulation, who had decompensated heart failure, who enrolled in an aerobic exercise program within the last 3 months, who had comorbidities or mental disorders that would prevent exercise, or who were otherwise unable to comply with the exercise program were excluded from the study.

#### Evaluation of subjects:

After obtaining consent, patients were randomized into 2 groups according to a scheme formed by a web-based random number generator (www.randomizer.org). The first group was deemed the hospital exercise group (case group), and the other was the home exercise group (control group).

All subjects underwent a thorough medical inspection, sociodemographic and clinical marital information including age, status. educational status, causes and duration of heart failure, date of LVAD implantation, presence/type pacemaker, anthropomorphic of features. comorbidities, and pharmacological interventions were recorded. At the start of the study and at the end of the 8th week, patients were evaluated with a cardiopulmonary exercise test (CPET) and their peak vO2 and pulmonary function tests were obtained. On each control visit, subjects were also given questionnaires and scales, including SF-36 to assess the quality of life, Beck depression Depression Index for (BDI), Minnesota Living with Heart Failure Questionnaire (MLHFQ) and State-Trait Anxiety Inventory (STAI). All of the measurement indices had been previously tested for validity and reliability of their Turkish versions and was appropriate to be used in cardiac patients (10– 18).

On evaluation days, patients were asked to dress suitable for exercise and continue their routine pharmacological treatment. Patients were also asked not to consume caffeinated drinks and alcohol in the 3 hours before and after each CPET session, and they were asked to have breakfast at least an hour before the test. For the patients with a pacemaker, their devices were arranged to be checked for battery and other issues in the 15 days leading to the test.

Before each evaluation session, O2 saturations and ECGs of all patients were recorded. 6-minute walk test (6MWT) was carried out under the supervision of a researcher. Patients with a significant decrease of O2 (<90%) after the 6MWT were not allowed to go forward with the exercise test. A spirometry based pulmonary function test was carried out and recorded.

During CPET, patients were assessed for exertion by Modified Borg scale and also a visual facial exertion scale. Tests were terminated if a patient demanded or contraindications to continuation were observed (19).

#### Exercise test protocol:

Exercise tests were done using the Master Screen ® CPX (Viasys Heathcare, Jaeger, Würzburg, Germany) device. Protocol started with a warm-up period of 2 minutes, after which the treadmill gradually increased in speed in 2minute intervals. Protocol started at 3 km/h and speed did not increase above 10 km/h. The inclination of the treadmill started at zero degrees and increased up to 7 degrees. At the end of the cardiopulmonary exercise test, patients' peak VO2 values were recorded. This value was later used to calculate the rate of rehabilitation exercises.

#### Rehabilitation program

All patients were enrolled in the rehabilitation program 3 days a week for 8 weeks. Their previous medical treatment modalities remained the same throughout the program.

#### Hospital exercise program (Hospital group):

The cardiac rehabilitation program in hospital setting was supervised by an experienced physiotherapist, to patient groups of 3 to 6 subjects. Patients were dressed suitable for exercise and had eaten at least one hour before sessions.

At the start of each session patients' weights, resting pulses, blood oxygen saturation levels, and LVAD outputs were recorded.

**Breathing and warming exercises**: Each session started with breathing exercises, done in a sitting position for 5 minutes. Chest and diaphragm respiration techniques were applied. Afterwards, stretching exercises and isotonic contraction exercises for the upper and lower extremities with 500 grams of weights were carried out. Patients who could not tolerate weights, exercised without any weights.

Walking exercises: After breathing and warming exercises, patients were taken to treadmill for the aerobic exercise phase. For the first 5 minutes, patients warmed up with intensities of up to 40% of peak VO2 values. Afterward, 50-70% of peak VO2 values were targeted for 30 minutes. Exercise intensity was increased by 10% every week, starting with 50% of peak VO2. Fatigue and exertion levels were evaluated with Visual Facial Exertion Scale and Modified Borg Scale. Patients' pulses were monitored throughout the session. The session was stopped if subject reported a Modified Borg Scale value of >7, breathing rate >40/minute, LVAD output lower than 3 L, or if they complained of chest pain, dyspnea, or dizziness.

After 30 minutes, 5 minutes of cooling phase was overseen (<40% VO2 max) after which, sessions were terminated.

#### Home Exercise group (Control group)

All of the evaluation visits were similar in both groups, carried out at baseline and at week 8. At the start of the intervention period, all patients in the home group were enrolled in a one-time training session for the same rehabilitation program and were also given instruction brochures to guide them through the home exercise sessions. Both verbal and written directions were also given to instruct subjects in how to achieve roughly 50% to 70% of peak VO2 value using the Modified Borg scale and how to assess their LVAD outputs. They were asked to carry out the exercises 3 days a week and were given a form to mark the days of the week in which exercises were completed.

#### Statistical analysis

Data obtained were analyzed using IBM SPSS Statistics, Windows version 20.0 (IBM Corporation, New York, US). Data showing a normal distribution were tested by Shapiro-Wilk test and data not having a normal distribution were analyzed using nonparametric tests. Chisquare test was used for the comparison of nominal data. Comparison of parameters between two groups was done by Mann-Whitney U test, and comparison of parameters within the same group was done by Wilcoxon Signed Ranks test. Correlation between parameters was assessed using Spearman Correlation Analysis. Statistical significance was accepted as p<0.05.

#### RESULTS

42 adult patients with end-stage cardiac failure who were implanted with an LVAD were recruited between October 2014-May 2015, from the cardiology and cardiovascular surgery departments of our hospital.

# Comparison of groups at the beginning of the study

50 patients were enrolled in the study and a total of 42 patients completed 8 weeks of rehabilitation. 5 patients were excluded from the hospital exercise group, and 3 from the control group due to loss in follow-up (2 received a transplant, 3 died and 3 were unable to complete the study period). We followed a per-protocol analysis, so their measurements were not included in the final analysis.

Demographic analyses and disease characteristics are presented in Table-1. Comparison analyses gave no difference between groups in any parameters at the baseline of study (p>0.05).

There was no significant difference between groups in initial  $pVO_2$ , 6MWT, and pulmonary function test values (FEV1, FVC, FEV1/FVC, VC) (p>0.05). MLHFQ, STAI, and BDI scores did not differ significantly between groups (p>0.05). Initial SF 36 scores did not differ significantly except for physical role functioning, vitality, and emotional role functioning, which were significantly worse for the home exercise group (p= 0.03, 0.02, and 0.01 respectively).

## Compliance with exercise

When compared with the home exercise group, the hospital exercise group was found to be better compliant and having spent more time doing exercise (p=0.002, Mean±SD 18.45±1.9 days for hospital vs 13.45±5.6 for home).

# Change in parameters after the intervention period

Changes in outcomes after the intervention period between groups are given in Table-2.

pVO<sub>2</sub> values and 6 MWT were found to be significantly better for the hospital group (p<0.001). Pulmonary function tests improved for both groups but there was no significant difference between the two groups.

self-reported parameters, Amona MLHFQ improved significantly for the hospital group, while in the home exercise group changes were not significant (p=0.01 and 0.49, respectively).

#### Correlations between parameters for the whole study group

A Spearman correlation analysis was performed

to assess the relationship between the clinical parameters and changes in study parameters after the rehabilitation program. Younger patients showed a better gain in FEV1 (r=-0.35, p<0.05) and 6MWT (r=-0.39, p<0.01). Gains in 6MWT correlated significantly with the gains in peak VO2 (r=0.54\*\*, p<0.01). Those patients with longer duration of HF showed a poorer response in the FEV1 (r=0.19, p<0.05) and 6MWT (r=-0.25, p<0.01) gains. We did not find among quality-oflife scores and the clinical parameters. Correlation analyses are presented in Table-3.

Table-1. Comparison of patient characteristics of hospital and home groups.

	Hospital group (n=20)	Home group (n=22)	р
Age, year			
Mean ± SD	48.9 ± 13.3	51.9 ± 12.1	
Median (min-max)	52.5 (22-66)	55 (20-66)	0.33
Gender, n (%)			
Female	3 (7.1)	4 (9.5)	
Male	17 (40.4)	18 (42.8)	0.78
Marital Status, n (%)			
Married	17 (40.4)	20 (47.6)	
Single	3 (7.1)	1(2.3)	
Widowed	0 (0)	1 (2.3)	0.34
Educational, n (%)			
Elementary	7 (16.6)	12 (28.5)	
Middle School	9 (21.4)	5 (11.9)	
Higher	4 (9.5)	5 (11.9)	0.28
Time with heart failure, year		· · · ·	
Mean ± SD	5.9 ± 3.3	$6.5 \pm 4.2$	
Median (min-max)	5 (2-14)	5.5 (2-16)	0.72
Time with LVAD, year			-
Mean ± SD	$1.5 \pm 0.7$	1.5 ± 0.8	
Median (min-max)	1.5 (0.5-3)	1.6 (0.5-3)	0.94
LVAD type			
Heartmate II	5 (11.9)	3 (7.1)	
Heartware	15 (35.7)	19 (45.2)	0.35
NYHA class, n (%) Class 1	0 (0)	1 (2.3)	
Class 2	18 (42.8)	17 (40.4)	
Class 3	2 (4.7)	4 (9.5)	
Class 4	0(0)	0 (0)	0.72
BMI, kg/m <sup>2</sup>			
Mean ± SD	26.5 ±4.8	27.8 ±5.5	
Median (min-max)	26.6 (17.3-35.2)	27.5 (19-39)	0.51
Obese, n (%)	5 (11.9)	8 (19.0)	0.42
Smoking status (%)	3 (11.3)	0 (10.0)	0.42
Smoking	1 (2.3)	0 (0)	
Non smoking	7 (16.6)	4 (9.5)	
Ex-smoker	12 (28.5)	18 (42.8)	0.23
Smoking, pack-year (mean ± SD)	34.0 ± 21.6	35.11 ± 28.3	0.84
Cause of heart failure, n (%) Dilated	6 (14.2)	4 (9.5)	
cardiomyopathy Ischemia	11 (26.1)	14 (33.3)	
Hypertension	3 (7.1)	2 (4.5)	
Other	0 (0)	2 (4.5)	0.41

.. . . ..

Chi-square test. SD: Standard deviation, BMI: Body mass index, LVAD: Left ventricle assist device, Obese: BMI≥30 kg/m<sup>2</sup> \* p<0.05 \*\* p<0.01

	Hos	spital group	p <sup>1</sup> =	Hom	e group	p <sup>1</sup> =	p <sup>2</sup> =
	Week 0	Week 8	p =	Week 0	Week 8		
Peak VO <sub>2</sub> , ml/kg/dk	9.7(5.9-14.3)	11.7(8.3-15.1)	0.00**	10.8 (6.0-18.7)	10.3 (6.1-15.7)	0.92	0.02*
6 Minute walk test (m)	305 (120-450)	405(210-500)	0.00**	345 (120-480)	360 (240-520)	0.06	0.02*
FEV1 (ml)	2090(1330-4460)	2170(1330-4450)	0.57	2025(750-3190)	2080 (710-2170)	0.79	0.76
FVC (ml)	2560(1960-5460)	2675(1800-5470)	0.13	2780(830-3990)	2915(820-4090)	0.21	0.99
FEV1/FVC (%)	80.1 (53-93)	77.9(52.4-91.9)	0.92	73.6 (60-97.7)	73.9 (65.7-90.5)	0.60	0.71
VC (ml)	2250(1340-5700)	2180(1420-5520)	0.39	2550(970-4310)	2365(930-4470)	0.28	0.15
MLHFQ	33.5 (11-95)	28.5(7-91)	0.01*	30.5 (12-74)	30(11-80)	0.49	0.00**
State-trait anxiety index							
State score	35 (20-50)	32.5(22-48)	0.06*	37.5(22-48)	39(20-50)	0.26	0.03*
Trait score	39 (25-52)	34(26-55)	0.02*	39.5(21-53)	42(22-50)	0.76	0.14
Beck depression index	7 (0-31)	6 (0-34)	0.17	17 (0-35)	17.5(0-37)	0.90	0.33
SF-36							
Physical summary	36.6 (25.2-54.6)	33.5(26.1-52.4)	0.88	32.7(20.9-51.6)	50(20-80)	0.26	0.9
Mental summary	46.7 (35.1-58.7)	47(36.1-59.3)	0.31	41.8(24.6-52.9)	45(30-67)	0.10	0.3
Physical functioning	50 (10-80)	47.5(15-88)	0.84	45 (25-70)	43.5(5-90)	0.17	0.1
Physical role	25 (0-100)	25(0-100)	0.69	0 (0-100)	23.5(0-100)	0.15	0.7
Pain	74 (41-100)	84(51-100)	0.27	62 (12-80)	72(32-100)	0.01*	0.4
General Health	37 (15-82)	33.5(20-80)	0.74	25 (10-87)	30(20-67)	0.09	0.4
Vitality	52.5 (30-85)	50(35-85)	0.94	50 (20-75)	50(30-80)	0.16	0.4
Social functioning	62.5 (38-100)	52.5(36-100)	0.54	50 (13-100)	50(37-100)	0.18	0.1
Emotional well being	66.7 (0-100)	66.7(33-100)	0.64	33.3 (0-100)	33.3(0-100)	0.81	0.5
Mental health	60 (44-80)	63(40-84)	0.29	50 (20-80)	56 (24-87)	0.27	0.8

Table-2. Changes in parameters after 8 weeks (Median (min-max)).

p1 In-group comparison Wilcoxon test. p2: Intergroup comparison of changes Mann Whitney U test \* p<0.05 \*\* p<0.01

	Age (rS)	Body Mass Index (rS)	Time with HF (rS)	Time with LVAD (rS)	Change in peak VO2 (rS)
Change in peak VO2	0.20	0.007	-0.13	0.01	-
Change in 6-minute walk test	-0.39**	0.09	-0.25**	0.14	0.54**
Change in FEV1	-0.35*	-0.11	-0.19*	0.07	0.14*
Change in FVC	-0.14	-0.19	-0.14	-0.03	0.31
Change in FEV1/FVC	-0.30	0.01	-0.30	0.06	0.09
Change in VC	-0.10	0.18	-0.29	0.20	0.03
MLHFQ	0.13	-0.19	-0.01	-0.08	0.25
Changes in STAI					
State score	-0.08	-0.06	-0.11	-0.008	0.51
Trait score	-0.04	-0.16	-0.18	0.19	-0.21
BDI	-0.17	-0.04	-0.16	-0.005	-0.03
SF-36					
Physical summary	0.08	-0.14	-0.26	-0.28	0.10
Mental summary	-0.22	-0.01	-0.06	-0.07	0.06
Physical functioning	-0.07	-0.19	-0.04	-0.26	0.07
Physical role functioning	-0.01	-0.22	-0.11	-0.23	0.36
Pain	0.00	-0.15	-0.05	-0.28	-0.13
General Health	0.19	0.05	0.13	0.02	0.16
Vitality	0.23	-0.02	0.04	0.11	0.24
Social functioning	0.00	-0.15	0.04	-0.11	0.09
Emotional well being	-0.22	-0.01	-0.21	-0.16	-0.01
Mental health	-0.12	-0.02	0.19	0.20	0.04

<b>Table-3.</b> Correlation analyses between parameters.
--

Spearman correlation analysis rS: Spearman correlation coefficient \* p<0.05 \*\*p<0.01 MLHFQ: Minnesota living with heart failure questionnaire, BDI: Beck depression inventory

#### DISCUSSION

The goal of cardiac rehabilitation is to improve the functional and psychosocial status of patients. Additionally, increasing myocardial perfusion, performance and slowing disease progression are among other goals (20). While LVAD implantation is a common procedure among patients with heart failure, studies evaluating efficacy of cardiac rehabilitation in such patients are scarce and small. Some of these studies were conducted in order to assess the safety and feasibility of cardiac rehabilitation in patients with LVADs. In most of these studies, patients with LVAD, heart transplantation, heart failure, and coronary artery disease were recruited in the same cohort.

There are few studies evaluating the efficacy of cardiac rehabilitation programs in LVAD patients. Marko et al. (21) investigated the efficacy of cardiac rehabilitation in 41 patients in a retrospective study. Alsara et al. (7) assessed the results of an early rehabilitation program in 94 patients with LVAD retrospectively. Chu et al. (22) also conducted a retrospective study for cardiac rehabilitation in 58 patients with LVAD. Prospective studies in this field are mainly limited in patient numbers, ranging from 14 to 26 (23,24). Our trial is one of those with the highest number of patients among these studies.

One differing side of our study is patient recruitment time after LVAD implantation (min=6 months, max=36 months), which refers to chronic stage unlike most studies. Most of the previous studies recruited patients in earlier stages after the operation. It is known that functional improvement after LVAD implantation continues for the first 12 weeks (7). Moreover, even without cardiac rehabilitation programs, functional improvement was reported in patients with LVADs in the first 3 months (25). Some of the reported benefits of cardiac rehabilitation in the early stages after LVAD operation could be attributed to physiological recovery. The earliest recruited patient in our study was 6 months postoperation, which makes it easier to attribute observed beneficial effects to cardiac that functional rehabilitation and shows improvement is possible even in chronic stage.

There is no consensus about the optimum intensity, duration, or frequency of cardiac rehabilitation. While Marko et al. (21) used a 21-day long hospital-based exercise program that

consisted of strengthening and aerobic exercises, Hayes et al. (23) preferred 8 weeks and Kerrigan et al. (24) preferred a 6-week approach. Since these approaches were found safe and resulted in functional improvement in those studies, we adapted an 8 week long approach with 3 days a week sessions, similar to the one which was found safe and efficient in heart failure, transplantation and LVAD patients in one of the studies we conducted (9).

The patients were divided into two groups, home, and hospital exercise groups. While we observed improvements in functional parameters in the hospital group, we could not observe the same effect in the home exercise group. In 2 Cochrane reviews comparing the effectiveness of home and hospital-based rehabilitation programs, home exercises were found as effective as hospital exercises (6,26). 17 studies that were included in one of the reviews possessed some differences compared to our study. Most of the included studies mainly included NYHA stage 1 patients who were asymptomatic, and only 5 studies also included NYHA stage 2 and 3 patients. Most of our patients were stage 2 (83.2%), with fewer stage 3 (14.2%) and only one stage 1 patient (2.3%). With lower functional status, compliance to exercise programs might be worse. Moreover, the said review consisted solely of patients with heart failure, and included no LVAD implanted patients, and subjects' adherence to exercise was assessed with telephone or postal service. While we didn't use such methods to check and strengthen adherence, we used an adherence form to assess the days subjects completed the exercises.

In the study conducted by Cowie et al. (27), adherence to exercise between hospital and home exercise groups was similar, resulting in improved functional outcomes in both groups. The reason for not achieving a significant increase in pVO2 and other parameters in the home exercise group in our study may be attributed to lower compliance to the exercise program.

Although there is no particular study comparing adherence to exercise and improvement in outcome measures in patients with implanted LVADs, it has been previously shown in other disease and subject groups that better adherence to exercise results in more favorable outcomes (26–29). Previous studies have shown that quality of life increases after LVAD implantation due to alleviation of symptoms. Jakovlevic et al. (25) LVAD reported that patients showed improvement in quality of life after the implantation in the first three months, and no increase beyond three months. Similarly, Kato et al. (30) stated that they detected improvement for first three months in quality of life in 33 patients with LVAD. We could not show any significant change in SF-36 scales in either group, except for improvement of pain subscale in the home exercise group. Yet, there was significant improvement in MLHFQ in the hospital group when compared to home exercise. The discrepancy between MLHFQ and SF-36 can be explained with SF-36's being a generic quality of life questionnaire, whereas MLHFQ being a questionnaire developed specifically for heart failure patients. Specific inventories such as MLHFQ might be more sensitive to changes in quality of life in cardiac patients.

Studies in LVAD-implanted patients show a depression prevalence of 51% (31). Cardiac rehabilitation is known to have beneficial effects on depressive symptoms, and our study reveals similar results. BDI for the hospital exercise group improved significantly more than the home group (p<0.05). Moreover, both state anxiety and trait anxiety sub-scores of STAI in hospital exercise group improved significantly, while home control group had no significant improvement in either BDI or STAI sub-scores (24). These findings can be explained with differences in adherence to exercise as well as improvement in functional capacity. A negative correlation was found between peak VO2 and depression in a previous study (32). Our correlation analyses did not show a significant correlation between these outcome measures.

Hospital exercise programs do not only guarantee better adherence, but they also allow patients to socialize and meet people in similar conditions to theirs, thus providing a form of psychosocial support. This may be caused by the effects of a group setting in contrast to the individual exercise sessions in the home group, as have been reported in other disease groups (32, 33).

#### Limitations and strengths of study:

As mentioned above, instead of a control group without intervention, a home exercise group was formed, due to ethical issues and the necessity of cardiac rehabilitation for all patients. Adherence of patients in the home exercise aroup to exercise was monitored by self-report forms included in exercise brochures. When we consider that compliance to exercise is reported to be lower in home-based exercise interventions, it would be more effective to monitor patients' adherence to the exercise program with more interactive methods such as telephone calls or teleconference. Due to the timeframe of limited our studv. patients' outcomes were monitored at 8 weeks. immediately after the end of study, so this study does not give us more insight about the long-term effects of cardiac rehabilitation.

# CONCLUSION

LVAD is being increasingly used in patients with heart failure, and safety and efficacy of cardiac rehabilitation in this patient group have previously been shown. We found that a cardiac rehabilitation program resulted in improvements in VO2 max, 6MWT, MLHFQ, and STAI scores in patients with LVAD implantations. Among these measures, VO2 max, 6MWT, MLHFQ and STAI scores improved significantly more in the hospital exercise group. Patients with a shorter duration of heart failure showed better outcomes in pulmonary function tests and 6MWT in correlation analyses. Most of previous studies reporting similar results in home and hospitalbased exercise programs were found to include NYHA stage 1 patients with better baseline functional status. We observed that patients in our home exercise group had worse adherence to the exercise program. Since studies involving patients with LVADs are few and utilize different outcome measures, comparison is not easy. More studies assessing the results of different exercise protocols with longer-term follow-ups are necessary to decide on the best rehabilitation program in this group of patients.

**Conflict of interest**: Authors declare no conflict of interest.

#### References

- 1. Cleland JGF, Gemmell I, Khand A, Boddy A. Is the prognosis of heart failure improving? Eur. J. Heart Fail. 1999; 1:229-41.
- Ketchum ES, Levy WC. Establishing Prognosis in Heart Failure: A Multimarker Approach. Prog Cardiovasc Dis. 2011 Sep 1;54(2):86–96.
- 3. Adebayo SO, Olunuga TO, Durodola A, Ogah OS. Quality of life in heart failure: A review. Niger J Cardiol. 2017 Jun;14(1):1-7.
- 4. Mpe MT, Klug EQ, Silwa KS, Hitzeroth J, Smith DA. Heart Failure Society of South Africa (HeFSSA) perspective on the European Society of Cardiology (ESC) 2012 chronic heart failure guideline. S. Afr. Med. J. 2013;103:660-7.
- 5. Adams EE, Wrightson ML. Quality of life with an LVAD: A misunderstood concept. Heart Lung. 2018 May 1;47(3):177-83
- 6. Taylor RS, Dalal HM, McDonagh STJ. The role of cardiac rehabilitation in improving cardiovascular outcomes. Nat Rev Cardiol. 2022 Mar;19(3):180–94.
- 7. Alsara O, Reeves RK, Pyfferoen MD, et al. Inpatient Rehabilitation Outcomes for Patients Receiving Left Ventricular Assist Device. Am. J. Phys. Med. 2014;93:860-8.
- Nguyen E, Stein J. Functional Outcomes of Adults with Left Ventricular Assist Devices Receiving Inpatient Rehabilitation. PM&R. 2013;5:99-103.
- Karapolat H, Engin C, Eroglu M, et al. Efficacy of the Cardiac Rehabilitation Program in Patients with End-Stage Heart Failure, Heart Transplant Patients, and Left Ventricular Assist Device Recipients. Transplant. Proc. 2013;45:3381-5.
- 10. Rector T. Patients' self-assessment of their congestive heart failure: Content, reliability, and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. Heart failure. 1987;3:198-209.
- 11. Uzunhasanoglu N. TF. Minnesota Kalp Yetmezliği ile Yasam Anketi (MKYYA) Türkçe Geçerlilik ve Guvenilirligi. 16 Ulusal Halk Sağlığı Kongresi. Antalya, Turkiye. 2013.
- Rector TS, Cohn JN. Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: Reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. Am. Heart J. 1992;124:1017-25.
- 13. Beck AT. An Inventory for Measuring Depression. Arch. Gen. Psychiatry. 1961;4:561.
- 14. Şahin N. Beck depresyon envanterinin üniversite öğrencileri için geçerliği güvenirliği. Türk Psikoloji Dergisi. 1989;23:3-13.
- Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). Medical Care. 1992;30:473-83.
- Kocyigit H, Aydemir O, Olmez N, Memis A. Reliability and validity of the Turkish version of Short-Form-36 (SF-36). Turkish J Drugs Therap. 1999;12:102-6.
- 17. Spielberger CD, Edwards CD, Montouri J, Lushene R. State-Trait Anxiety Inventory for Children. PsycTESTS Dataset: American Psychological Association (APA); 1973.
- Oner N. Le Comte A. Durumluk-Sürekli Kaygı Envanteri El kitabi. Oner N. Le Comte A. (Ed) 2nd ed. Bogazici Universitesi Yayinlari. Istanbul, Turkey. 1985. 20-6
- Ferguson B. ACSM's Guidelines for Exercise Testing and Prescription 9th Ed. 2014. J Can Chiropr Assoc. Sep;58(3):328
- 20. El Demerdash S, Khorshid H, Salah I, Abdel-Rahman MA, Salem AM. Cardiac rehabilitation improves the ischemic burden in patients with ischemic heart disease who are not suitable for revascularization. Cardiovasc Revasc Med. 2015;16:280-3.
- 21. Marko C, Danzinger G, Käferbäck M, et al. Safety and efficacy of cardiac rehabilitation for patients with continuous flow left ventricular assist devices. Eur J Prev Cardiol. 2014;22:1378-84.
- 22. Chu SK, McCormick Z, Hwang S, Sliwa JA, Rydberg L. Outcomes of Acute Inpatient Rehabilitation of Patients With Left Ventricular Assist Devices. PM&R. 2014;6:1008-12.

- Hayes K, Leet AS, Bradley SJ, Holland AE. Effects of exercise training on exercise capacity and quality of life in patients with a left ventricular assist device: A preliminary randomized controlled trial. J. Heart Lung Transplant. 2012;31:729-34.
- Kerrigan DJ, Williams CT, Ehrman JK, et al. Cardiac Rehabilitation Improves Functional Capacity and Patient-Reported Health Status in Patients With Continuous-Flow Left Ventricular Assist Devices. JACC: Heart Fail. 2014;2:653-9.
- 25. Jakovljevic DG, McDiarmid A, Hallsworth K, et al. Effect of Left Ventricular Assist Device Implantation and Heart Transplantation on Habitual Physical Activity and Quality of Life. Am. J. Cardiol. 2014;114:88-93.
- 26. Anderson L, Sharp GA, Norton RJ, Dalal H, Dean SG, Jolly K, Cowie A, Zawada A, Taylor RS. Home-based versus centre-based cardiac rehabilitation. Cochrane Database Syst Rev. 2017 Jun 30;6(6):CD007130
- 27. Cowie A, Thow MK, Granat MH, Mitchell SL. Effects of home versus hospital-based exercise training in chronic heart failure. Int. J. Cardiol. 2012;158:296-8.
- 28. Beinart NA, Goodchild CE, Weinman JA, Ayis S, Godfrey EL. Individual and intervention-related factors associated with adherence to home exercise in chronic low back pain: a systematic review. J. Spine. 2013;13:1940-50.
- 29. Arena R, Cahalin LP, Borghi-Silva A, Myers J. The effect of exercise training on the pulmonary arterial system in patients with pulmonary hypertension. Prog Cardiovasc Dis. 2015;57:480-8.
- 30. Kato NP, Okada I, Imamura T, et al. Quality of Life and Influential Factors in Patients Implanted With a Left Ventricular Assist Device. Circ. J. 2015;79:2186-92.
- 31. Opasich C, Cobelli F, Assandri J, et al. Is old age a contraindication to cardiac rehabilitation after acute myocardial infarction? Eur. Heart J. 1984;5:105-7.
- 32. Kanamori S, Takamiya T, Inoue S, Kai Y, Kawachi I, Kondo K. Exercising alone versus with others and associations with subjective health status in older Japanese: The JAGES Cohort Study. Sci Rep. 2016 Dec 15;6: 39151
- 33. Komatsu H, Yagasaki K, Saito Y, Oguma Y. Regular group exercise contributes to balanced health in older adults in Japan: a qualitative study. BMC Geriatr. 2017 Aug 22;17(1):190.