

Association between the low percentage of forced vital capacity and increased mortality after left ventricular assist device implantation

Sol ventrikül destek cihazı yerleştirilmesinden sonra artmış mortalite ve düşük zorlu vital kapasite yüzdesi arasındaki ilişki

Pervin Korkmaz Ekren¹, Pelin Öztürk², Serkan Ertugay², Ali Özdiil³, Sanem Nalbantgil⁴, Çağatay Engin², Tahir Yağdı², Mustafa Özbaran²

¹Department of Chest Diseases, Ege University Medical Faculty, Izmir, Turkey

²Department of Cardiovascular Surgery, Ege University Medical Faculty, Izmir, Turkey

³Department of Thoracic Surgery, Ege University Medical Faculty, Izmir, Turkey

⁴Department of Cardiology, Ege University Medical Faculty, Izmir, Turkey

ABSTRACT

Background: This study aims to investigate the effect of low percentage of forced vital capacity measured in the preoperative period on the 28-day mortality in patients undergoing left ventricular assist device implantation.

Methods: A total of 131 patients (111 males, 20 females; median age 54 years; range, 47 to 59 years) who underwent left ventricular assist device implantation with HeartWare™ between December 2010 and January 2016 were retrospectively analyzed. The patients were divided into two groups according to the results of pulmonary function test as a forced vital capacity percentage of $\geq 60\%$ (n=113) and $< 60\%$ (n=18). Both groups were compared in terms of laboratory and clinical characteristics, and postoperative complications. Risk factors for postoperative 28-day mortality were analyzed.

Results: Pre- and intraoperative characteristics were similar in both groups, except for left ventricular end-diastolic diameter. The ventilator-free days up to 28 days was shorter (p=0.046) and the length of intensive care unit stay was longer (p=0.011) in the low percentage of forced vital capacity group. The 28-day mortality rate was also higher (22.2% vs. 9.7%, respectively; p=0.12) in this group. The history of prior cardiac operation (odds ratio: 4.40; 95% confidence interval 1.19-16.20, p=0.026) and tricuspid valve repair at the time of device implantation (odds ratio: 5.30; 95% confidence interval 1.33-21.00, p=0.018) were found to be independent risk factors for mortality. Multivariate analysis showed that a forced vital capacity of $< 60\%$ was not associated with mortality (odds ratio: 3.96; 95% confidence interval 0.95-16.43, p=0.058).

Conclusion: The length of intensive care unit stay and duration of mechanical ventilation may be longer in patients with a low percentage of forced vital capacity. Although the association between 28-day mortality and low percentage of forced vital capacity is not significant, the risk of 28-day mortality is higher in this group. Therefore, the patients should be assessed carefully before the left ventricular assist device operation.

Keywords: Complication, heart failure, heart-assist device, mortality, pulmonary function test.

ÖZ

Amaç: Bu çalışmada, sol ventrikül destek cihazı yerleştirilen hastalarda ameliyat öncesi dönemde ölçülen düşük zorlu vital kapasite yüzdesinin 28 günlük mortalite üzerindeki etkisi incelendi.

Çalışma planı: Aralık 2010 - Ocak 2016 arasında, HeartWare™ ile sol ventrikül destek cihazı yerleştirilen toplam 131 hasta (111 erkek, 20 kadın; median yaş 54 yıl; dağılım, 47-59 yıl) retrospektif olarak değerlendirildi. Hastalar solunum fonksiyon test sonuçlarına göre, zorlu vital kapasite yüzdesi $\geq 60\%$ (n=113) ve $< 60\%$ (n=18) olmak üzere iki gruba ayrıldı. İki grup laboratuvar ve klinik özellikler ile ameliyat sonrası komplikasyonlar açısından karşılaştırıldı. Ameliyat sonrası 28 günlük mortalite için risk faktörleri analiz edildi.

Bulgular: Ameliyat öncesi ve ameliyat sırası özellikler sol ventrikül diyastol sonu çapı dışında iki grupta da benzerdi. Düşük zorlu vital kapasite yüzdesi olan grupta 28 güne kadar ventilatörsüz gün sayısı daha kısa (p=0.046) ve yoğun bakım ünitesinde kalış süresi daha uzun (p=0.011) idi. Bu grupta 28 günlük mortalite oranı da daha yüksek idi (sırasıyla %9.7'ye kıyasla %22.2; p=0.12). Kalp ameliyatı öyküsü (olasılık oranı: 4.40; %95 güven aralığı 1.19-16.20; p=0.026) ve cihaz yerleştirme sırasında triküspit kapak tamiri (olasılık oranı: 5.30; %95 güven aralığı 1.33-21.00; p=0.018) mortalitenin bağımsız risk faktörleri olarak bulundu. Çok değişkenli analizde $< 60\%$ zorlu vital kapasite ile mortalite arasında ilişki saptanmadı (olasılık oranı: 3.96; %95 güven aralığı 0.95-16.43; p=0.058).

Sonuç: Zorlu vital kapasite yüzdesi düşük olan hastalarda, yoğun bakım ünitesinde kalış süresi ve mekanik ventilasyon süresi daha uzun olabilmektedir. Her ne kadar 28 günlük mortalite ile düşük zorlu vital kapasite yüzdesi arasında anlamlı bir ilişki olmasa da, 28 günlük mortalite riski bu grupta daha yüksek olabilir. Bu nedenle, bu hastalar sol ventrikül destek cihazı ameliyatından önce dikkatle değerlendirilmelidir.

Anahtar sözcükler: Komplikasyon, kalp yetmezliği; kalp destek cihazı; mortalite, solunum fonksiyon testi.

Received: April 01, 2020 Accepted: August 19, 2020 Published online: October 21, 2020

Correspondence: Ali Özdiil, MD. Ege Üniversitesi Tıp Fakültesi Göğüs Cerrahisi Anabilim Dalı, 35040 Bornova, İzmir, Türkiye.

Tel: +90 232 - 390 43 34 e-mail: dr_aliozdiil@yahoo.com

Cite this article as:

Korkmaz Ekren P, Öztürk P, Ertugay S, Özdiil A, Nalbantgil S, Engin Ç, et al. Association between the low percentage of forced vital capacity and increased mortality after left ventricular assist device implantation. Turk Gogus Kalp Dama 2020;28(4):576-585

©2020 All right reserved by the Turkish Society of Cardiovascular Surgery.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes (<http://creativecommons.org/licenses/by-nc/4.0/>).

Left ventricular assist device (LVAD) is the common circulatory support system worldwide in which the pump system receives blood from the left ventricle and delivers it to the aorta. The LVAD implantation and heart transplantation are accepted as the main therapy for patients with advanced heart failure who do not recover with the best medical therapies. These devices are administered as a bridge to transplant, a bridge to recovery or destination therapy. The LVAD implementation has been increasing currently, due to the increased number of patients with newly diagnosed heart failure and shortage of donor hearts.^[1-8] The selection procedure of these patients who have multiple comorbidities has become crucial before the operation to prevent postoperative morbidity and mortality. Hence, numerous cardiovascular risk profiles have been evaluated to guide clinical decision-making during the preoperative period. The models developed for risk identification for LVAD implantation have been developed to predict 90-day mortality (Destination Therapy Risk Score, HeartMate II™ [Abbott Laboratories Inc., IL, USA] risk score).^[2,9] However, none of these models consider the effect of pulmonary function tests (PFTs).

Patients with heart failure may have restrictive type impairment on PFTs caused by different mechanisms before an operation. The volume of heart chambers shows limited reverse remodeling following LVAD implant, and the device is also placed into this thoracic cavity. Mohamedali *et al.*^[10] showed that the PFT significantly reduced after LVAD implantation in their study, despite a limited number of patients. Additionally, we have insufficient data regarding the management of this patient group in cases where the patient has impaired pulmonary function before the operation in the literature. As a result, the effect of preoperative impaired PFT is still an unanswered question for these recipients.

In the present study, we hypothesized that low percentage of forced vital capacity (FVC%; <60%) in the preoperative period could increase the risk of 28-day mortality and this parameter could be used in the postoperative risk stratification. We, therefore, aimed to investigate whether low FVC% measured in the preoperative period was associated with an increased risk of 28-day mortality and to compare ventilator-free days up to 28 days and evaluate respiratory complications within the first week after operation.

PATIENTS AND METHODS

This retrospective cohort study included the patients who underwent LVAD implantation at Ege University, Faculty of Medicine, Department of Cardiovascular Surgery between December 2010 and January 2016. The goals of implantation were to bridge to transplantation or destination therapy. Inclusion criteria were as follows: age ≥ 18 years, having spirometry before operation; presence of chest X-ray before operation, being implanted with HeartWare™ (Medtronic, MN, USA). Exclusion criteria were as follows: absence of PFT, having unacceptable PFT results indicating that the patient was unable to perform successful respiratory maneuvers necessary to obtain clinically meaningful results, those directly admitted to the intensive care unit (ICU) from the outpatient centers due to severe clinical conditions/emergency operations (their preoperative examinations were done bedside without PFT), being implanted with a different device, and undergoing heart transplantation within 28 days after LVAD implantation due to the increased risk of mortality and morbidity. During the study period, LVAD was implanted in 246 patients in our institution and only 131 patients (111 males, 20 females; median age 54 years; range, 47 to 59 years) who were considered eligible for the study. The study flowchart is shown in Figure 1. A written informed consent was obtained from each patient. The study protocol was approved by the Ege University, Faculty of Medicine, Ethics Committee (No. 16-2.1/6, 21.07.2016). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Spirometric measurement was performed three times with SensorMedics 2400 (Yorba Linda, CA, USA) spirometer in the PFT laboratory of the chest disease department. The best of the three results was accepted as the outcome measure. The assessment of PFT consisted of FVC, forced expiratory volume in 1 sec (FEV₁), and FEV₁/FVC ratio. The study population was divided into two groups according to their percentage of FVC (FVC%) as $\geq 60\%$ (n=113) or $<60\%$ (n=18). The cut-off value of FVC% was defined according to the restrictive pattern classification of the American Thoracic Society (ATS).^[11]

The medical records of the patients were reviewed and relevant data were recorded. Demographic and clinical characteristics, comorbid diseases, indications for operation, preoperative laboratory values, right heart catheterization measurements, preoperative support and echocardiography findings, operative procedures, and postoperative complications were noted. Mortality within 28 days after the operation, ventilator-free days

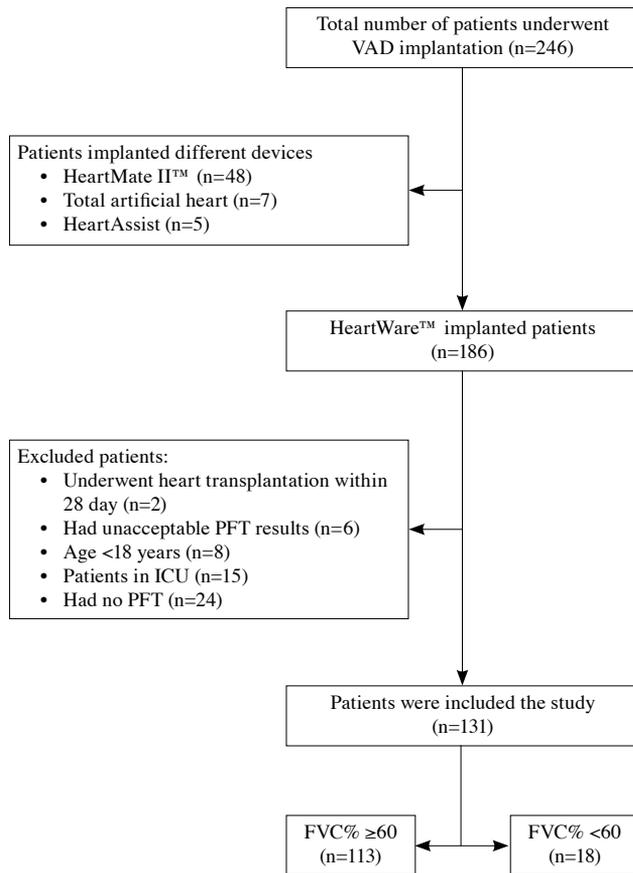


Figure 1. Study flowchart.

VAD: Ventricular assist device; PFT: Pulmonary function test; ICU: Intensive care unit; FVC: Forced vital capacity.

up to 28 days, and respiratory complications such as pneumonia and atelectasis within the first week of the operation were retrieved from the inpatient and outpatient files. For patients who died before Day 28, the value for ventilator-free days was accepted as “0”.^[12]

The spirometer device in the PFT laboratory of the chest disease department was calibrated regularly on a daily basis. The test was performed by two experienced technicians. Case report forms were used for data collection by the investigators.

Statistical analysis

Statistical analysis was performed using the PASW version 18.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented in mean ± standard deviation (SD) or median (75th-25th percentile), while categorical variables were expressed in number and frequency. The Kolmogorov-Smirnov test was used for the assessment of the data distribution.

Categorical data were compared using the Fisher’s exact test for ≤2 groups and the Pearson chi-square test for >2 groups. The Student’s t-test and Mann-Whitney U test were performed for normally and abnormally distributed data, respectively. Univariate analysis was performed for mortality. Covariates with p<0.05 and clinically important variables were included in the multivariate logistic regression analyses. Models were constructed using the forward stepwise method. The Hosmer-Lemeshow test was used for goodness of fit for logistic regression models. A p value of <0.05 was considered statistically significant.

RESULTS

The common etiology of heart failure was ischemic and dilated cardiomyopathy. Most of the patients were classified in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) Level 3 in terms of clinical status before implantation. History of cardiac procedure was detected in 22.9% of the patients. There were no significant differences between the two groups in terms of demographic characteristics, comorbid diseases, or presence of chronic obstructive pulmonary disease (Table 1). Both groups had similar preoperative laboratory parameters, cardiac catheterization measurements, and echocardiographic findings, except for the left ventricular end-diastolic diameter (LVEDD). The use of preoperative cardiopulmonary support such as intra-aortic balloon pump, extracorporeal membrane oxygenation, and mechanical ventilation was similar between the two groups (Table 2).

No significant difference was observed between two groups in terms of surgical procedure and complications after LVAD operation, such as re-exploration for bleeding or requirement of postoperative hemodialysis. The presence of pulmonary complications was also observed to be similar in both groups during the first week after operation. However, the ventilator-free days up to 28 days was shorter (p=0.046) and the length of ICU stay was significantly longer (p=0.011) in the patient group with low FVC% (Table 3).

The overall 28-day mortality rate was 11.4% in the all study groups, whereas the rate was higher in the low FVC% group (22.2% vs. 9.7%, respectively; p=0.12) (Table 3). A total of 26.7% of patients who died and 12.1% of survivors had low FVC%. Additionally, the median FVC% in the deceased group was lower than the survivors (69 vs. 78, respectively; p=0.06). A prior cardiac operation history, high total bilirubin level, and requirement of postoperative dialysis were significantly higher in deceased patients. Pneumonia

Table 1. Demographic and clinical characteristics and pulmonary function test results of patients

	Total (n=131)			FVC% ≥60 (n=113)			FVC% <60 (n=18)			P	
	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median		IQR
Age (year)	111	84.7	54	47-59	47-60	55	47-60	53	43-58	43-58	0.15
Sex											
Male	98	86.7				98	86.7				0.25
Ischemic cardiomyopathy	66	50.4				58	51.3				0.62
Smoking history	91	69.5				79	69.9				0.78
Smoking pack/years			25	15-36	15-36	25	15-36	23.5	7-37	7-37	0.66
Body mass index (kg/m ²)			25.5±4.2			25.7±4.2		25.8±4.1			0.78
INTERMACS											0.59
Class 1	6	4.6				4	3.5				
Class 2	34	26.0				4	3.5				
Class 3	57	43.5				32	25.7				
Class 4	32	24.4				43.4					
Class 5	2	1.5				25.7					
Class 5	2	1.5				2	1.8				
Comorbid disease											
Hypertension	53	40.5				47	41.6				0.61
Diabetes mellitus	41	31.3				32	28.3				0.09
Hyperlipidemia	22	16.8				19	16.8				1.0
Cerebrovascular disease	12	9.2				10	8.8				0.67
Prior hemodialysis	3	2.3				3	2.7				1.0
COPD	26	19.8				23	20.4				1.0
Prior cardiac operation history	30	22.9				25	22.1				0.55
Pulmonary function test											
FVC (%)			76±15					79±12			<0.001
FEV ₁ (%)			71±15					74±13			<0.001
FEV ₁ /FVC			77	71-82	71-82	76	71-82	81	73-84	73-84	0.08

FVC: Forced vital capacity; SD: Standard deviation; IQR: Interquartile range; INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; COPD: Chronic pulmonary obstructive disease; FEV₁: Forced expiratory volume.

Table 2. Preoperative baseline laboratory and clinical characteristics

	Total (n=131)			FVC% ≥60 (n=113)			FVC% <60 (n=18)			p	
	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median		IQR
Laboratories											
Hemoglobin (g/dL)			12.3±1.9	228	186-285			11.9±1.9	228	162-280	0.38
Platelets (10 ³ /μL)				136	133-140				135	133-138	0.57
Sodium (mEq/L)				42	28-68				50	29-75	0.64
Urea (mg/dL)				1.1	0.9-1.3				1.1	0.9-1.4	0.57
Creatinine (mg/dL)				25	19-42				28	20-51	0.38
Aspartate transaminase (U/L)				24	16-42				29	21-37	0.60
Alanine transaminase (U/L)				1.1	0.7-1.9				1.8	0.87-4.06	0.06
Total bilirubin (mg/dL)			3.9±0.5					3.7±0.6			0.16
Albumin (g/dL)				1.2	1.1-2.4				1.3	1.0-2.0	0.18
INR											
Cardiac catheterization											
mPAP (mmHg)				35	26-45				34	26-39	0.27
RAP (mmHg)				8	5-14				8	4-14	0.71
PCWP (mmHg)				28	18-31				25.5	18-30	0.45
TPG (mmHg)				8	4-13				4	4-10	0.48
Echocardiographic data											
LVEDD (cm)				6.7	6.15-7.55				6.1	5.9-7.1	0.036
LVESD (cm)				6.0	5.4-6.8				5.4	4.6-6.4	0.11
LVEF (%)				20	18-23				20	17-23	0.66
Systolic PAP (mmHg)				49.5	40-60				50	40-60	0.52
TAPSE (mm)				14	11-16				11	10-13	0.05
Pre-operation life support											
Intra-aortic balloon pump	7	5.3				7	6.2		0		0.59
ECMO support	2	1.5				1	0.9		1	5.6	0.25
Mechanical ventilator support	8	6.1				7	6.2		1	5.6	1.0

FVC: Forced vital capacity; SD: Standard deviation; IQR: Interquartile range; INR: International normalized ratio; PAP: Pulmonary artery pressure; PCWP: Pulmonary capillary wedge pressure; TPG: Transpulmonary gradient; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; LVEF: Left ventricular ejection fraction; TAPSE: Tricuspid Annular Plane Systolic Excursion; ECMO: Extracorporeal membrane oxygenation.

Table 3. Surgical procedures and complications after operation

	FVC% ≥60 (n=113)				FVC% <60 (n=18)				p
	n	%	Median	IQR	n	%	Median	IQR	
Sternotomy	96	85.0			12	66.7			0.08
Thoracotomy	18	15.9			5	27.8			0.31
Mini-thoracotomy	2	1.8			1	5.6			0.36
Tricuspid valve repair	18	15.9			3	16.7			1.0
Re-exploration for bleeding	11	9.7			1	5.6			1.0
Postoperative hemodialysis	10	8.8			3	16.7			0.38
Pulmonary complication within one week									
Pneumonia	15	13.3			1	5.6			0.69
Atelectasia	1	0.9			0	0			1.0
Ventilator free day to 28 days (day)			27	26-27			26	21.2-27	0.046
Length of ICU (day)			5	4-7			9	5-20	0.011
Length of hospitalization (day)			20	14.5-26			20.5	16-47	0.28
Mortality	11	9.7			4	22.2			0.12

FVC: Forced vital capacity; IQR: Interquartile range; ICU: Intensive care unit.

occurred in 46.7% of patients who died during the first week after operation; however, the pneumonia rate was 7.8% in the surviving group ($p < 0.001$). The length of ICU stay was significantly longer in the deceased patients ($p < 0.001$) (Table 4).

Multivariate logistic regression was performed to identify pre- and perioperative mortality risk factors. The prior cardiac operation history (odds ratio [OR]: 4.40; 95% confidence interval [CI]: 1.19-16.20; $p = 0.026$) and tricuspid valve repair at the LVAD operation (OR: 5.30; 95% CI: 1.33-21.00; $p = 0.018$) were independent risk factors for 28-day mortality. However, there was no significant correlation between the low FVC% (<60) and increased 28-day mortality (OR: 3.96; 95% CI: 0.95-16.43; $p = 0.058$). After adjustment, total bilirubin level, LVEDD, and right atrium pressure measured with cardiac catheterization before the operation did not continue in the regression model (Table 5).

DISCUSSION

To the best of our knowledge, this is the first study to assess the effect of low FVC% on mortality within 28 days after LVAD operation. Our study showed that 28-day mortality rate was higher in the low FVC% group. However, low FVC% (<60) was no longer significantly associated with mortality in the multivariate analysis. The presence of a cardiac operation history and tricuspid valve repair at the time

of LVAD operation were found to be independent risk factors for mortality. Morbidities such as duration of ventilation or length of ICU stay were more common in the patient group with low FVC% (<60).

Patients with advanced heart failure are screened in a detailed manner to select patients and to optimize preparation before LVAD implantation. Patients with various cardiovascular risk profiles are usually assessed by pulmonary physicians. The PFT and chest X-rays are performed to plan the operation and postoperative risks. The FVC is an important parameter on the PFT and is measured with spirometry. It is the total amount of air exhaled during force expiratory maneuver. Reduced FVC, more so than FEV₁, is shown in restrictive defects.^[11] Patients with heart failure may have restrictive type impairment on PFT. The restrictive pattern occurs with many different mechanisms, which are alveolar and interstitial edema, reactive fibrosis, previous pulmonary infarction, pleural effusion, compressive atelectasis, and enlarged cardiac dimension. Also, the remarkable reduction in lung compliance, increased respiratory work, and redistribution of pulmonary blood flow adversely affect the PFT.^[13-18] This patient group has severe respiratory muscle dysfunction which occurs due to chronic increased respiratory workload and dead space ventilation.^[19,20] All of these changes cause decreased lung function. In addition to these preoperative changes, pain and considerable reduction of respiratory

Table 4. Comparison of baseline laboratory, clinic, operation and postoperative complication in terms of 28-day mortality

	Alive (n=116)				Deceased (n=15)				p
	n	%	Median	IQR	n	%	Median	IQR	
FVC% <60	14	12.1			4		26.7		0.12
FVC%			78	66-87	69		56-80		0.06
Age (year)			54	47-59	49		31-60		0.23
Body mass index (kg/m ²)			25.7	22.9-27.7	25.2		22.1-28.7		0.75
Ischemic cardiomyopathy	60	51.7			6		40.0		0.42
Comorbid disease									
Hypertension	48	41.4			5	33.3			0.38
Diabetes mellitus	35	30.2			6	40.0			0.55
Hyperlipidemia	20	17.2			2	13.3			1.0
Cerebrovascular disease	12	10.3			0	0			0.35
COPD	24	20.7			2	13.3			0.73
Prior cardiac operation	23	19.8			7	46.7			0.043
Laboratories									
Hemoglobin (g/dL)			12.5	11.0-13.9	12.2		10.6-13.3		0.41
Platelets (10 ³ /μL)			228	188-286	204		144-283		0.26
Sodium (mEq/L)			136	134-140	133		128-142		0.08
Urea (mg/dL)			41	27-62	49		28-81		0.22
Creatinine (mg/dL)			1.0	0.9-1.3	1.3		1.0-1.6		0.07
Aspartate transaminase (U/L)			25	19-44	24		15-44		0.74
Alanine transaminase (U/L)			24	16-43	32		21-37		0.63
Total bilirubin (mg/dL)			1.1	0.7-1.6	1.9		1.0-4.1		0.034
Albumin (g/dL)			3.9	3.6-4.4	3.6		3.0-4.3		0.09
International normalized ratio			1.2	1.1-1.4	1.3		1.1-2.3		0.10
Cardiac catheterization									
mPAP (mmHg)			35.5	25.5-44	35		26-45		0.70
RAP (mmHg)			8	5-14	11		5-14		0.50
PCWP (mmHg)			28	18-31	26		20-32		0.74
TPG (mmHg)			8	4-13	9		5-12		0.82
Echocardiographic data									
LVEDD (cm)			6.7	6.1-7.5	6.5		6.1-7.7		0.92
LVESD (cm)			6	5.3-6.8	6		5.4-6.9		0.76
LVEF (%)			20	18-22	20		19-25		0.18
Systolic PAP (mmHg)			49	40-60	49		41-58		0.81
TAPSE (mm)			14	11-16	13.5		9.5-16.5		0.56
Pre-operation support									
Intra-aortic balloon pump	5	4.3			2	13.3			0.18
ECMO support	2	1.7			0	0			1.0
Mechanical ventilator support	7	6.0			1	6.7			1.0
Sternotomy	96	82.8			12	80			0.72
Thoracotomy	20	17.2			3	20			0.72
Mini-thoracotomy	3	2.6			0	0			1.0
Tricuspid valve repair	16	13.8			5	33.3			0.06
Re-exploration for bleeding	11	9.5			1	6.7			1.0
Post-operation dialysis	2	1.7			11	73.3			<0.001
Pulmonary complication within one week									
Pneumonia	9	7.8			7	46.7			<0.001
Atelectasia	1	0.9			0	0			1.0
Length of ICU (day)			5	4-7	15		8.5-19.5		<0.001
Length of hospitalization (day)			20	15-28.5	18		9-21		0.040

IQR: Interquartile range; FVC: Forced vital capacity; COPD: Chronic pulmonary obstructive disease; PAP: Pulmonary artery pressure; RAP: Right atrial pressure; PCWP: Pulmonary capillary wedge pressure; TPG: Transpulmonary gradient; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular systolic diameter; LVEF: Left ventricular ejection fraction; TAPSE: Tricuspid annular plane systolic excursion; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit.

Table 5. The multivariate logistic regression for preoperative and postoperative mortality risk factors

Parameters	OR	95% CI lower-upper	<i>p</i>
Low FVC% (<60)	3.96	0.95-16.43	0.058
Prior cardiac operation history	4.40	1.19-16.20	0.026
Tricuspid valve repair at operation	5.30	1.33-21.00	0.018

FVC: Forced vital capacity; OR: Odds ratio; CI: Confidence interval.

muscle function after the surgical procedure were observed in the operated patients with increased lung dysfunction as a result of atelectasis.^[21,22] The LVAD is placed into the thoracic cavity, and the volume of heart chambers shows limited reverse remodeling following LVAD implant. All of the factors described above may cause the respiratory mechanism to be affected poorly.

Furthermore, pulmonary function improves after heart transplantation. This improvement may be explained with diminishing cardiothoracic index, decreased left ventricular end-diastolic pressure, decompression of the pulmonary circulation, and reverse remodeling of pulmonary vascular resistance after transplantation.^[23-25] Likewise, review of the literature reveals that spirometric values return to baseline within three months after the surgical procedure in patients undergoing thoracotomy for coronary artery bypass graft or valvular heart disease.^[26,27] However, it is not the case for patients with LVAD implantation. Mohamedali *et al.*^[10] evaluated PFTs in the pre- and postoperative periods. They showed a significant reduction in lung volumes after LVAD operation. However, they used two different types of devices (Heartmate II™ and HeartWare™) for operation. Pulmonary functions were found to worsen after implantation of the HeartWare™ patients, although the difference was not statistically significant, while a significant decline in pulmonary functions according to the baseline was shown in the Heartmate II™-implanted patients after the operation. These results support that poor PFT results before operation may not improve after operation; they can even be worse than baseline values in this particular patient group. Device type may have an effect on the impairment of pulmonary function. This situation can be explained by the different operation procedures and how device dimensions affect the diaphragm's motion during breathing. Therefore, we assessed the HeartWare™-implanted patients in the present study to prevent confounders. According to our study results, although the low FVC% group had a higher

mortality ratio, we found no significant association between the low FVC% (<60) and 28-day mortality.

The secondary outcome measures of the study suggest that the number of ventilator-free days is shorter and the length of ICU stay is longer in patients with a low FVC% (<60). The long-term mechanical ventilation use may explain the prolonged ICU stay in this group. In light of these findings, low respiratory volume in the preoperative period can be used to predict complications and morbidity rates after device implantation. According to the results, the quality of life of these patients may not be improved quickly or completely on the following days after the operation.

This study is the first to investigate the effect of low FVC% (<60%) on early mortality following LVAD implantation. Although our study population was homogeneous in terms of the implanted device in the same timeframe, it has several limitations. First, the sample size is small, particularly for the low FVC% group; therefore, the study is underpowered. This may be the cause of the insignificant statistical results. As the patients with low FVC% may be considered high-risk patients for this operation in the preoperative period due to frailty situation, they may not be referred to the operation. Of note, it should be considered that reaching a sufficient number of patients with low FVC% for cardiac surgery may be difficult. Second, this is a single-center study and, thus, it is difficult to generalize the study results to the overall population. Third, missing data due to the absence of PFTs and the exclusion of ICU patients whose health situation was not suitable to perform PFTs may have led to a selection bias. Although there are many confounders for mortality in this patient group, our variables used in the logistic regression model are consistent with the literature. Another limitation is that chest X-ray examination for complications is difficult, particularly for patients having thoracic surgery and under follow-up in the ICU. There is no data about preoperative pulmonary function evaluation in the literature for this patient group. Therefore, we adapted the restrictive pattern classification of the ATS to assess the patients.

Although we were unable to reach a positive result on mortality with this classification. Longer ICU and hospitalization time in the low FVC% group may point to increased cost in treatment.

In conclusion, patients with low percentage of forced vital capacity had an increased 28-day mortality rate, although it did not reach statistical significance. These findings suggest an increased morbidity of this type related to prolonged duration of mechanical ventilation and length of intensive care unit stay in these patients. Therefore, this special patient group should be assessed carefully before the operation. Additionally, further large-scale studies using different evaluation methods for pulmonary function stratification would guide the assessment of patients with low percentage of forced vital capacity.

Acknowledgment

The authors acknowledge and thank the American Thoracic Society (ATS); the ATS Methods in Epidemiologic, Clinical, and Operations Research (MECOR) Program; and particularly Damon Scales and Neill Adhikari for their supports about designing of the study.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Wiesenthaler GM, O Driscoll G, Jansz P, Khaghani A, Strueber M; HVAD Clinical Investigators. Initial clinical experience with a novel left ventricular assist device with a magnetically levitated rotor in a multi-institutional trial. *J Heart Lung Transplant* 2010;29:1218-25.
2. Lietz K, Long JW, Kfoury AG, Slaughter MS, Silver MA, Milano CA, et al. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. *Circulation* 2007;116:497-505.
3. Birks EJ, George RS, Hedger M, Bahrami T, Wilton P, Bowles CT, et al. Reversal of severe heart failure with a continuous-flow left ventricular assist device and pharmacological therapy: a prospective study. *Circulation* 2011;123:381-90.
4. Meyer AL, Malehsa D, Bara C, Haverich A, Strueber M. Implantation of rotary blood pumps into 115 patients: a single-centre experience. *Eur J Cardiothorac Surg* 2013;43:1233-6.
5. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009;361:2241-51.
6. Dell'Aquila AM, Schneider SR, Schlarb D, Redwan B, Sindermann JR, Ellger B, et al. Initial clinical experience with the HeartWare left ventricular assist system: a single-center report. *Ann Thorac Surg* 2013;95:170-7.
7. Goldstein DJ, Oz MC, Rose EA. Implantable left ventricular assist devices. *N Engl J Med* 1998;339:1522-33.
8. Birks EJ, Yacoub MH, Banner NR, Khaghani A. The role of bridge to transplantation: should LVAD patients be transplanted? *Curr Opin Cardiol* 2004;19:148-53.
9. Cowger J, Sundaeswaran K, Rogers JG, Park SJ, Pagani FD, Bhat G, et al. Predicting survival in patients receiving continuous flow left ventricular assist devices: the HeartMate II risk score. *J Am Coll Cardiol* 2013;61:313-21.
10. Mohamedali B, Bhat G, Yost G, Tatoes A. Changes in Spirometry After Left Ventricular Assist Device Implantation. *Artif Organs* 2015;39:1046-50.
11. Lung function testing: selection of reference values and interpretative strategies. American Thoracic Society. *Am Rev Respir Dis* 1991;144:1202-18.
12. Rubenfeld GD, Angus DC, Pinsky MR, Curtis JR, Connors AF Jr, Bernard GR. Outcomes research in critical care: results of the American Thoracic Society Critical Care Assembly Workshop on Outcomes Research. The Members of the Outcomes Research Workshop. *Am J Respir Crit Care Med* 1999;160:358-67.
13. Saxena P, Luthra S, Dhaliwal RS, Rana SS, Behera D. Early changes in pulmonary functions after mitral valve replacement. *Ann Thorac Med* 2007;2:111-7.
14. Hosenpud JD, Stibolt TA, Atwal K, Shelley D. Abnormal pulmonary function specifically related to congestive heart failure: comparison of patients before and after cardiac transplantation. *Am J Med* 1990;88:493-6.
15. Cohen A, Katz M, Katz R, Hauptman E, Schachner A. Chronic obstructive pulmonary disease in patients undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1995;109:574-81.
16. Naum CC, Sciruba FC, Rogers RM. Pulmonary function abnormalities in chronic severe cardiomyopathy preceding cardiac transplantation. *Am Rev Respir Dis* 1992;145:1334-8.
17. Dimopoulou I, Daganou M, Tsintzas OK, Tzelepis GE. Effects of severity of long-standing congestive heart failure on pulmonary function. *Respir Med* 1998;92:1321-5.
18. Olson TP, Denzer DL, Sinnett WL, Wilson T, Johnson BD. Prognostic value of resting pulmonary function in heart failure. *Clin Med Insights Circ Respir Pulm Med* 2013;7:35-43.
19. Nanas S, Nanas J, Kassiotis C, Alexopoulos G, Samakovli A, Kanakakis J, et al. Respiratory muscles performance is related to oxygen kinetics during maximal exercise and early recovery in patients with congestive heart failure. *Circulation* 1999;100:503-8.
20. Meyer FJ, Borst MM, Zugck C, Kirschke A, Schellberg D, Kübler W, et al. Respiratory muscle dysfunction in congestive heart failure: clinical correlation and prognostic significance. *Circulation* 2001;103:2153-8.
21. Lichtenberg A, Hagl C, Harringer W, Klima U, Haverich A. Effects of minimal invasive coronary artery bypass on pulmonary function and postoperative pain. *Ann Thorac Surg* 2000;70:461-5.

22. Johnson D, Kelm C, To T, Hurst T, Naik C, Gulka I, et al. Postoperative physical therapy after coronary artery bypass surgery. *Am J Respir Crit Care Med* 1995;152:953-8.
23. Agostoni P, Cattadori G, Guazzi M, Palermo P, Bussotti M, Marenzi G. Cardiomegaly as a possible cause of lung dysfunction in patients with heart failure. *Am Heart J* 2000;140:e24.
24. Krüger S, Hoffmann R, Skobel E, Breuer C, Janssens U, Hanrath P. Impairment of ventilatory parameters and exercise capacity in patients with pulmonary hypertension and chronic heart insufficiency. *Dtsch Med Wochenschr* 2002;127:839-44.
25. Agostoni PG, Guazzi M, Bussotti M, Grazi M, Palermo P, Marenzi G. Lack of improvement of lung diffusing capacity following fluid withdrawal by ultrafiltration in chronic heart failure. *J Am Coll Cardiol* 2000;36:1600-4.
26. Vaidya R, Husain T, Ghosh PK. Spirometric changes after open mitral surgery. *J Cardiovasc Surg (Torino)* 1996;37:295-300.
27. Mustafa KY, Nour MM, Shuhaiber H, Yousof AM. Pulmonary function before and sequentially after valve replacement surgery with correlation to preoperative hemodynamic data. *Am Rev Respir Dis* 1984;130:400-6.
28. Sabashnikov A, Mohite PN, Zych B, García D, Popov AF, Weymann A, et al. Outcomes and predictors of early mortality after continuous-flow left ventricular assist device implantation as a bridge to transplantation. *ASAIO J* 2014;60:162-9.