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Original Article

The effect of left ventricular assist device implantation on pulmonary vascular resistance: a single center experience

Sol ventrikül destek cihazı implantasyonunun pulmoner vasküler rezistans üzerine etkisi: tek merkez deneyimi

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Abstract

Aim: We aimed to show our single center experience on patients with left ventricular assist device (LVAD) who have higher pulmonary vascular resistance (PVR) and their follow-up.

Material and Methods: Between May 2013 and March 2022, 62 LVAD implantations performed as destination therapy because they had pulmonary vascular resistance of 4 WU or higher. During the follow-up, pulmonary artery catheterization was performed in 17 (14 males, 82,4%) of patients and analyzed performed retrospectively. The duration of follow-up, mortality, post-operative drainage, duration of intubation and intensive care unit stay, pre- and post-operative pulmonary artery catheterization parameters were analyzed.

Results: The mean age was 38±11 years. Primary etiology was dilated cardiomyopathy in 13 (76.5%) patients and ischemic cardiomyopathy in 4 (23.5%) patients. The need of post-operative extracorporeal membrane oxygenator was not seen. The median duration of intubation was 1 (range 1 to 7) day. The mean duration of pulmonary artery catheterization after LVAD implantation was 638±305 days. The PVR was 5.2WU±1.5WU and 1.9WU±1.4WU before and after the operation, respectively ($p<0.001$). Five (29.4%) of the patients were bridged to the transplantation, seven (41.2%) of patients died and five (29.4%) of patients were still alive with LVAD. The mean survival time was 53±5 months. The cumulative survival rates were 93.8%, 76.7%, and 42.6% at 2nd, 3rd, and 5th year respectively.

Conclusions: In patients who are contraindicated to heart transplantation due to high PVR, PVR decreases after LVAD and these patients can be listed for the heart transplantation.

Keywords: Heart failure; ventricular assist device; pulmonary vascular resistance

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Öz

Amaç: Pulmoner vasküler rezistansı (PVR) yüksek olan sol ventrikül destek cihazı (LVAD) implante edilmiş hastaları ve takiplerini sunmayı amaçladık.

Gereç ve Yöntemler: Mayıs 2013 ile Mart 2022 arasında, pulmoner vasküler rezistansı 4 WU veya daha yüksek olduğu için destinasyon tedavisi olarak 62 hastaya LVAD implantasyonu yapıldı. Takiplerde hastaların 17'sine (14 erkek, %82,4) pulmoner arter kateterizasyonu uygulandı ve geriye dönük olarak incelendi. Takip süresi, mortalite, ameliyat sonrası drenaj, entübasyon ve yoğun bakımda kalış süresi, ameliyat öncesi ve sonrası pulmoner arter kateterizasyon parametreleri analiz edildi.

Bulgular: Ortalama yaş 38±11 idi. Primer etyoloji 13 (%76.5) hastada dilate kardiyomiyopati ve 4 (%23.5) hastada iskemik kardiyomiyopatiydi. Ameliyat sonrası ekstrakorporeal membran oksijenatör ihtiyacı görülmedi. Medyan entübasyon süresi 1 (dağılım 1-7 gün) idi. LVAD implantasyonu sonrası ortalama pulmoner arter kateterizasyon süresi 638±305 gündü. PVR operasyon öncesi ve sonrası sırasıyla 5.2WU±1.5WU ve 1.9WU±1.4WU idi ($p<0.001$). Hastaların beşi (%29.4) nakil için köprülenmiş, yedisi (%41.2) ölmüş ve beşi (%29.4) LVAD ile yaşamına devam etmiştir. Ortalama sağkalım süresi 53±5 aydı. Kümülatif sağkalım oranları 2., 3. ve 5. yılda sırasıyla %93.8, %76.7 ve %42.6 idi.

Sonuç: Yüksek PVR nedeniyle kalp transplantasyonu kontrendike olan hastalarda LVAD sonrası PVR azalmakta ve bu hastalar kalp transplantasyonu için listeye alınabilmektedirler.

Anahtar Kelimeler: Kalp yetmezliği; ventriküler destek cihazı; pulmoner vasküler rezistans

Introduction

The gold treatment method in advanced heart failure is heart transplantation, but the small number of donors is the challenge in this regard[1]. The left ventricular assist device (LVAD) is an important treatment option in patients for whom heart transplantation is contraindicated due to high pulmonary vascular resistance (PVR)[2].

Pulmonary hypertension (PHT) is a condition that may develop secondary to left ventricular failure and is associated with increased mortality in patients with heart failure[3]. Moreover, higher PVR that is refractory to medical therapy is considered a contraindication because it is associated with high mortality after heart transplantation[4, 5]. It has been shown that heart transplantation have worse results with PVR values of 4 WU and above [5, 6].

In this study, we aimed to show our single center experience on patients with LVAD who have higher PVR and their follow-up.

Material and Methods

Between May 2013 and March 2022, 251 ventricular assist device implantations were performed in our center. Of these, 207 were isolated adult LVAD cases. 62 of them had LVAD implantation as destination therapy because they had pulmonary vascular resistance of 4 WU or higher. During the follow-up, patients who had no contraindication to being included in the heart transplantation list except for high PVR were selected and pulmonary artery catheterization was performed in 17 of patients. Data of these patients were collected and retrospectively analyzed. The duration of follow-up, mortality, post-operative drainage, duration of intubation and intensive care unit stay, pre- and post-operative pulmonary artery catheterization parameters were analyzed.

Three different LVAD devices were used: HeartWare (Medtronic Inc., Minneapolis, Minnesota, USA), HeartMate 2, and HeartMate 3 (Abbott Inc., Chicago, IL, USA). These were the devices that we implanted either via median sternotomy or via left thoracotomy, as we described previously(7).

All devices were implanted under cardiopulmonary bypass (CPB). Inhaled nitric oxide was started in all patients while weaning from CPB. Day after surgery, unfractioned heparin administration and vitamin K antagonist were started. After extubation, all patients were given sildenafil and iloprost until discharge.

Pulmonary artery catheterization was performed for all patients at least six months after implantation. Patients should be treated at least 6 months after implantation. Central venous pressure, mean pulmonary artery pressure, transpulmonary gradient, cardiac output, cardiac index, pulmonary capillary wedge pressure and pulmonary vascular resistance were calculated.

The study was approved by the local ethical committee (ASH E1/2839/2022). A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed using the SPSS software version 15 (SPSS Inc., Chicago, IL, USA). Continuous variables with normal distribution were expressed as mean ± standard deviation, with non-normal distribution were expressed as median, minimum and maximum; and categorical variables were expressed as number and percentage. The Shapiro-Wilk test, skewness and kurtosis was used for continuous variables. Paired samples T-test was used for the significance of the difference between two homogeneously distributed dependent groups, and Wilcoxon Rank Test was used for those that were non-normally distributed. Kaplan-Meier survival analysis was used. $p<0.05$ were considered statistically significant.

Results

A total of 17 patients (14 males, 82,4%) were analyzed for study. The mean age was 38±11 years and mean body mass index was 23,08±4,51 kg/m^2. The mean of right ventricle fractional area change (RV-FAC) was 24,7%±6,6%, tricuspid annular plane systolic excursion (TAPSE) 14,6mm±3mm and left ventricle end-diastolic diameter (LVEDD) 67mm±6mm. Primary etiology was dilated cardiomyopathy in 13 (76.5%) patients and ischemic cardiomyopathy in 4 (23.5%) patients. Three (17.6%) of the patients were at INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) Profile 2 and ten (58.8%) of patients were at Profile 3. Moderate and lower grade tricuspid regurgitation was present in 12 (70.6%) patients and trivial aortic regurgitation was present in only 9 (52.9%) patients. The demographics and pre-operative evaluation were summarized in Table 1.

HeartWare was implanted in 10 (58.8%) patients, HeartMate 2 in 2 (11.8%) and HeartMate 3 in 5 (29.4%) patients. The implantation was performed via median sternotomy in 12 (70.6%) patients, and left thoracotomy in 5 (29.4%) patients. Post-operative right ventricular failure was seen in only 2 (11.8%) patients and all of them were treated with medical therapy and the need of post-operative extracorporeal membrane oxygenator was not seen. The median duration of intubation was 1 (range 1 to 7) day and median duration of intensive care unit stay was 7 (range 1 to 21) days. The median post-operative day 0 drainage was 450mL (range 300 to 1450). Intra- and post-operative parameters were shown in Table 2.

The mean duration of pulmonary artery catheterization after LVAD implantation was 638±305 days. The mean follow-up duration after LVAD implantation was 1207±478 days. The pulmonary vascular resistance was 5.2WU±1.5WU and 1.9WU±1.4WU before and after the operation, respectively (p<0.001) (Figure 1). Moreover, post-operative pulmonary artery catheterization parameters were also improved compared to pre-operative period (Table 3) The mean pulmonary artery pressure decreased from 36mmHg±8mmHg to 16±6mmHg after the operation (p<0,001).

As a result of the follow-up, five (29.4%) of the patients were bridged to the transplantation, seven (41.2%) of patients died and five (29.4%) of patients were still alive with LVAD. The mean survival time was 53±5 months. The cumulative survival rates were 93.8%, 76.7%, and 42.6% at 2nd, 3rd, and 5th year respectively (Figure 2).

Table 1. Demographics and pre-operative evaluation

Male gender		n (%)
		14 (82,4%)
Height (cm)		170±10
Weight (kg)		67±17
Body Surface Area (m^2)		1,79±0,26
Body Mass Index (kg/m^2)		23,08±4,51
Age (year)		38±11
Systolic Blood Pressure (mmHg)		83±12
Heart Rate (bpm)		91±12
C-reactive Protein (mg/L)		11,98±9,55
White Blood Cell (x10^9/L)		8,6±3,5
Platelet g/dL (x10^9/L)		218±60
Hemoglobin (g/dL)		12,19±2,23
International Normalized Ratio (INR)		1,31±0,25
Albumin (g/L)		38±10
Aspartate aminotransferase (U/L)		28 (13-207)
Alanine aminotransferase (U/L)		34 (13-418)
Total Bilirubin (mg/dL)		1,6 (0,5-7,8)
Urea (mg/dL)		44 (10-147)
Creatinine (mg/dL)		1,03±0,46
Potassium (mEq/L)		4,03±0,48
Sodium (mEq/L)		134±5
Hematocrit (%)		38±6
Total Cholesterol (mg/dL)		138±42
Left Ventricle Ejection Fraction (%)		17,8±4,5
Right Ventricle Fractional Area Change (%)		24,7±6,6
Tricuspid Annular Plane Systolic Excursion (mm)		14,6±3
Left Ventricle End-Diastolic Diameter (mm)		67±6
Etiology	DCMP	13 (76.5%)
	ICMP	4 (23.5%)
Previous cardiac surgery		1 (5.9%)
INTERMACS Profile	INTERMACS 2	3 (17.6%)
	INTERMACS 3	10 (58.8%)
	INTERMACS 4	4 (23.5%)
Mechanical ventilation		0
Pre-operative IABP		3 (17.6%)
Pre-operative ECMO		0
Heart rhythm	Sinus rhythm	15 (88.2%)
	Atrial fibrillation	2 (11.8%)
Tricuspid insufficiency	Mild	5 (29.4%)
	Moderate	7 (41.2%)
	Moderate-severe	3 (17.6%)
	Severe	2 (11.8%)
Aortic insufficiency	None	8 (47.1%)
	Trivial	9 (52.9%)

DCMP: dilated cardiomyopathy, ICMP: ischemic cardiomyopathy, INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support

Table 2. Intra- and post-operative parameters		
Device type	Heartware	10 (58.8%)
	HeartMate 2	2 (11.8%)
	HeartMate 3	5 (29.4%)
Incision	Median sternotomy	12 (70.6%)
	Left thoracotomy	5 (29.4%)
Outflow anastomosis	Ascending aorta	16 (94.1%)
	Descending aorta	5 (29.4%)
Post-operative RVF		2 (11.8%)
The need of post-operative ECMO		0
Median of duration of intubation (days)		1 (1-7)
Median of duration of intensive care unit stay (days)		7 (1-21)
Median of post-operative day 0 drainage (mL)		450 (300-1450)
Median of post-operative day 1 drainage (mL)		350 (200-800)
RVF: right ventricular failure, ECMO: extracorporeal membrane oxygenator		

Table 3. Pre-, and post-operative pulmonary artery catheterization			
	Pre-operative	Post-operative	p value
Central venous pressure (mmHg)	11±4	8±3	p=0,012
Mean pulmonary artery pressure (mmHg)	36±8	16±6	p<0,001
Transpulmonary gradient (mmHg)	12±7	7±3	p=0,009
Cardiac Output (L/min)	2,5±0,7	4,2±0,8	p<0,001
Cardiac Index (L/min/m2)	1,4±0,3	2,3±0,5	p<0,001
Pulmonary capillary wedge pressure (mmHg)	25±7	15±6	p<0,001

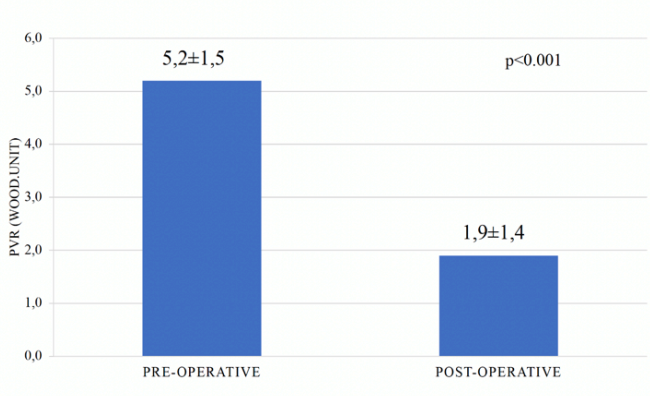

Figure 1: Pre-, and post-operative pulmonary vascular resistance

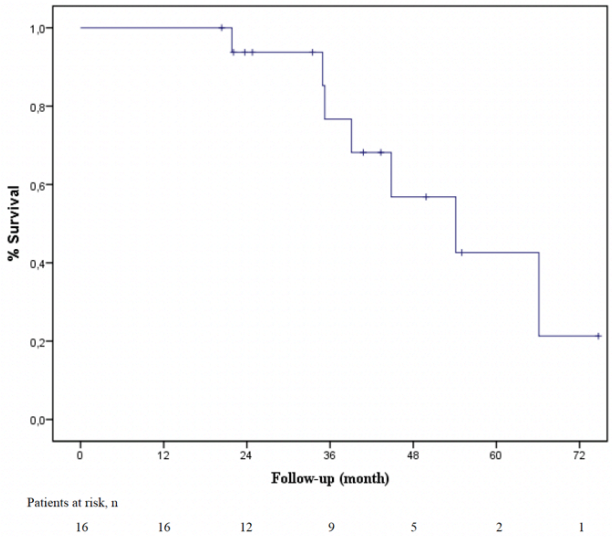

Figure 2: Survival curve of the patients

Discussion

In our study, we showed the changes in pulmonary artery catheterization parameters before and after LVAD implantation. Beside, we implanted three different continuous-flow LVADs (one axial pump and two centrifugal pumps) to the patients, and it was shown that PVR decreased statistically after device implantation. Thus, patients who could not be on the heart transplantation list before had a chance to be on the list after the LVAD's improvement for the PVR, and 30% of the patients were able to get a heart transplantation.

PHT is an important condition that increases the load on the pulmonary artery secondary to heart failure and increases the mortality of the patient by causing right heart failure[8]. Almost two-thirds of patients on the heart transplantation list have PHT[9]. The most important underlying factor in the pathophysiology of PHT is left atrial hypertension caused by left heart failure. This increases the post-capillary pressure in the pulmonary circulation[10]. Thus, the emergence of some processes that may cause remodeling in the pulmonary tree becomes inevitable.

The result of PHT developing secondary to heart failure is seen as increase in PVR during pulmonary artery catheterization, and it has been shown that high PVR measured before transplantation is associated with mortality after heart transplantation[4] . With the transplantation of the donor heart to a new recipient, the right ventricle that was previously working against normal PVR faces higher PVR in its new recipient[11]. Therefore, pre-operative evaluation should be performed in a multi-faceted manner in order to prevent right heart failure after heart transplantation.

In our study, the survival of patients with LVAD implanted with PVR high enough to be contraindication for heart transplantation

was not lower than the survival reported by international registry[12]. Although the mortality of patients with higher PVR could be increase, it can be thought that the decreased left atrial pressure after LVAD implantation contributes to the prevention of right failure with sildenafil, as well as the heart failure medications we routinely use, thus reducing mortality.

After LVAD implantation, there is a decrease in pulmonary vascular resistance due to the removal of the load on the pulmonary circulation. It has been shown that this process could take up to 6 months[13]. However, strict follow-up of the pulmonary artery catheterization after LVAD implantation is not recommended.

In the clinical evaluations of the patient groups that were bridged and not bridged with LVAD before heart transplantation; although in-hospital mortality was higher in the group with high PVR after heart transplantation, this difference was disappeared at the end of the 3rd year[14]. Survival of heart transplantation outcomes bridged with LVAD differ from each other[15].

Limitations

First, this study was not a randomized study. Second, the study had small number of patients.

Conclusion

In patients who are contraindicated to heart transplantation due to high PVR, PVR decreases after LVAD and these patients can be listed for the heart transplantation.

Declaration of conflict of interest

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

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