ORIGINAL ARTICLE

A LEFT VENTRICULAR ASSIST DEVICE IS THE BEST TREATMENT METHOD FOR ELDERLY PATIENTS WITH ADVANCED HEART FAILURE

Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2024.412
2024; 27(4):390−397

Deniz Sarp BEYAZPINAR[1]
Mehmet Emir EROL[1]
Denizhan AKPINAR[2]
Arif Okay KARSLIOĞLU[2]
Hakkı Tankut AKAY[2]
Atilla SEZGIN[2]

CORRESPONDANCE

Deniz Sarp BEYAZPINAR
Phone : +90 5324882366
e-mail : dsarpbeyazpinar@gmail.com

Received : Sep 13, 2024
Accepted : Oct 25, 2024

[1] Etlik City Hospital, Cardiovascular Surgery Department, Ankara, Turkey

[2] Başkent University, Cardiovascular Surgery Department, Ankara, Turkey

Abstract

Introduction: In end stage heart failure, cardiac transplantation is the gold standart treatment. But advance age (>65 years old) is one of the relative contrindication for cardiac trasnplantation. So these patients were left to their faith out of medical treatment.

Material and Methods: Between april 2012 to december 2023, 98 left ventricular assit device implantation patients were retrospectively analysed. Patients divided into two group according to their ages (>65; <65 years old). Group were compared according to preoperative, perioperative and postoperative parameters.

Results: The demographic datas, preoperative cardiac parameters, perioperative datas, postoperative datas and complication were similar according to statistically analyses. Statistically, the only difference between the groups is the day on which device thrombosis developed.

Conclusion: Although the number of patients on the heart transplant list increases day by day, the number of donors does not increase. For this reason, advanced age is considered a relative contraindication for heart transplantation in many clinics. For this reason, the elderly patient group is left helpless apart from medical treatment. This study showed that left ventricular assist device therapy is a good alternative to transplantation in the group of patients sentenced to medical treatment.

Keywords: Heart-Assist Devices; Heart Transplantation; Heart Failure.

INTRODUCTION

The prevalence of advanced heart failure has increased due to greater life expectancy, and the mortality rate among elderly patients (over 65 years) with advanced heart failure who are followed-up with only maximal medical treatment is 20%-30% annually (1). In addition to the high mortality rate, a greater number of hospitalization episodes and prolonged hospital stays are causing a significant rise in healthcare costs (1).

Although cardiac transplantation is accepted as the gold standard treatment for advanced heart failure, the number of patients waiting for cardiac transplantation increases daily due to a lack of donors (2). Because of this scarcity, younger patients with fewer comorbidities are prioritized over older patients. Although age is not an absolute contraindication for cardiac transplantation, many centers establish an age greater than 60 to 70 years as a relative contraindication for cardiac transplantation. Consequently, this age group is left with no hope except medical treatment.

With the increased use of left ventricular assist devices (LVADs) as a bridging therapy for cardiac transplantation in the early stages of heart failure, destination therapy has been added as an indication for ventricular assist devices (VADs). In the US in the early 2000s, patients of 70 years or older constituted only 3.5% of patients implanted with a VAD, but this proportion had increased to 10.4% by 2014 (3). Interagency Registry for Mecanically Assisted Circulatory Support (INTERMACS) reports also show that 30% of patients who have undergone a LVAD implantation were 65 years or older (4).

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial and other trials by Rose, Dembitsky, and Sarling have all shown that patients who undergo a VAD implantation have significantly better survival rates and quality of life improvement than patients receiving only medical treatment (5-8). It has also been shown, however, that the risk of developing a major complication (device thrombosis or malfunction, stroke, hemorrhage, infection, etc.) increases with every day spent with a VAD (4).

The current study compared patients 65 years of age and older using VADs as destination therapy with patients 50 to 64 years of age in terms of mortality and morbidity to determine whether this treatment choice represents a good alternative in the elderly patient population.

MATERIAL AND METHODS

After receiving Baskent University Institutional Review Board (No. KA23/280) approval according to ethical quidelines of the 1975 Declaration of Helsinki. We retrospectively analyzed 98 patients who underwent LVAD implantation as a destination therapy in our clinic between April 2012 and December 2023. Eighty-four patients received the HeartWare LVAD (Medtronic, St. Paul, MN, USA), seven received the HeartMate II (St. Jude Medical, Minneapolis, MN, USA), and seven received the HeartMate III (St. Jude Medical).The exclusion criteria embraced postoperative early mortality, cardiac transplantation in the first postoperative year, presence of a congenital heart disease, right VAD implantation, presence of preoperative acute kidney injury (AKI), chronic kidney disease, patients who were not New York Heart Assosiation (NYHA) class 3 or 4, and patients 50 years of age or younger. After the exclusion criteria were applied, 64 patients were included in the study. The patients were divided into two groups according to their age. Patients who were at least 65 years old were labeled as Group 1 (n=12; 18.75%; 10 HeartWare, 2 HeartMate III), and patients from 50 to 64 years of age were identified as Group 2 (control group) (n=42; 62.625%; 38 HeartWare, 2 HeartMate II, 2 HeartMate III). The two groups were compared by their demographic, perioperative, and postoperative data. Additionally, the groups were compared

regarding the medical treatments they received during follow-up, stroke incidence, development of right heart failure, device/driveline infection, AKI development, gastrointestinal complications, gastrointestinal and/or nose bleedings that could not be stopped via simple medical treatment, and mortality. All patients who were included in the trial were started on warfarin sodium (dosage titrated to maintain an International Normalised Ratio of blood clots time (INR) of 3.0–3.5) and acetylsalicylic acid 100 mg per oral daily for anticoagulation after VAD implantation; in cases of nontherapeutic levels of INR during routine follow-up, temporary subcutaneous injections of enoxaparin sodium were added to the anticoagulation therapy. All follow-up was done monthly, including management of LVAD device parameters and transthoracic echocardiography (TTE) to evaluate cardiac functions. Right ventricle functions were evaluated by transannular systolic plane excursion (TAPSE) and right ventricle fractional area change (FAC). All patient data included in the trial were obtained from the database of the Başkent University School of Medicine Ankara Hospital.

Statistical Anaylsis

Kolmogorov Smirnov test was used for analyzing the normal distribution of the data. Continuous variables were expressed as mean ± SD, or median values if abnormally distributed. Categorical variables were expressed as numbers and percentages. Demographic characteristics and perioperative variables were compared using "independent samples t-test" or "Mann-Whitney-U test" for continuous variables and "chi-square test" or "Fisher's exact test" for categorical variables between patients aged 65 and under 65 after surgery. Patients were compared between groups in terms of cerebro vascular events, asist device driveline infection, assist device thrombosis, and bleeding during follow-up using Kaplan-Meier survival test. Differences between Kaplan-Meier curves were tested for significance using log-rank test. In all statistical tests, p value <0.05 was accepted as significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (Armonk, NY: IBM Corp.).

RESULTS

Table 1 presents the demographic data and preoperative cardiac parameters of both groups. No statistically significant difference between the two groups was found with the exception of age.

When compared by reoperation, there were 3 (25%) patients in the older age group and 6 (14.3%) patients in the younger age group, which was not statistically significant (*p=.99)*

Table 2 lists the perioperative data of both groups. There was no statistically significant difference between them.

In the postoperative period, 2 patients (16.6%) in the older age group and 2 patients (2.4%) in the younger group were taken into revision because of bleeding in the first 24 hours postoperatively. One patient (8.3%) in the older group and 2 (2.4%) in the younger group were taken into revision because of bleeding after the first 24 hours. There was no statistically significant difference between the groups in terms of revision due to surgical bleeding (*p*=.324).

Table 3 shows the days of hospitalization and length of intensive care unit (ICU) stay. Both of those factors were longer in the older age group, but there was no statistically significant difference.

Table 4 gives the data on postoperative AKI development, renal replacement therapy, and postoperative complications after VAD implantation. In the postoperative parameters, there was no statistically significant difference between the two groups except in day of LVAD thrombosis.

Of the 42 patients in the younger age group, 19 patients (19 HeartWare) had a stroke, whereas 9

patients (8 HeartWare, 1 HeartMate II) in the older age group had a stroke. Twelve patients (29%; 10 HeartWare, 2 HeartMate II) in the younger age group had a device thrombosis, whereas 1 patient (8.3%; HeartWare) had a device thrombosis in the older age group. Twenty patients (48%; 19 HeartWare, 1 HeartMate II) in the younger age group had a driveline infection, whereas 4 patients (25%; 4 HeartWare) in the older age group had a driveline infection.

Table 1. Preoperative demographic data and cardiac parameters

	Group 1	Group 2	p-value
Age	68.41±2.77	54.21±3.01	.001
Male gender	9 (75%)	40 (95%)	.06
BSA (m²)	1.58±0.67	1.85±0.34	.97
DM	4 (33.3%)	19 (45.2%)	.525
AF	3 (25%)	7 (16.6%)	.674
COPD	2 (16.6%)	1 (2.4%)	.121
PVD	2 (16.6%)	1 (2.4%)	.121
Preoperative EF	21.00±3.01	18.80±4.12	.09
Preoperative TAPSE	14.08±1.83	15.71±3.66	.144
Preoperative FAC	27.83±6.32	27.33±5.71	.795
Mean PAP (mmHg)	37.83±10.22	36.66±9.56	.715
PCWP (mmHg)	24.08±6.20	27.02±7.62	.227
PVR (wood unite)	5.92±18.4	4.31±10.6	.794

AF: atrial fibrillation; BSA: body surface area; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; EF: ejection fraction; FAC: fractional area change of right vetricle;PAP: pulmonary artery pressure; PCWP: pulmonary capillary wedge pressure; PVD: peripheral vascular disease; PVR: pulmonary vascular resistance; TAPSE: transannular systolic plane excursion

Table 2. Perioperative data

	Group 1	Group 2	*p*-value
CPB (min)	137.41±35.29	133.21±46.32	.773
Concomitant procedure	6 (50.0%)	18 (42.85%)	.748
Tricuspid valve annuloplasty	4 (33.3%)	10 (23.8%)	.485
Urinary output in CPB	327.5±170.93	405.83±321.22	.422

CPB: cardiopulmonary bypass

Table 3. Days of hospitalization and length of ICU stay

	Group 1	Group 2	*p*-value
Stay in hospital (days)	46.41±32.10	32.90±35.22	.238
Stay in ICU (days)	30.83±35.34	20.95±34.70	.390

ICU: intensive care unit

Table 4. Postoperative AKI development, renal replacement therapy and postoperative complications after VAD implantation

	Group 1	Group 2	p-value
Number of patients who developed AKI	7 (58.3%)	18 (42.87%)	.322
Stage of AKI			.552
0	5 (41.7%)	24 (57.13%)	
1	3 (25.0%)	7 (16.6%)	
2	3 (25.0%)	5 (11.9%)	
3	1 (16.6%)	6 (14.3%)	
Renal replacement therapy	3 (25.0%)	7 (16.6%)	.674
CVE	9 (75.0%)	19 (45.23%)	.103
Day of CVE	269.58±265.07	176.07±295.01	.327
Bleeding	4 (33.3%)	10 (23.8%)	.485
Day of bleeding	77.58±166.47	64.54±194.26	.834
LVAD thrombosis	1 (8.3%)	12 (28.6%)	.254
Day of LVAD thrombosis	14.6±50.80	165.66±328.75	.006
Driveline infection	4 (33.3%)	20 (47.6%)	.515
Day of driveline infection	149.41±255.54	178.02±315.03	.774

CVE: cerebrovascular event; LVAD: left ventricular assist device

Days spent with the device were 788.75±255.54 for the older age group and 952.95±798.17 for the younger age group. There was no statistically significant difference between the groups in this comparison (p=.367). There were 8 (66.6%) mortalities in the older age group and 17 (40.5%) in the younger group. There was no statistically significant difference (p=.188). Six patients (14.3%) were bridged to cardiac transplantation in the younger age group during the first year after LVAD implantation, whereas no patients were bridged to cardiac transplantation in the older group.

DISCUSSION

Since LVAD began being used as a destination therapy, the number of patients over 65 years of age undergoing LVAD implantation has continually increased. According to the annual INTERMACS reports, approximately 40% of patients undergoing a LVAD implantation are 65 or older, and the average age of a patient undergoing a LVAD implantation has increased to 57±1.0 year (9).

The main finding of our trial is that LVAD systems can be used in the treatment of advanced stage heart failure in older patients equally and as effectively as in younger patients. The data that inspired this conclusion include the absence of difference in the preoperative comorbidities of the groups, both groups having very similar preoperative TTE and catheterization findings, and there being no statistically significant difference regarding mortality. Despite the older group having a longer hospitalization time and longer ICU stay, there was no statistically significant difference between the groups.

LVAD systems are lifesaving technologies for treating advanced stage heart failure as a bridge to transplantation or as destination therapy, but device-related complications, complications

secondary to medical treatment started after device implantation, and complications secondary to the patient's comorbidities are possible. Stroke is the complication that most reduces quality of life in patients who have undergone LVAD implantation. Coffin and Yoshioka show that there is a correlation between age and stroke, with the risk of stroke being double in patients older than 70 years (10,11), but our study found no statistically significant difference between the groups in terms of stroke incidence or day of cerebrovascular event. Studies by Harvey and Frontera have similarly shown that age is not a risk factor for stroke (12,13).

Lushaj et al. report similar results to those of our study, finding no statistically significant difference between age groups regarding revision due to surgical bleeding (14). In our study, there was no statistically significant difference between the groups in terms of major bleeding or the postoperative day on which the bleeding occurred. By contrast, a study by Caraballo found that the risk of bleeding was greater in the older age group (15). Increased tissue fragility and acquired-type von Willebrand syndrome were shown as the causes of this result. That study also states that the older patients had more comorbidities and worse preoperative right ventricle functions (15). Yoshioka et al. (10) describe similar findings to those of Caraballo. The major difference between our study and those two is that, in our study, the patient groups had no differences in preoperative comorbidities, right ventricle functions, or perioperative parameters, so the groups were more homogeneous.

One of the more feared complications after LVAD implantation is device thrombosis. In addition to causing device malfunction, device thrombosis is an important cause of mortality, morbidity, and stroke.

In our study, there was no statistically significant difference between the two groups in terms of device thrombosis incidence. Yoshioka et al. found that LVAD thrombosis is seen more often in the older age group, whereas Carabello et al. found the opposite (10-15). When we compared groups according to day of thrombosis, there was a statistically significant difference in terms of the day of thrombosis development,we showed that device thrombosis developed earlier in the older patient group if it did occur. No other study was found in the literature that examined the day of implantation thrombosis development. One of the more significant causes of LVAD thrombosis development is the inflow cannula drawing in adjacent tissues. We believe that the reason for earlier thrombosis development in older patients may be the elongation of tissues caused by the degradation of the tissue collagen, especially in the chordae. Additionally, adaptation to medications can be lower in elderly patients than in younger patients.

Another possible major complication after LVAD implantation is AKI. Our study found no statistically significant difference between the two groups in terms of AKI development, which is similar to the result of Lushaj's study (14). The risk of AKI development is greater in older patients after LVAD implantation (16).

There was no statistically significant difference between the two groups in terms of infection. Critsinelis et al. found a correlation between age and infection, which they hypothesize is caused by older patients having lower serum albumin levels because of malnutrition (17). In that study, patients older than 75 years were compared with all age groups. In our study, the two compared groups had closer ages. Consequently, there was a conflicting result.

Postoperative right ventricular failure is one of the more significant causes of morbidity and mortality after LVAD implantation (4). In our study, there was no statistically significant difference between the two groups in terms of postoperative right ventricular failure. We believe that this is explained by correct patient selection in the preoperative period.

Age is a risk factor for prolonged hospital stay after LVAD implantation (18-20). In our study, there was no statistically significant difference between the two groups in terms of length of stay in the hospital or length of stay in the ICU, but there was a numerical difference, albeit not statistically significant. This is an expected result considering that older patients are more fragile and their healing process is slower and longer. Additionally, Kirklin et al. found no difference in terms of hospital and ICU stay between different age groups, but they indicate that some of the older patients went to rehabilitation centers instead of their homes after being discharged (18).

In our study, there was no statistically significant difference between the groups in terms of mortality. This result contributes to our main hypothesis that LVAD implantation is an efficacious method of treatment in the older patient group with advanced heart failure. By contrast, age was identified as a risk factor for prolonged hospital stay and mortality after LVAD implantation in studies conducted by Kirklin and Colts (18,19).

Every day spent with a device after LVAD implantation increases the risk for any complication. In our study, there was no statistically significant difference between the groups in terms of days spent with a device. Similarly, statistical analysis showed no statistically significant difference between the groups regarding complications. Morgan et al. report similar results (20). In that study, there was no statistically significant difference between patients older than 70 years and young patients in terms of mortality, morbidity, and complications. There was also no difference in hospital or ICU stay, but the sample group was small. Advanced age is not a negative predictor for survival and is not a contraindication for LVAD implantation. There was no statistically significant difference between the groups in terms of survival. Studies by Frazier and Rao have shown no correlation between age and survival (21,22), but age was a risk factor for high mortality and worse survival in studies by Kirklin and Sandler (4,18).

Our results show that LVAD implantation has similar risks in the older age group compared to younger patients except in the occurrence of day of assist device thrombosis. We believe that the use of LVAD is a very good alternative choice of treatment for older patients with a relative contraindication for cardiac transplantation.

Consequently, we consider that LVAD implantation is an important modality in the treatment of advanced heart failure and can be implemented with acceptable mortality and morbidity rates in patients older than 65 years with advanced heart failure and relative contraindications for cardiac transplantation in the presence of correct echocardiographic assessment, appropriate management of the patients' preoperative comorbidities, and close monitoring and follow-up during the perioperative and postoperative periods.

The most important limitation in our study is that it was a single-center study with a relatively small patient sample group. Multicenter studies with much larger sample sizes will deepen the understanding of the best medical and surgical treatment in the elderly patient population.

REFERENCES

1. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics.—2020 update: a report from the American Heart Association. Circulation 2020;141(9):e139-e596. (DOI: 10.1161/CIR.0000000000000757).
2. Gude E, Andreassen AK, Arora S, et al. Acute renal failure early after heart transplant: risk factors and clinical consequences. ClinTransplant. 2010;24(6):E207-E213. (DOI: 10.1111/j.1399-0012.2010.01225.x).
3. Rali AS, Vuddanda V, Masoomi R, et al. Trends in LVADs in the geriatric population: demographics for 2003–2014. J Card Fail 2017;23:S17. (DOI: 10.1016/j.card-fail.2017.07.059).
4. Kirklin JK, Naftel DC, Pagani FD, et al. Sixth INTERMACS annual report: a 10,000-patients database. J Heart Lung Transplant 2014;33(6):555–64. (DOI: 10.1016/j.healun.2014.04.010).

5. Rose EA, Moskowitz AJ, Packer M, et al. The REMATCH trial: rationale design and end points Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure. Ann Thoracic surg, 1999; 67(3); 723-30. (DOI: 10.1016/s0003-4975(99)00042-9).

6. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 2001;345(20);1435-43. (DOI: 1056/NEJMoa012175).

7. Dembitsky WP, Tector AJ, Park S, et al. Left ventricular assist device performance with long-term circulatory support: lessons from the REMATCH trial. Ann Thorac Surg 2004;78(6);2123-30. (DOI: 10.1016/j.athoracsur.2004.02.030).

8. Starling RC, Naka Y, Boyle AJ, et al. Results of the post-U.S. Food and Drug Administration approval study with a continuous flow left ventricular assist device as a bridge to heart transplantation: a prospective study using the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). J Am Coll Cardiol 2011;57(19):1890-8. (DOI: 10.1016/j.jacc.2010.10.062).

9. Kormos RL , Cowger J , Pagani FD, et al. The Society of Thoracic Surgeons Intermacs Database Annual Report: Evolving Indications, Outcomes, and Scientific Partnerships. Ann Thorac Surg 2019;107(2):341-353. (DOI: 10.1016/j.athoracsur.2018.11.011).

10. Yoshioka D, Toda K, Ono M, et al. Clinical Results, Adverse Events, and Change in End-Organ Function in Elderly Patients With HeartMateII Left Ventricular Assist Device. Circ J. 2018;82(2):409-418. (DOI: 10.1253/circj.CJ-17-0881).

11. Harvey L, Holley C, Roy SS, et al. Stroke after left ventricular assist device implantation: Outcomes in the continuous-flow era. Ann Thorac Surg 2015;100(2):535–541. (DOI: 10.1016/j.athoracsur.2015.02.094).

12. Frontera JA, Starling R, Cho SM, et al. Risk factors, mortality, and timing of ischemic and hemorrhagic stroke with left ventricular assist devices. J Heart Lung Transplant 2017;36(6): 673–683. (DOI:10.1016/j.healun.2016.12.010).

13. Coffin ST, Haglund NA, Davis ME, et al. Adverse neurologic events in patients bridged with long-term mechanical circulatory support: A device-specific comparative analysis. J Heart Lung Transplant 2015;34(12):1578–85. (DOI:10.1016/j.healun.2015.08.017).

14. Lushaj EB, Badami A, Osaki S, et al. Impact of age on outcomes following continuous-flow left ventricular assist device implantation. Interac Cardiovasc Thorac Surg 2015;20(16);743–748. (DOI:10.1093/icvts/ivv051).

15. Caraballo C, DeFilippis EM, Nakagawa S, et al. Clinical Outcomes After Left Ventricular Assist Device Implantation in Older Adults. JACC Heart Fail 2019;7(12):1069–78. (DOI: 10.1016/j.jchf.2019.10.004).

16. Sandner SE, Zimpfer D, Zrunek P, et al. Age and outcome after continuous-flow left ventricular assist device implantation as bridge to transplantation. J Heart Lung Transplant 2009;28(4):367–72. (DOI: 10.1016/j.healun.2009.01.008).

17. Critsinelis AC, Kurihara C, Kawabori M, et al. Predictive value of preoperative serum albümin levels on outcomes in patients undergoing LVAD implantation. J Card Surg. 2018;33(8):469-478. (DOI:10.1111/jocs.13745).

18. Kirklin JK, Naftel DC, Pagani FD, et al. Seventh INTERMACS annual report: 15,000 patients and counting. J Heart Lung Transplant 2015;34(12):1495–1504. (DOI: 10.1016/j.healun.2015.10.003).

19. Cotts WG, McGee EC, Myers SL, et al. Predictors of hospital length of stay after implantation of a left ventricular assist device: an analysis of the INTERMACS registry. J Heart Lung Transplant 2014;33(7):682–688. (DOI: 10.1016/j.healun.2014.02.022).

20. Morgan JA, Nemeh HW, Paone G, et al. Should Left Ventricular Assist Devices be Implanted in Patients Seventy Years of Age and Older: A Comparative Analysis. Heart Surg Forum 2014;17(4):E182-6. (DOI: 10.1532/hsf98.2014386).

21. Frazier OH, Rose EA, Oz MC, et al. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. J Thorac Cardiovasc Surg 2011;122(6):1186–95. (DOI: 10.1067/mtc.2001.118274)

22. Rao V, Oz MC, Flannery MA, Catanese KA, Argenziano M, Naka Y. Revised screening scale to predict survival after insertion of a left ventricular assist device. J Thorac Cardiovasc Surg 2003;125:855–62. (DOI: 10.1067/mtc.2003.111).