Outcomes of orthotopic heart transplantation and left ventricular assist device in patients aged 65 years or more with end-stage heart failure

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ABSTRACT

Age has traditionally been a limiting factor for advanced heart failure (HF) therapies. Orthotopic heart transplantation (OHT) age guidelines have become less restrictive, and left ventricular assist devices (LVADs) are increasingly utilized as destination therapy for patients ≥ 65 years. Although indications differ, we assessed outcomes for both modalities in this older population. We reviewed charts of consecutive advanced HF therapy recipients aged ≥ 65 years at our center from 2012 to 2016. Of 118 patients evaluated, 46 (39%) received an LVAD and 72 (61%) received OHT. Gender, body mass index, and rate of prior sternotomy were similar between groups; OHT recipients were younger, less likely to have diabetes mellitus, and more likely to have HF due to ischemic etiology. Forty-six percent of patients receiving LVADs were urgent need (Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS] profile 1–2), compared to 29% of patients receiving OHT (United Network for Organ Sharing 1A criteria; $P = 0.068$). OHT recipients had shorter lengths of stay and better 1-year survival compared to LVAD recipients. Although many centers do not offer advanced HF therapy to patients aged ≥ 65 years, our results indicate that age alone should not be prohibitive for advanced HF therapy, particularly OHT.

KEYWORDS Advanced age; heart failure; left ventricular assist device; orthotopic heart transplantation

Heart failure (HF) is a burden known firsthand by approximately 6 million Americans.¹ Nearly half of these individuals die within 5 years of their initial diagnosis, with the overwhelming majority of HF deaths occurring in persons aged ≥ 65 years.^{1,2} In 2006, the International Society for Heart and Lung Transplantation increased the age of orthotopic heart transplantation (OHT) eligibility to 70 years³; however, many transplant centers remain hesitant to consider patients ≥ 65 years of age as candidates for OHT due, in part, to concerns regarding quality years of life gained.^{3,4} Although some studies revealed that OHT in the geriatric population yields outcomes similar to those in the younger, general population, the utilization of left ventricular assist devices (LVAD) in the geriatric population has been postulated as an

acceptable alternative therapy for these end-stage HF patients.^{5,6} Unfortunately, largely attributable to low center volume, there are few studies that simultaneously evaluate outcomes of these two interventions for patients aged ≥ 65 years.^{7,8} Our analysis describes 1-year surgical outcomes of patients aged ≥ 65 years who underwent advanced HF therapy (OHT or LVAD) at our high-volume center.

METHODS

We reviewed charts of consecutive advanced HF patients aged ≥ 65 years who underwent surgery (OHT or LVAD) at the Baylor Annette C. and Harold C. Simmons Transplant Institute at Baylor University Medical Center in Dallas, Texas, between 2012 and 2016. Patient demographics,

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Table 1. Characteristics of patients aged ≥ 65 years with heart failure receiving a left ventricular assist device or orthotopic heart transplantation ($n = 118$)

Variable	LVAD ($n = 46$)	OHT ($n = 72$)	<i>P</i> value
Age (years)	71 $\pm$ 4	68 $\pm$ 2	<0.001
Men	39 (85%)	61 (85%)	0.993
Body mass index (kg/m ²)	28 $\pm$ 5	28 $\pm$ 4	0.442
Prior sternotomy	27 (59%)	46 (64%)	0.571
Diabetes mellitus	23 (50%)	13 (18%)	<0.001
Ischemic etiology	5 (11%)	48 (67%)	<0.001
Urgent need ^a	21 (46%)	21 (29%)	0.068

LVAD indicates left ventricular assist device; OHT, orthotopic heart transplant.

^aFor left ventricular assist device recipients, this means Interagency Registry for Mechanically Assisted Circulatory Support profile 1 or 2. For transplant recipients, this means United Network for Organ Sharing status code 1A.

comorbidities, and outcomes were recorded. We used United Network for Organ Sharing status designation of 1A and Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles of 1 or 2 to indicate “urgent need” for OHT and LVAD recipients, respectively. This study was approved by the Baylor University Medical Center institutional review board with a waiver of informed consent.

Comparisons between OHT and LVAD recipients’ demographics and presurgical clinical states were evaluated using two-sample *t* and chi-square tests or Wilcoxon rank sum and Fisher’s exact tests, as appropriate. Individuals who received an LVAD and subsequently underwent OHT were analyzed as LVAD-only and were censored at the time of OHT. Continuous variables are reported as mean $\pm$ standard deviation or median (quartile 1, quartile 3) if skewed. Categorical variables are presented as frequency (percentage). Hypothesis testing was conducted using two-tailed alternatives and a type I error rate of 5%. Analyses were performed in SAS 9.4.

RESULTS

Of 118 patients, 72 (61%) received OHT and 46 (39%) received an LVAD. Gender, body mass index, and rates of prior sternotomy were similar between groups; however, OHT recipients were younger (68 $\pm$ 2 years vs 71 $\pm$ 4 years; $P < 0.001$), had a lower rate of diabetes (18% vs 50%; $P < 0.001$), and had a higher rate of ischemic etiology of HF (67% vs 11%; $P < 0.001$) (Table 1). Twenty-one (29%) OHT and 21 (46%) LVAD recipients were urgent need ($P = 0.068$). The OHT recipients had shorter postoperative lengths of stay (9 [7, 17] days vs 15 [11, 24] days; $P < 0.001$) and better 1-year survival compared to LVAD recipients (mortality: 11% vs 33%; $P = 0.004$). Of the LVAD recipients who died within 1 year, 8 (53%) were urgent

Table 2. Surgical outcomes of patients aged ≥ 65 years with heart failure receiving a left ventricular assist device or orthotopic heart transplantation

	LVAD ($n = 46$)	OHT ($n = 72$)	<i>P</i> value
Length of stay (days)	15 [11, 24]	9 [7, 17]	<0.001
Rejection > 1R ^a	—	3 (4%)	—
Infection	—	11 (15%)	—
Cancer	—	12 (17%)	—
Gastrointestinal bleed	4 (9%)	—	—
Stroke	4 (9%)	—	—
Pump thrombus/exchange	5 (11%)	—	—
LVAD to OHT	5 (11%)	—	—
Average hospitalizations per person per year ^b	0.5 [0, 2]	0 [0, 1]	0.153
1-Year mortality	15 (33%)	8 (11%)	0.004

LVAD indicates left ventricular assist device; OHT, orthotopic heart transplant.

^aInternational Society for Heart and Lung Transplant rejection scale.

^bAdjusted for time alive during study time frame.

need. The median mortality-adjusted hospitalizations per person per year were similar between the therapy types (0.5 [0, 2] vs 0 [0, 1]; $P = 0.119$). Though the nature of complications was not directly comparable, the frequencies of complications were similar between the therapy groups (Table 2).

DISCUSSION

In this study of 118 patients aged ≥ 65 years who received either OHT or LVAD for end-stage HF, we found that LVAD recipients were significantly older, had more comorbidities, and were more critically ill than OHT recipients. The 1-year survival rate was significantly better for those who received OHT, and OHT recipients also experienced a significantly shorter postoperative length of stay than LVAD recipients.

Previous studies report comparable survival rates between these two interventions, regardless of age.^{7,9} Yet, many candidates are deemed ineligible for OHT due to advanced age.¹⁰ Though our results indicate a worse survival outcome for LVAD recipients, it is important to emphasize that 46% of LVAD recipients had an INTERMACS profile of 1 or 2, which is associated with increased mortality.^{11,12} With this degree of criticality, it would be unreasonable to expect these urgent-need patients to be considered for OHT listing in the setting of prolonged wait times for a suitable donor. With a limited supply of donor organs and vast improvements in LVAD technology, LVADs have become the default destination therapy for older, high-risk HF patients.¹³ As a result, patients with (ambiguously defined) advanced age are more likely to receive an LVAD than OHT, if they receive any intervention at all. Our center is somewhat of an anomaly,

with 72 (61%) receiving OHT and 46 (39%) receiving treatment via LVAD.

Age remains a limiting factor for advanced HF therapy; however, larger recent studies have further elucidated that patients of advanced age and few comorbidities have a survival rate similar to that of their younger counterparts.^{4,6,14–16} Jha et al demonstrated that frailty, independent of age, increases mortality and morbidity following advanced HF therapy.¹⁷ Though advanced age is associated with increased frailty, characteristics of overall functionality (i.e., grip strength, agility, energy level, cognition) more fully determine an individual's frailty and future ability of self-care.^{18,19} Jha et al found that the severity of patients' frailty and quality of life (QoL) significantly improved following surgery.¹⁷ Because LVADs require more maintenance and self-care following implantation than OHT, LVAD recipients who have greater capacity for self-care have larger gains in postsurgical QoL than those who are care dependent.²⁰ It has been shown that both OHT and LVAD improve the QoL and physical ability of patients within the first 3 months following surgery.²¹ Patients receiving OHT had more sustained increased physical ability beyond 3 months and fewer hospital visits between 3 and 12 months compared to patients receiving LVAD. Arnold et al acknowledged that LVADs are capable of improving QoL but reported that up to one-third of LVAD recipients continue to experience poor QoL in the year following implantation, particularly among recipients with severe comorbidities.¹⁰ A comprehensive evaluation incorporating both frailty and cognition would be a more sophisticated approach to advanced HF therapy selection than ruling out individuals based on chronological age alone.²²

Our study's analytic framework, which simultaneously analyzed two advanced HF therapies in patients aged ≥ 65 years, brings with it new scientific insights. With stringent, universal guidelines for OHT eligibility, candidates for LVAD are often more diverse in both population (i.e., gender and race) and health status.²³ Without universally accepted guidelines for LVAD candidacy, LVAD recipients are nearly always significantly more ill than their OHT counterparts, which creates an inherent selection bias.²⁴ In our experience, patients aged ≥ 65 years had more favorable outcomes with OHT than LVAD, although LVAD recipients were more critically ill. It may be beneficial to act earlier with LVAD implantation to prevent further decompensation by decelerating comorbidities and decreasing frailty while waiting for OHT.^{25,26} Given our findings, knowing that patients aged ≥ 65 are less likely to receive OHT and that studies reveal no differences in survival or rejection following OHT with young or old donor hearts, it is crucial that transplant centers also consider expanding the donor age criterion to help decrease the overall organ shortage and demand.^{27,28}

Because these results are from a single center, the data may not be widely generalizable. Additionally, the complications between therapy types were not directly comparable; for

example, rejection and malignancies are relevant complications following OHT but are not relevant following LVAD (Table 2). The definition we created for urgent need may not be equivalent between treatment groups. Finally, we were unable to perform fully adjusted analyses to examine the independent effect of treatment type on mortality due to the small number of events.

In conclusion, in our study of patients with end-stage HF aged ≥ 65 years, we found that LVAD recipients were significantly older, had more comorbidities, and were more critically ill than OHT recipients. We also observed an approximate 89% 1-year survival rate among OHT recipients. Although many centers do not offer advanced HF therapy in patients aged ≥ 65 years, our results indicate that age alone should not be prohibitive for advanced HF therapy, particularly OHT.

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