

Retrospective Cohort Study

# Optimal timing of same-admission orthotopic heart transplantation after left ventricular assist device implantation

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## Abstract

### AIM

To investigate the impact of timing of same-admission orthotopic heart transplant (OHT) after left ventricular assist device (LVAD) implantation on in-hospital mortality and post-transplant length of stay.

### METHODS

Using data from the Nationwide Inpatient Sample from 1998 to 2011, we identified patients 18 years of age or older who underwent implantation of a LVAD and for whom the procedure date was available. We calculated in-hospital mortality for those patients who underwent OHT during the same admission as a function of time from LVAD to OHT, adjusting for age, sex, race, household income, and number of comorbid diagnoses. Finally, we analyzed the effect of time to OHT after LVAD implantation on the length of hospital stay post-transplant.

### RESULTS

Two thousand and two hundred patients underwent implantation of a LVAD in this cohort. One hundred and sixty-four (7.5%) patients also underwent OHT during

the same admission, which occurred on average 32 d (IQR 7.75–66 d) after LVAD implantation. Of patients who underwent OHT, patients who underwent transplantation within 7 d of LVAD implantation ("early") experienced increased in-hospital mortality (26.8% *vs* 12.2%,  $P = 0.0483$ ) compared to patients who underwent transplant after 8 d ("late"). There was no statistically significant difference in age, sex, race, household income, or number of comorbid diagnoses between the early and late groups. Post-transplant length of stay after LVAD implantation was also not significantly different between patients who underwent early *vs* late OHT.

## CONCLUSION

In this cohort of patients who received LVADs, the rate of in-hospital mortality after OHT was lower for patients who underwent late OHT (at least 8 d after LVAD implantation) compared to patients who underwent early OHT. Delayed timing of OHT after LVAD implantation did not correlate with longer hospital stays post-transplant.

**Key words:** Mechanical circulatory support; Orthotopic heart transplant; Bridge to transplant; Left ventricular assist device outcomes

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**Core tip:** The optimal timing of same-admission orthotopic heart transplantation (OHT) after the implantation of a left ventricular assist device (LVAD) is unknown. The need for clinical stability and time to recover from surgery is counterbalanced by the risk of LVAD complications and formation of adhesions and scarring, particularly when OHT is considered early after LVAD implantation. We reviewed adult patients in the Nationwide Inpatient Sample who underwent same-admission OHT after LVAD between 1998 and 2011. Compared to early transplantation after LVAD, OHT after 8 d of LVAD implantation was associated with decreased mortality risk without increased post-transplant length of stay.

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## INTRODUCTION

Heart failure (HF) affects an estimated 5.8 million people in the United States and contributes to over 300000 deaths every year<sup>[1,2]</sup>. It is the most common cause of hospital admission and readmission in people greater than 65 years of age, annually accounting for over 2.4 million hospitalizations<sup>[2,3]</sup> and \$39 billion in healthcare costs<sup>[1,4]</sup>. Although most patients respond favorably to standard medical treatment, a considerable number of

patients progress to end-stage HF refractory to medical therapy<sup>[5]</sup>. Currently, orthotopic heart transplant (OHT) is the gold standard therapy for these patients<sup>[6-8]</sup>, but the number of donor hearts available for transplantation is far fewer than the number of patients on the transplant list. For this reason, left ventricular assist devices (LVADs), a class of electromechanical devices used for cardiac circulatory support, are increasingly being used to bridge patients to cardiac transplantation<sup>[5]</sup>.

The REMATCH trial in 2001 showed significant mortality reductions in patients placed on a pulsatile-flow LVAD compared to standard medical treatment<sup>[9]</sup>. Several subsequent studies since have confirmed the survival benefit of both the older pulsatile and newer continuous-flow LVADs<sup>[10-13]</sup>. Although LVADs have substantially reduced mortality in end-stage HF patients, the absolute mortality rates still remain high. A large portion of this mortality is attributable to complications and other occurrences during the patient's stay in the hospital<sup>[14]</sup>. In-hospital mortality rates as high as 27% have been reported in patients after LVAD surgery<sup>[15-18]</sup>.

As the rate of LVAD implantation in the United States continues to increase<sup>[19-22]</sup>, effective recommendations for the in-hospital management of LVAD implantation are needed. Although the majority of cardiac transplants performed after LVAD implantation occur after a patient has been discharged from hospital, there is an important cohort of patients who cannot be discharged from hospital post-LVAD implant due to severe right ventricular failure, arrhythmias refractory to oral therapy, and infectious complications. Patients bridged to OHT with a LVAD achieve similar survival rates as patients who undergo direct heart transplant<sup>[14]</sup>, but there is little data to guide clinicians on the optimal timing of same-admission OHT after LVAD implantation. Though patients receiving LVADs may be considered for OHT while still inpatients, some have argued that performing OHT early after LVAD placement poses an increased risk of morbidity and mortality to patients.

Past studies on the appropriate use and outcomes of LVADs have been mostly limited to institutional experience and case series of select populations. While such descriptive investigations are useful, they are often limited by small sample size and variation between institutions and comparison groups. We used the Nationwide Inpatient Sample (NIS), the largest national database of hospitalizations in the United States with data from over 36 million hospitalizations, to assess the optimal timing of OHT after LVAD implantation. The NIS dataset complements the UNOS database and INTERMACS dataset with additional information on patient comorbidities, additional same-hospitalization procedures, hospital and center characteristics, and markers of patient's socioeconomic status including insurance provider and regional income quartiles. In addition, the NIS dataset contains data on both LVAD and inpatient OHT, which are not simultaneously available in the UNOS or INTERMACS databases.

We analyzed a patient cohort who had OHT performed

during the same admission after LVAD implantation. We hypothesized that early OHT after LVAD implantation would be associated with higher mortality than late OHT, and that the hospital length of stay (LOS) after early OHT would be less than LOS after late OHT.

## MATERIALS AND METHODS

### Data source

The NIS, from the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality is the largest database of all-payer inpatient discharge information, sampling approximately 20% of all non-federal United States hospitals and including approximately 9 million hospital admissions each year. It contains discharge data from over 5000 hospitals located across 45 states, of which approximately 1200 hospitals are sampled each year to create a stratified sample of United States hospitals. Each NIS entry includes all diagnosis and procedure codes of activity during the patient's hospitalization at the time of discharge, as well as patient demographics, hospital characteristics, and short-term complications of the hospitalization.

### Study design and cohorts

This was a retrospective cross-sectional study using the NIS between 1998 and 2011. We identified all hospitalizations from 1998 to 2011 of patients 18 years of age or older who underwent LVAD implantation and for whom the hospital day of each procedure was available. Procedures during the hospitalization in addition to LVAD placement, including OHT, extracorporeal membrane oxygenation, intubation, hemodialysis, invasive hemodynamic monitoring, and surgical revision were identified by associated ICD9 codes (Supplementary Table 1). Additionally, hospital mortality and perioperative morbidity such as post-operative infections, cardiopulmonary complications, and hemorrhagic complications requiring endoscopy were identified.

### Statistical analysis

The statistical methods of this study were reviewed by Dr. David Ouyang from the Stanford University Department of Medicine. Python 2.7 (Python Software Foundation, [www.python.org](http://www.python.org)) and R 2.13 (R Foundation, [www.r-project.org](http://www.r-project.org)) were used for statistical analysis. *P*-values for numerical and count data were calculated by two-sided *t*-tests and  $\chi^2$  tests, respectively, with significance thresholds of 0.05. The multivariate linear model evaluating post-LVAD OHT mortality was performed using a generalized linear model with input variable selection by Bayesian Information Criteria (BIC). The dependent variable was in-hospital mortality. Independent variables of age, gender, median income, race, number of comorbidities, LVAD era, and timing of OHT were evaluated in the model.

## RESULTS

### Baseline patient characteristics

We identified 2200 patients greater than 18 years of

age between 1998 and 2011 who underwent LVAD implantation and for whom hospital day of procedure was listed (66.4% of all LVAD patients in the NIS database 1998-2011). Comparison of baseline characteristics between this study sample and all LVAD patients in the NIS 1998-2011 database confirmed that our study sample is representative of the entire patient population. The two groups were well matched based on age, sex, household income, prevalence of comorbidities, length of stay, and number of comorbidities, however there were more patients without documented race in the overall group (Supplementary Table 2). The mean age of all patients was 53.4 years (SD = 13.7, range = 18-92 years). Baseline patient demographics, patient comorbidities, and hospital characteristics were well matched between LVAD patients with and without same-admission OHT (Table 1). Most LVAD implantations were performed in large (87.8%), urban (99.1%), teaching hospitals (92.4%). The most common comorbidities were diabetes (17.8%), disorders of lipid metabolism (14.1%), hypertension (13.7%), history of or current use of tobacco (6.5%), and BMI  $\geq 30$  kg/m<sup>2</sup> (4.4%). The mean day of LVAD implantation was 9.4 d (SD = 12.5 d) into the hospitalization. The overall in-hospital mortality rate was 26.8%, with respiratory failure, cardiac dysrhythmias, right HF, and renal failure among the most frequent in-hospital complications immediately following LVAD implantation (Table 2).

Our dataset includes patients from both the pulsatile-flow era (1998-2005) and the continuous-flow era (2006-2011) of mechanical support (Table 3). Comparing the two eras, there was significantly less mortality in the continuous-flow era compared to the pulsatile-flow era (20.4% vs 43.0%; *P* < 0.001) even as patients were older (55.4 years vs 53.2 years; *P* < 0.001) and suffering more comorbid diagnoses (13.5 vs 10.6; *P* < 0.001). During the continuous-flow era, fewer patients received OHT during the same admission as LVAD implantation (3.8% vs 17.3%; *P* < 0.001), and mechanical support was more frequently initiated in large (88.8% vs 85.1%; *P* = 0.002), teaching (94.4% vs 87.1%; *P* < 0.001) institutions. Median household income quartile and race distribution also were different between the two eras, although there was no difference in gender ratio of patients.

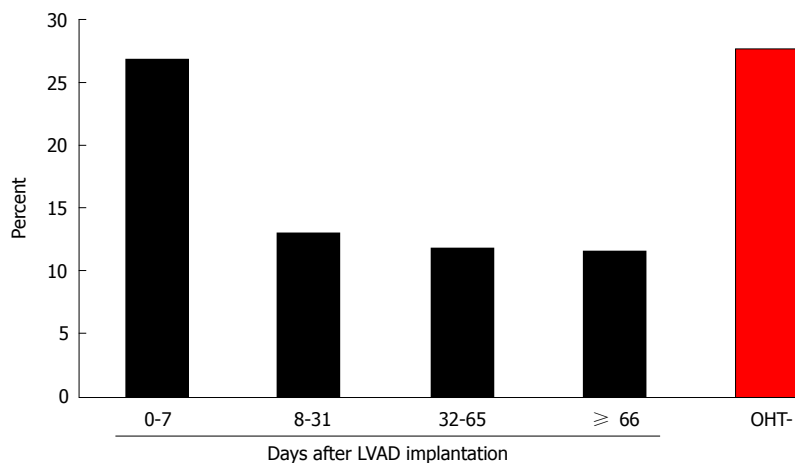
### Timing of post-LVAD OHT

Of the patients who underwent LVAD implantation, 164 (7.5%) also underwent OHT during the same admission. OHT occurred a median of 32 d (IQR 7.75-66 d) after LVAD implantation. Patients who underwent OHT at least 8 d after LVAD implantation experienced significantly lower mortality compared to patients who underwent OHT earlier (26.8% vs 12.2%; *P* = 0.048; Table 1 and Figure 1). Baseline patient demographics, patient comorbidities, and hospital characteristics were similar between the early and late OHT groups. LVAD patients who underwent late OHT also had lower mortality compared to LVAD patients who were not transplanted (12.2% vs 27.0%; *P* < 0.001). However, LVAD patients who underwent early

**Table 1** Baseline demographics for patients who waited 0-7 d, 8-31 d, 32-65 d, and  $\geq 66$  d for an orthotopic heart transplant after left ventricular assist device implantation

	0-7 d (n = 41)	8-31 d (n = 38)	32-65 d (n = 42)	$\geq 66$ d (n = 43)	No OHT (n = 2036)
Length of stay, mean $\pm$ SD	39.3 $\pm$ 33.2	48.9 $\pm$ 25.6	85.8 $\pm$ 40.1	151.2 $\pm$ 52.6	37.1 $\pm$ 34.6
Length of stay after OHT, mean $\pm$ SD	23.8 $\pm$ 21.4	21.7 $\pm$ 15.8	27.6 $\pm$ 37.1	27.1 $\pm$ 22.8	NA
Mortality, n (%)	11 (26.8)	5 (13.2)	5 (11.9)	5 (11.6)	564 (27.3)
Age, mean $\pm$ SD	50.6 $\pm$ 12.6	48.6 $\pm$ 12.7	47.4 $\pm$ 15.3	46.3 $\pm$ 13.1	55.4 $\pm$ 13.2
Sex, n (%)					
Male	33 (80.5)	32 (84.2)	35 (83.3)	34 (79.1)	1525 (74.9)
Female	8 (19.5)	6 (15.8)	7 (16.7)	9 (20.9)	511 (25.1)
Race, n (%)					
White	25 (61.0)	19 (50.0)	23 (54.8)	22 (51.2)	1185 (58.2)
Black	3 (7.3)	5 (13.2)	8 (19.0)	6 (14.0)	330 (16.2)
Hispanic	3 (7.3)	7 (18.4)	2 (4.8)	5 (11.6)	125 (6.1)
Asian/Pacific Islander	2 (4.9)	0 (0.0)	1 (2.4)	4 (9.3)	44 (2.2)
Native American	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.2)
Other or unknown	8 (19.5)	7 (18.4)	8 (19.0)	6 (14.0)	347 (17.0)
Median household income, n (%)					
\$1-24999	4 (9.8)	8 (21.1)	8 (19.0)	8 (18.6)	447 (22.0)
\$25000-34999	10 (24.4)	10 (26.3)	10 (23.8)	7 (16.3)	454 (22.3)
\$35000-44999	12 (29.3)	8 (21.1)	10 (23.8)	13 (30.2)	509 (25.0)
\$45000 or more	129 (29.3)	12 (31.6)	14 (33.3)	14 (32.6)	579 (28.4)
Unknown	3 (7.3)	0 (0.0)	0 (0.0)	1 (2.3)	47 (2.3)
Comorbidities					
Diabetes	8 (19.5)	5 (13.2)	4 (9.5)	2 (4.7)	373 (18.3)
Hyperlipidemia	5 (12.2)	2 (5.3)	3 (7.1)	3 (7.0)	297 (14.6)
Hypertension	5 (12.2)	1 (2.6)	2 (4.8)	2 (4.7)	291 (14.3)
History of smoking	5 (12.2)	2 (5.3)	0 (0.0)	0 (0.0)	137 (6.7)
BMI $\geq 30$ kg/m <sup>2</sup>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	96 (4.7)
No. of comorbid diagnoses, mean $\pm$ SD	11.9 $\pm$ 3.1	12.3 $\pm$ 3.0	12.5 $\pm$ 3.2	12.5 $\pm$ 3.2	12.8 $\pm$ 2.9
Location of hospital, n (%)					
Rural	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	17 (0.8)
Urban	41 (100.0)	38 (100.0)	42 (100.0)	43 (100.0)	2017 (99.1)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
Size of hospital, n (%)					
Small	4 (9.8)	0 (0.0)	0 (0.0)	2 (4.7)	32 (1.6)
Medium	7 (17.0)	6 (15.8)	5 (11.9)	0 (0.0)	211 (10.4)
Large	30 (73.2)	32 (84.2)	37 (88.1)	41 (95.3)	1791 (88.0)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
Teaching status of hospital, n (%)					
Nonteaching	1 (2.4)	1 (2.6)	2 (4.8)	1 (2.3)	160 (7.9)
Teaching	40 (97.6)	37 (97.4)	40 (95.2)	42 (97.7)	1874 (92.0)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)

SD: Standard deviation; BMI: Body mass index; LVAD: Left ventricular assist device; OHT: Orthotopic heart transplant.

**Figure 1** Percent in-hospital mortality by quartiles of wait time for orthotopic heart transplant after left ventricular assist device implantation and no orthotopic heart transplant after left ventricular assist device implantation. Percent mortality for each quartile was calculated as number of deaths per quartile by total number of patients per quartile. LVAD: Left ventricular assist device; OHT: Orthotopic heart transplant.

transplant did not experience a similar mortality benefit (26.8% vs 27.0%;  $P = 0.946$ ). The reduced mortality

trend with delayed OHT post-LVAD was observed in both the pulsatile-flow (13.8% vs 36.4%;  $P = 0.081$ )

**Table 2** Complications in hospitalized patients with or without same admission orthotopic heart transplant after left ventricular assist device

	Early OHT ( <i>n</i> = 41)	Late OHT ( <i>n</i> = 123)	OHT- ( <i>n</i> = 2036)	Total ( <i>n</i> = 2200)
Acute renal failure	24 (58.5)	64 (52.0)	963 (47.3)	1051 (47.8)
Reoperation	28 (68.3)	87 (70.7)	803 (39.4)	918 (41.7)
Bleeding requiring transfusion	7 (17.1)	30 (24.4)	780 (38.3)	817 (37.1)
Acute respiratory failure	8 (19.5)	37 (30.1)	518 (25.4)	563 (25.6)
Sepsis	2 (4.9)	17 (13.8)	233 (11.4)	252 (11.5)
Postoperative cardiac complication	7 (17.1)	15 (12.2)	234 (11.5)	256 (11.6)
Acute liver failure	3 (7.3)	9 (7.3)	224 (11.0)	236 (10.7)
Device failure	0 (0.0)	4 (3.3)	62 (3.0)	66 (3.0)
Stroke	1 (2.4)	1 (0.8)	53 (2.6)	55 (2.5)

All pairwise comparisons of early *vs* late OHT were not statistically significant ( $P > 0.05$ ). OHT: Orthotopic heart transplant.

**Table 3** Baseline demographics of all left ventricular assist device patients, left ventricular assist device patients from 1998-2005 (pulsatile-flow era), and left ventricular assist device patients from 2006-2011 (continuous-flow era)

	All LVADs ( <i>n</i> = 2200)	1998-2005 ( <i>n</i> = 589)	2006-2011 ( <i>n</i> = 1611)	<i>P</i> -value <sup>a</sup>
Mortality, <i>n</i> (%)	590 (26.5)	253 (43.0)	329 (20.4)	< 0.001
Same admission OHT, <i>n</i> (%)	164 (7.5)	102 (17.3)	62 (3.8)	< 0.001
Early same admission OHT, <i>n</i> (%)	41 (25.0)	22 (21.6)	19 (30.6)	0.373
Early same admission OHT mortality, <i>n</i> (%)	11 (26.8)	8 (36.4)	3 (15.8)	0.319
Length of stay after early OHT, mean $\pm$ SD	23.8 $\pm$ 21.4	30.9 $\pm$ 26.0	17.6 $\pm$ 14.3	0.054
Late same admission OHT, <i>n</i> (%)	123 (75.0)	80 (78.4)	43 (69.4)	0.849
Late same admission OHT mortality, <i>n</i> (%)	15 (12.2)	11 (13.8)	4 (9.3)	0.774
Length of stay after late OHT, mean $\pm$ SD	25.6 $\pm$ 26.9	26.1 $\pm$ 22.9	25.4 $\pm$ 29.0	0.883
Length of stay, mean $\pm$ SD	40.5 $\pm$ 38.9	44.7 $\pm$ 48.6	39.0 $\pm$ 34.6	0.008
Age, mean $\pm$ SD	53.4 $\pm$ 13.7	53.2 $\pm$ 13.4	55.4 $\pm$ 13.4	< 0.001
Sex, <i>n</i> (%)				
Male	1659 (75.4)	433 (73.5)	1226 (76.1)	0.23
Female	541 (24.6)	156 (26.5)	385 (23.9)	
Race, <i>n</i> (%)				< 0.001
White	1274 (57.9)	327 (55.5)	947 (58.8)	
Black	352 (16.0)	62 (10.5)	290 (18.0)	
Hispanic	142 (6.5)	28 (4.8)	114 (7.1)	
Asian/Pacific Islander	51 (2.3)	13 (2.2)	38 (2.4)	
Native American	5 (0.2)	1 (0.2)	4 (0.2)	
Other or unknown	376 (17.1)	143 (24.3)	148 (9.2)	
Median household income, <i>n</i> (%)				< 0.001
\$1-24999	475 (21.6)	88 (14.9)	387 (24.0)	
\$25000-34999	491 (22.3)	126 (21.4)	365 (22.7)	
\$35000-44999	552 (25.1)	141 (23.9)	411 (25.5)	
\$45000 or more	631 (28.7)	214 (36.3)	417 (25.9)	
Unknown	51 (2.3)	20 (3.4)	31 (2.4)	
Comorbidities				
Diabetes	391 (17.8)	91 (15.4)	300 (18.6)	0.097
Hyperlipidemia	310 (14.1)	61 (10.4)	249 (15.5)	0.003
Hypertension	309 (14.0)	88 (14.9)	221 (13.7)	0.508
History of smoking	131 (6.0)	29 (4.9)	102 (6.3)	0.257
BMI $\geq$ 30 kg/m <sup>2</sup>	96 (4.4)	12 (2.0)	84 (5.2)	0.002
No. of comorbid diagnosis, mean $\pm$ SD	12.7 $\pm$ 2.9	10.6 $\pm$ 2.9	13.5 $\pm$ 2.5	< 0.001
Location of hospital, <i>n</i> (%)				0.73
Rural	17 (0.8)	5 (0.8)	12 (0.7)	
Urban	2181 (99.1)	583 (99.0)	1598 (99.2)	
Unknown	2 (0.1)	1 (0.2)	1 (0.1)	
Size of hospital, <i>n</i> (%)				0.002
Small	38 (1.7)	20 (3.4)	18 (1.1)	
Medium	229 (10.4)	67 (11.4)	162 (10.1)	
Large	1931 (87.8)	501 (85.1)	1430 (88.8)	
Unknown	2 (0.1)	1 (0.2)	1 (0.1)	
Teaching status of hospital, <i>n</i> (%)				< 0.001
Nonteaching	165 (7.5)	75 (12.7)	90 (5.6)	
Teaching	2033 (92.4)	513 (87.1)	1520 (94.4)	
Unknown	2 (0.1)	1 (0.2)	1 (0.1)	

<sup>a</sup>Pairwise *t*-test or  $\chi^2$  test for patients before 2006 and patients 2006 and afterwards. SD: Standard deviation; BMI: Body mass index; LVAD: Left ventricular assist device; OHT: Orthotopic heart transplant.



**Table 4** A generalized multivariate linear model to evaluate post-left ventricular assist device orthotopic heart transplant mortality (positive estimates reflect positive association with increased mortality)

	Regression coefficient	Standard error	P-value
Age	0.003	0.002	0.158
Female sex	0.071	0.075	0.342
Caucasian race	-0.01	0.027	0.695
Median household income	0.013	0.027	0.638
Number of comorbidities	0.006	0.010	0.518
Years 1998-2005	0.096	0.060	0.113
Early OHT	0.2	0.067	0.004 <sup>a</sup>

<sup>a</sup>P-value < 0.05. OHT: Orthotopic heart transplant.

and continuous-flow eras (9.3% vs 15.8%;  $P = 0.672$ ), although due to small sample numbers in each subgroup, the differences were not statistically significant (Table 2). Multivariate linear model also confirmed the strong association between early OHT after LVAD and in-hospital mortality, independent of patient age, LVAD era, comorbidities, and demographics (Table 4).

Comparing the quartiles of post-LVAD OHT transplant times, there was no statistically significant difference in post-transplant length of stay ( $23.8 \pm 21.4$  d for the first quartile,  $21.7 \pm 15.8$  d for the second quartile,  $27.6 \pm 37.1$  d for the third quartile,  $27.1 \pm 22.8$  d for the fourth quartile;  $P = 0.6571$  comparing first quartile to other quartiles; Table 1). However, as expected, patients who waited longer after LVAD implantation for OHT had longer overall hospital stays ( $39.3 \pm 33.2$  d for the first quartile,  $48.87 \pm 25.6$  d for the second quartile,  $85.8 \pm 40.1$  d for the third quartile,  $151.2 \pm 52.6$  d for the fourth quartile;  $P < 0.001$  comparing first quartile to other quartiles; Table 1).

## DISCUSSION

Our study addresses the difficult question of timing of same-admission OHT after LVAD implantation. Using the inpatient data on procedure timing from the NIS 1998-2011, we show that mortality risk significantly decreases in patients who undergo OHT at least 8 d after LVAD implantation. We also report that post-transplant length of stay is independent of the timing of OHT after LVAD.

For patients who receive an LVAD for bridge to transplant therapy (BTT), the optimal timing of post-LVAD OHT is controversial. The need for clinical stability and time to recover from major surgery is counterbalanced by the risk of LVAD complications and the formation of adhesions and scarring, particularly when OHT is considered early after LVAD implantation.

The high failure rate of the early, pulsatile-flow LVADs had in part led to the initial 1999 UNOS allocation algorithm giving LVAD patients 30 d of IA status on the transplant list. The elective nature of the 30-d IA status allows for optimization of management prior to transplant and suggests the time period immediately post-mechanical support is often not the optimal time for transplant. Our data showing that delaying post-

LVAD transplant can lead to superior outcomes is consistent with the excellent long term outcomes of BTT mechanical support, pushing some groups to question the justification of elective IA status<sup>[23]</sup>.

Our study, using a large national database, solidifies and extends previous findings that early transplantation after initiation of BTT mechanical support is associated with worse outcomes. In the pulsatile-flow era of LVAD, John *et al*<sup>[24]</sup> (2010) had shown that cardiac transplants done less than 6 wk after LVAD confer higher mortality risk in patients, and Gammie *et al*<sup>[25]</sup> (2003) and Ashton *et al*<sup>[26]</sup> (1996) have similarly reported optimal timing to be 2 wk after LVAD implantation. With the advantage of procedural timing data of patients who underwent same admission LVAD implantation and transplant, we add to those findings by showing there is an increased mortality associated with early same-admission transplant after LVAD in the continuous flow era.

During the study period between 1998 and 2011, there was a significant increase in the number of LVAD implantations, but patient characteristics of this population - including timing of LVAD, usage of invasive hemodynamic monitoring, and timing of post-LVAD OHT - has remained relatively unchanged. Our sample patient population is representative of LVAD patients studied in other databases with regards to age, gender, race, and other demographic characteristics and also mortality trends between the pulsatile and continuous-flow eras. Without randomized control trials to better characterize the optimal management and timing of transplant after LVAD, our study describes representative clinical practice and trends in outcomes associated with changing practice patterns.

Our study has a few limitations. First, the NIS is a deidentified administrative database dependent on the appropriate coding of individual ICD-9-CM codes. Studies using such databases are susceptible to errors related to coding such as undercoding complications or variation in the application of diagnostic codes. This database also lacks many details available in registries, and unmeasured confounders cannot be excluded. Additionally, the NIS only captures events during the hospitalization, so complications and adverse events after discharge are not recorded. This limitation is counterbalanced by the larger sample size relative to other studies and the absence of reporting bias as compared to studies relying upon the

institutional experiences from a few specialized centers. Additionally, patients who undergo LVAD implantation have long hospital stays that capture most, if not all, of the acute complications causing morbidity and mortality. Finally, the ability of the NIS to capture detailed LVAD implantation and OHT data provided advantages in answering our central question over either the INTERMACS or UNOS databases, which capture largely LVAD or transplant data, respectively.

It is important to note that our cohort only assessed outcomes of OHT after LVAD placement in hospitalized patients. This represents a minority of patients (7.5%) in practice, as most institutions prefer to wait 2-3 mo after LVAD implantation to list patients for cardiac transplantation. Nevertheless, there will continue to be patients in the future who receive same-admission OHT after LVAD implantation, and our study provides meaningful guidelines on the timing of such OHT.

In conclusion, our analysis suggests that delayed same-admission OHT after LVAD implantation decreases mortality risk without increasing post-transplant length of stay, and, therefore, may be the preferred option in such a clinical setting. This new understanding of the optimal timing of same-admission OHT after LVAD implantation can greatly improve patient outcomes, although prospective data will be needed to enhance the validity of our findings.

## COMMENTS

### Background

Heart failure (HF) affects an estimated 5.8 million people in the United States and contributes to over 300,000 deaths every year. Although most patients respond favorably to standard medical treatment, a considerable number of patients progress to end-stage HF refractory to medical therapy. Orthotopic heart transplant (OHT) is currently the gold standard therapy for these patients, but the number of donor hearts available for transplantation is far fewer than the number of patients on the transplant list. For this reason, left ventricular assist devices (LVADs), a class of electromechanical devices used for cardiac circulatory support, are increasingly being used to bridge patients to OHT. The optimal timing of when patients with LVADs should be bridged to OHT is an important consideration for patient care and has yet to be characterized.

### Research frontiers

As the rate of LVAD implantation in the United States continues to increase, effective recommendations on the in-hospital management of LVAD implantation are needed. The optimal timing of when to bridge patients with LVADs to OHT remains controversial and is an active area of research.

### Innovations and breakthroughs

Few groups have studied the impact of timing of same-admission OHT after LVAD on patient outcomes. Past studies on the appropriate use and outcomes of LVADs have been mostly limited to institutional experience and case series of select populations. The authors used the Nationwide Inpatient Sample (NIS), the largest national database of hospitalizations in the United States with data from over 36 million hospitalizations, to assess the optimal timing of OHT after LVAD implantation. It has been suggested that performing OHT early after LVAD placement confers an increased risk to patient. The study corroborates these claims and concludes that early OHT after LVAD placement (less than 8 d) is associated with increased in-hospital mortality. Therefore, depending on the clinical scenario, it might be reasonable for physicians to defer OHT immediately after LVAD placement.

## Applications

This study offers recommendations for cardiologists and cardiac surgeons on the optimal timing of same-admission OHT after LVAD implantation. It also summarizes the demographics and characteristics of LVAD and post-LVAD OHT patients in the United States.

## Terminology

Left ventricular assist device (LVAD): A class of electromechanical devices that help the left ventricle pump blood to the rest of the body; Orthotopic heart transplant (OHT): A procedure in which the patient's heart is removed and replaced with a donor heart.

## Peer-review

Very interesting and clinically relevant question with novel use of the NIS database. Overall well written with interesting findings.

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