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What If the Destination Is Transplant? Outcomes of Destination Therapy Patients Who Were Transplanted

Pavan Atluri,* Scott C. Silvestry,† Jeffrey J. Teuteberg,‡ Carmelo A. Milano,§ Craig H. Selzman,¶ and Jennifer A. Cowger‖

Abstract: We sought to characterize patients who underwent heart transplant (HTx) following destination therapy (DT) implant in the combined ENDURANCE/ENDURANCE Supplemental Trials (DT/DT2). A post hoc analysis of the DT/DT2 trials was performed. Baseline characteristics and adverse events between the HTx and no-HTx cohorts were analyzed. Reasons for transplant were examined. Time to HTx was compared with contemporaneous HVAD BTT trial patients. Of the 604 DT/DT2 HVAD patients, 80 (13%) underwent HTx. The HTx cohort was younger (53.6 ± 11.1 *vs.* 65.2 ± 10.8, $P < 0.0001$) with fewer Caucasians (60.0% *vs.* 76.5%, $P = 0.002$), less ischemic cardiomyopathy (42.5% *vs.* 58.8%, $P = 0.01$), and atrial fibrillation (38.8% *vs.* 54.4%, $P = 0.01$). The HTx cohort had longer 6-minute walk distances (183.6 *vs.* 38.0 m, $P = 0.02$). Most HTx in DT/DT2 were categorized as elective (n = 63, 79%) and, of these, 70% were due to modification of behavioral issues and weight loss. Adverse events were the main indication for urgent HTx (n = 17, 21%). Median times to HTx were longer in DT/DT2 (550.0 days) *versus* BTT/lateral (285.2 days). In this post hoc analysis of the DT/DT2 trials, over 1 in 10 underwent heart transplantation within 3 years of HVAD support. In DT therapy patients, consideration for transplant following DT VAD implant may be feasible. *ASAIO Journal* 2022; 68;178–183

Key Words: Left-ventricular assist device, heart transplant, destination therapy, HVAD

The gold standard of care for patients with advanced heart failure resistant to medical therapy is heart transplantation.[1] However, due to the limited availability of donor hearts and restrictive transplant eligibility criteria, only a group of carefully selected patients may receive a heart transplant.[2] Due to the scarcity of donor hearts, left-ventricular assist devices (LVAD) were developed to bridge transplant-eligible, advanced heart failure patients to a suitable donor heart (BTT). The use of LVAD as BTT provides additional time to optimize hemodynamics, improves end-organ function, and allows patients to be discharged home for further rehabilitation, all of which may reduce waitlist mortality and improve posttransplant outcomes. While originally utilized for BTT strategies, VAD therapy has advanced technologically, allowing for long-term support for the duration of a patient's life, termed destination therapy (DT).

Based upon historical reasons, reimbursement policies of the Center of Medicare and Medicaid Services and many private payors require patients to be assigned a DT or BTT indication preimplant based on the intended treatment strategy for the LVAD. However, predicting transplant eligibility at the time of LVAD can be challenging. Despite limitations in forecasting a patient's ultimate transplant candidacy following VAD, many payors require transplant listing before LVAD implant to quality for BTT reimbursement. In the Society of Thoracic Surgery INTERMACS database, only 25% of patients were categorized as BTT at the time of implant, yet 34% underwent transplant by 5 years.[3] Furthermore, as patients experience extended time on LVAD support, their treatment goals and transplant candidacy may change such that the original designation may not mirror the eventual postimplant strategy.[4–8]

Recent clinical trials and publications have focused on the use of long-term LVAD support for advanced heart failure patients.[9–13] The combined ENDURANCE and ENDURANCE Supplemental trials sought to evaluate the use of the HeartWare HVAD System (Medtronic, Inc. Minneapolis, MN) implanted as DT in patients deemed ineligible for heart transplant.[12,13] Reported reasons a patient was not a transplant candidate in the ENDURANCE and ENDURANCE Supplemental trials included the following: age, IDDM, obesity, renal insufficiency, pulmonary hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, cancers, and social issue/compliance. Notably, since some of these exclusion criteria are modifiable, some of the patients enrolled in the ENDURANCE Trials ultimately went on to heart transplantation. This report seeks to describe the characteristics and adverse event profiles of all transplanted DT patients, comparing them to a contemporary cohort of patients enrolled into a BTT trial utilizing the same device (LATERAL).[14] In addition, we aimed to examine the rationale and primary factors that allow selective DT patients to become transplant eligible.

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Methods

Study Design and Definitions

The ENDURANCE and ENDURANCE Supplemental trials have been described previously.[12,13] The ENDURANCE trial was a multicenter, prospective, randomized, controlled, unblinded trial comparing the safety and efficacy of the HeartWare HVAD System to a Food and Drug Administration-approved control LVAD (HeartMate II, HMII, Abbott, Inc., Abbott Park, IL) in heart transplant ineligible, end-stage heart failure patients (n = 296 HVAD patients). The ENDURANCE Supplemental trial was a prospective, multicenter, randomized, unblinded, controlled trial to prospectively determine the effectiveness of a blood pressure management strategy on neurologic injury in patients receiving the HVAD System as DT (n = 308 HVAD patients) compared to the same control. Patients in both trials were censored if consent was withdrawn or patients were lost to follow up. The current study reports on outcomes for the combined trials through 5 years of follow up.

The DT patients on HVAD support from each trial were combined into a single DT cohort. A subgroup analysis was performed on those who received heart transplantation during the ENDURANCE and ENDURANCE Supplemental trial and those who did not. Baseline characteristics and adverse events were compared between the two cohorts. In addition, the sample of DT patients who underwent transplant were compared to those in a contemporaneous BTT cohort of HVAD patients (n = 144) enrolled into the LATERAL trial.

See Figure 1 for enrollment start and stop dates for each of the trials discussed herein.

Outcomes

Adverse Events

Adverse event rates are reported in events per patient-years through 5 years. Documented adverse events included major bleeding events, stroke, pump exchange due to thrombus, cardiac arrhythmia, major infections, renal dysfunction, and right heart failure as classified according to the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) definitions (version 3.0).

Reasons for Transplant

Reasons for transplant were reported as either "Elective" or "Urgent" with further reasoning listed within each category. Thirteen patients (16.3%) had more than one reason for transitioning to heart transplant and were, therefore, captured in more than one category.

Statistical Analysis

Descriptive statistics were used to evaluate baseline clinical and demographic characteristics. Results are reported as mean ± standard deviation for continuous variables, as percentage for binary variables, and as median [25th percentile, 75th percentile] for skewed continuous variables. Comparisons between the transplanted and nontransplanted groups are made with a Wilcoxon test for continuous variables and Fisher's exact test for categoric variables. Adverse events are reported in events per patient-year and comparisons between the transplanted and nontransplanted groups were made with Poisson regression. For all analyses, a $P \leq 0.05$ was considered statistically significant. SAS v.9.4 software (SAS Institute, Cary, NC) was used to perform all statistical analyses.

The studies were conducted in compliance with FDA regulations for Good Clinical Practice. Institutional IRB approval and patient (or authorized representative) consent was obtained before patient enrollment in the listed clinical trials above.

Results

Comparison of Characteristics of Destination Therapy Patients According to Transplant Status

A total of 604 DT patients were included in this study. Within this patient cohort, 80 patients (13%) received heart transplant over the course of five years with a median time to transplant of 550 days. At baseline, DT patients receiving a transplant were significantly younger than nontransplant DT patients (53.6 ± 11.1 *vs.* 65.2 ± 10.8 years, $P < 0.0001$), less likely to be white (60.0% *vs.* 76.5%, $P = 0.002$) and had a lower frequency of ischemic cardiomyopathy (42.5% *vs.* 58.8%, $P = 0.01$). Transplanted DT patients were also less likely to have major comorbidities, including atrial fibrillation, PVD, and CAD. DT patients undergoing subsequent transplant also had better preimplant renal function (BUN 23.4 ± 12.9 *vs.* 28.5 ± 14.4 mg/dL, $P = 0.003$; creatinine 1.3 ± 0.4 *vs.* 1.4 ± 0.4 mg/dL, $P = 0.01$) compared with DT patients who were not transplanted. Although the INTERMACS profiles were similar between DT patient cohorts, functional capacity using the six-minute walk test revealed transplanted DT patients walked significantly

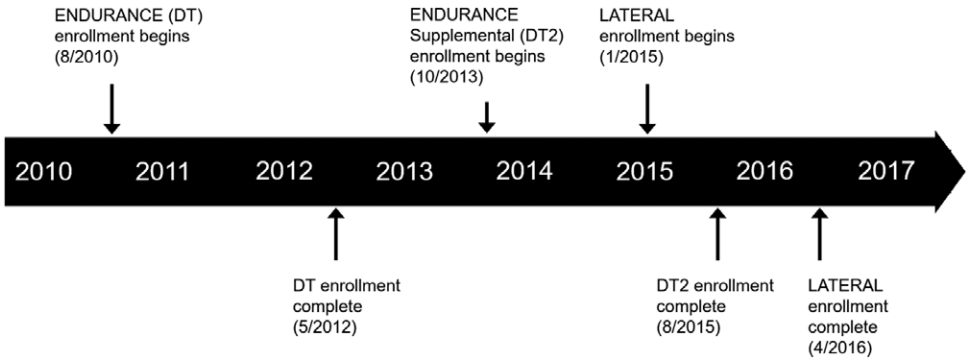

Figure 1. Enrollment for ENDURANCE, ENDURANCE Supplemental, and LATERAL trials.

farther at pre-VAD baseline than DT patients who did not receive a transplant (183.6 [0, 279.5] *vs.* 38.0 [0, 220.7] meters, $P=0.02$).

Intraoperatively at the time of HVAD implant, DT patients who later went on to heart transplant received significantly fewer transfusions with PRBCs (1.0 [0.0, 2.0] *vs.* 2.0 [1.0, 4.0] units, $P=0.0001$) and cryoprecipitate (0.0 [0.0, 0.0] *vs.* 0.0 [0.0, 2.0] units, $P=0.0007$). Although length of initial ICU stay was similar between cohorts, DT patients who were eventually transplanted had significantly shorter length of initial hospital stay (20.9 ± 11.4 *vs.* 25.4 ± 18.7, $P=0.02$) (Table 1).

A subgroup analysis was conducted on DT patients <60 years to compare the characteristics of transplanted *versus* nontransplanted patients in an age group more representative of transplant. Within the subgroup of DT patients under the age 60, those undergoing eventual transplant had lower CVP at baseline (8.6 ± 4.1 *vs.* 11.7 ± 6.1 mm Hg, $P=0.01$), fewer PRCB transfusions at implant (1.3 ± 1.6 *vs.* 3.2 ± 7.8 units, $P=0.008$), fewer cryoprecipitate transfusions at implant (1.1 ± 3.6 *vs.* 3.2 ± 7.8 units, $P=0.03$), longer 6MW test at baseline (128.1 ± 147.3 *vs.* 81.9 ± 116.8, $P=0.04$), and shorter length of index hospital stay (20.3 ± 10.1 *vs.* 25.6 ± 18.3 days,

Table 1. Baseline characteristics of patients who did or did not undergo transplant in the combined DT cohort

Characteristics	DT: Transplanted, n = 80	DT: No Transplant n = 524	*P*
Demographics			
Age, mean ± standard deviation	53.6 ± 11.1	65.2 ± 10.8	**<0.0001**
BMI (kg/m^2), mean ± standard deviation	28.8 ± 6.6	27.5 ± 5.7	0.08
Female, %	23.8%	20.4%	0.55
White, %	60.0%	76.5%	**0.002**
Medical history, %			
Ischemic etiology of heart failure	42.5%	58.8%	**0.01**
History of smoking	67.5%	68.1%	0.90
History of diabetes mellitus	43.8%	47.5%	0.55
History of atrial fibrillation	38.8%	54.4%	**0.01**
History of COPD	26.3%	25.2%	0.89
History of peripheral vascular disease	3.8%	12.2%	**0.02**
History of carotid artery disease	6.3%	15.3%	**0.04**
History of hypertension, requiring med	62.5%	71.6%	0.11
History of stroke/TIA	15.0%	17.7%	0.64
History of ICD Implant	85.0%	83.0%	0.75
History of CABG	18.8%	31.9%	**0.02**
Laboratory & hemodynamic values, mean ± standard deviation			
Blood urea nitrogen (mg/dL)	23.4 ± 12.9	28.5 ± 14.4	**0.003**
Creatinine (mg/dL)	1.3 ± 0.4	1.4 ± 0.4	**0.01**
Total bilirubin (mg/dL)	1.0 ± 0.6	1.0 ± 0.7	0.60
ALT (U/L)	36.2 ± 26.5	34.8 ± 38.4	0.31
Albumin (g/L)	35.3 ± 5.3	34.8 ± 5.1	0.42
Platelets (10^9/L)	211.7 ± 83.1	198.6 ± 72.5	0.15
Mean arterial pressure (mm Hg)	78.3 ± 10.6	78.2 ± 10.8	0.95
Mean PA pressure (mm Hg)	35.3 ± 9.5	32.3 ± 9.1	**0.04**
Central venous pressure (mm Hg)	9.6 ± 5.2	10.2 ± 5.9	0.63
PCW pressure (mm Hg)	23.5 ± 6.7	21.5 ± 7.7	0.08
PVR (Wood)	3.0 ± 1.7	2.9 ± 3.3	0.41
Echocardiogram			
LVEF (%), mean ± standard deviation	16.6 ± 5.2	17.3 ± 4.8	0.27
LVEDD (mm), mean ± standard deviation	69.4 ± 11.4	67.5 ± 11.3	0.20
Presence of LV thrombus, %	2.5%	4.4%	0.76
Tricuspid regurgitation (moderate/severe), %	40.0%	41.2%	0.90
Aortic insufficiency (moderate/severe), %	1.3%	3.6%	0.50
Intraoperative variables, mean ± standard deviation			
Cardiopulmonary bypass time (min)	87.3 ± 37.2	90.7 ± 45.5	0.89
Packed red blood cells (units)	1.0 [0.0, 2.0]*	2.0 [1.0, 4.0]*	**0.0001**
Fresh frozen plasma (units)	2.0 [0.0, 4.0]*	2.0 [1.0, 4.0]*	0.10
Platelets (units)	1.0 [0.0, 4.0]*	2.0 [1.0, 4.0]*	0.32
Cryoprecipitate (units)	0.0 [0.0, 0.0]*	0.0 [0.0, 2.0]*	**0.0007**
Concomitant tricuspid repair, %	21.3%	14.5%	0.13
Functional classification, quality of life, and length of stay, mean ± standard deviation			
KCCQ: Overall Summary Score	40.0 ± 23.5	38.7 ± 20.3	0.94
Six-minute Walk Test (m)	183.6 [0.0, 279.5]*	38.0 [0.0, 220.7]*	**0.02**
Length of ICU stay (days)	10.0 ± 9.1	11.8 ± 12.2	0.15
Length of hospital stay (days)	20.9 ± 11.4	25.4 ± 18.7	**0.02**
INTERMACS profiles, %			
1	3.8%	3.8%	>0.99
2	25.0%	31.3%	0.30
3	43.8%	41.6%	0.72
4–7	26.3%	22.9%	0.57

*Due to skewness of data, summary statistics are provided as median [25th percentile, 75th percentile].

ALT, alanine aminotransferase; BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DT, destination therapy; ICD, implantable cardioverter defibrillator; ICU, intensive care unit; KCCQ, Kansas City cardiomyopathy questionnaire; LV, left ventricle; LVEDD, left-ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; PA, pulmonary artery; PCW, pulmonary capillary wedge; PVR, pulmonary vascular resistance; TIA, transient ischemic attack.

$P=0.01$) than those under 60 years of age who remained on DT LVAD support (Table 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A623).

Comparison of Characteristics of Destination Therapy Patients Undergoing Transplant Versus Bridge to Transplant Patients

In a contemporary cohort of BTT HVAD patients (LATERAL trial, n = 144), 77 (53.5%) patients underwent transplant within 2 years. When comparing the baseline characteristics of the 80 transplanted DT patients to the BTT patients, the transplanted patients in the DT trials were statistically and clinically similar with respect to age, sex, race, BMI, BUN, Creatinine, and hospital length of stay. DT patients who were transplanted had more history of smoking (67.5% *vs.* 34.7%, $P<0.0001$), more hypertension requiring medication (62.5% *vs.* 16.7%, $P<0.0001$), larger history of stroke (15% *vs.* 4.9%, $P=0.01$), longer CPB times (87.3 ± 37.2 *vs.* 69.7 ± 48.6 minutes, $P<0.01$), higher self-reported quality of life score (40.0 ± 23.5 *vs.* 38.0 ± 21.0, $P<0.0001$), and walked further in the 6-minute walk test (135.0 ± 146.2 *vs.* 76.7 ± 135.5 meters, $P=0.01$) (**Table 2**).

Adverse Events in Patients on DT Support

During the 5-year follow-up period, rates of major adverse events on VAD were compared between heart transplant and nontransplant DT trial patients. Transplanted DT patients had significantly higher rates of GI bleeding (0.64 *vs.* 0.45 eppy, $P<0.01$) and pump exchange secondary to thrombus (0.08 *vs.* 0.03 eppy, $P<0.01$) with a lower incidence of major infection (0.62 *vs.* 0.87; $P<0.01$) and HCVA (0.02 *vs.* 0.08; $P=0.04$) compared with nontransplanted DT patients. Major bleeding, cardiac arrhythmia, driveline infection, renal dysfunction, and right heart failure events were not significantly different between the DT groups (Table 3).

The 2-year rates of major adverse events such as GI bleeding (0.70 *vs.* 0.30 eppy), stroke (0.18 *vs.* 0.10 eppy), thrombus with pump exchange (0.09 *vs.* 0.01), and driveline infection (0.21 *vs.* 0.10 eppy) in the DT transplanted patients were higher than those in the BTT lateral patients (Table 4).

Reason for Transplant in the Destination Therapy Subgroup

Of the 80 DT patients transplanted, 63 (78.8%) were transplanted electively at a median of 16.4 months after LVAD. Patients could have multiple reasons given for transitioning to elective heart transplantation. Of these reasons, the most common included improvement in compliance/social risk factors (n = 26, 41.3%), weight loss (n = 12, 19.0%), improvement in pulmonary hypertension (n = 10, 15.9%), cessation of tobacco (n = 6, 9.5%), and cancer remission (n = 4, 6.3%), transfer to or from an outside institution (n = 3, 4.8%), improved glycemic control (n = 3, 4.8%), worsening aortic insufficiency (n = 2, 3.2%), improved renal function (n = 2, 3.2%), refractory GI bleed (n = 1, 1.6%), improved cardiac function (n = 1, 1.6%), improved physical condition (n = 1, 1.6%), improved COPD (n = 1, 1.6%), and donor heart became available (n = 1, 1.6%). In the remaining 17 (21.3%) patients, transplant was urgent, occurring a median 21.6 months after implant. Reasons for transitioning to urgent transplant included 5 (26.3%) pump thrombosis, 5 (26.3%) driveline infection, 2 (10.5%) ICVA, 2 (10.5%) hemolysis, 1 (5.3%) GI bleed, 1 (5.3%) cardiac arrythmia, 1 (5.3%) aortic insufficiency, 1 (5.3%) right heart failure, 1 (5.3%) decompensated heart failure, and 1 (5.3%) improved patient condition (Table 5).

Table 2. Baseline Characteristics of Transplanted DT Patients *Versus* BTT Patients

Characteristics	DT: Transplanted (N = 80)	BTT: Lateral (N = 144)	*p*
Age, mean ± SD	53.6 ± 11.1	54.2 ± 11.5	0.74
BMI (kg/m2), mean ± SD	28.8 ± 6.6	27.1 ± 5.1	0.07
Female	23.8%	28.8%	0.53
White	60.0%	62.5%	0.77
Ischemic etiology of heart failure	42.5%	32.6%	0.15
History of smoking	67.5%	34.7%	**<0.0001**
History of atrial fibrillation	38.8%	30.6%	0.24
History of peripheral vascular disease	3.8%	0.0%	**0.04**
History of hypertension, requiring medication	62.5%	16.7%	**<0.0001**
History of stroke/TIA	15.0%	4.9%	**0.01**
History of ICD implant	85.0%	82.6%	0.71
History of CABG	18.8%	11.1%	0.16
Blood urea nitrogen (mg/dL), mean ± SD	23.4 ± 12.9	24.7 ± 14.4	0.55
Creatinine (mg/dL), mean ± SD	1.3 ± 0.4	1.3 ± 0.7	1.00
Bilirubin (mg/dL), mean ± SD	1.0 ± 0.6	1.1 ± 0.7	0.33
ALT (U/L), mean ± SD	36.2 ± 26.5	36.5 ± 34.9	0.95
Platelets (109/L), mean ± SD	211.7 ± 83.1	204.4 ± 66.7	0.54
CPB (min), mean ± SD	87.3 ± 37.2	69.7 ± 48.6	**0.01**
Intermacs 1	3.8%	3.5%	1.00
Intermacs 2	25%	31.3%	0.36
Intermacs 3	43.8%	47.2%	0.68
Intermacs 4–7	26.3%	18.1%	0.17
KCCQ: Overall Summary Score, mean ± SD	40.0 ± 23.5	38.0 ± 21.0	**< 0.0001**
Six-minute walk test (m), mean ± SD	135.0 ± 146.2	76.7 ± 135.5	**0.01**
Length of ICU stay (days), mean ± SD	10.0 ± 9.1	7.8 ± 9.8	0.15
Length of hospital stay (days), mean ± SD	20.9 ± 11.4	17.6 ± 11.7	0.07

ALT, alanine aminotransferase; BMI, body mass index; BTT, bridge to transplant; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; DT, destination therapy; ICD, implantable cardioverter defibrillator; ICU, intensive care unit; KCCQ, Kansas City cardiomyopathy questionnaire; PRBC, packed red blood cells; SD, standard deviation; TIA, transient ischemic attack.

Table 3. 5-year Adverse Event Rates in Transplanted Versus Nontransplanted Destination Therapy Patients

Adverse Event	Transplanted No. of Events	Transplanted EPPY (PY: 122) n = 80	No Transplant No. of Events	No Transplant EPPY (PY: 1344) n = 524	*p*
Major bleeding	100	0.82	1010	0.75	0.39
GI bleeding	78	0.64	598	0.45	**<0.01**
Stroke	20	0.16	267	0.20	0.41
HCVA	3	0.02	112	0.08	**0.04**
ICVA	17	0.14	155	0.12	0.45
Thrombus with exchange	10	0.08	44	0.03	**<0.01**
Cardiac arrhythmia	38	0.31	413	0.31	0.93
Ventricular arrhythmia	25	0.21	268	0.20	0.89
Infection	75	0.62	1175	0.87	**<0.01**
Driveline infection	26	0.21	245	0.18	0.44
Renal dysfunction	2	0.05	120	0.09	0.16
Right heart failure	32	0.26	252	0.19	0.07

EPPY, events per patient year; GI, gastrointestinal; HCVA, hemorrhagic cerebrovascular accident; ICVA, ischemic cerebrovascular accident; PY, patient-year.

The reasons given for why patients were listed as DT at the time of enrollment were only collected for the ENDURANCE (n = 296) cohort. The most common reasons were age-related (n = 131, 44.3%), cancer-related (n = 32, 10.8%), social issue/compliance-related (n = 26, 8.8%), pulmonary hypertension-related (n = 25, 8.4%), and obesity-related (n = 24, 8.1%).

Discussion

In this posthoc analysis of patient undergoing LVAD support as destination therapy, we identified a subgroup of patients who were categorically ineligible for transplant in the preoperative period who subsequently underwent heart transplantation. When compared with the DT patients who did not transition to transplant, the pre-VAD implant characteristics of the transplanted DT patients suggest a profile more amenable to transplant if exclusion criteria are addressed, being younger with less atherosclerosis, better kidney function and functional capacity, and lower requirements for potentially allosensitizing blood transfusions at implant. Aside from age, these patients also shared many similar preoperative characteristics with patients categorized as BTT in the LATERAL Trial. These results demonstrate that modification of measured and unmeasured risk factors during extended LVAD support can allow a considerable (over 1:10 in this analysis) number of patients the ability to transition to transplant for management of end-stage heart failure. However, this transition takes considerable time (median 1.5 years), highlighting the need for ongoing close follow-up, lifestyle coaching, nutritional counseling, and aggressive treatment of comorbidities.

Others have highlighted the challenges with predicting transplant candidacy in patients being considered for LVAD support.[3] The severity with which many patients present for advanced heart failure therapy evaluation (e.g., INTERMACS profiles 1-2) often limits the ability to complete the extensive pretransplant testing needing for listing. In addition, this analysis shows that LVAD support allows many previously ineligible patients time to address relative contraindications for transplant through improvement in obesity (in 16%) and amelioration of perceived social contraindications to transplant (in 36%), demonstrating the necessary rehabilitation, compliance, and self-care for successful transplant candidacy. The results also show that achieving transplant candidacy takes considerable time, delaying transplant by nearly a year compared with BTT patients. Many centers require at least 6 months of smoking cessation to achieve transplant candidacy, and it is reasonable to assume that other measures of compliance and self-care will require similarly long periods of time to achieve transplant candidacy. Weight loss, especially in the morbidly obese, takes a considerable amount of time in patients with a limited ability to perform sustained aerobic exercise.

While we see a continued focus on transplant as the "gold standard" optimal treatment strategy for end-stage heart failure, this remains a continuously evolving algorithm as VAD technology

Table 4. 2-year Adverse Event Rates for DT Transplanted and BTT Lateral Patients

Adverse Event	DT: Transplanted No. of Events	DT: Transplanted EPPY(PY: 106) n = 80	BTT: Lateral No. of Events	BTT: Lateral EPPY (PY: 162.5) n = 144	*p*
Major bleeding*	95	0.90	83	0.51	0.0005
GI bleeding*	74	0.70	50	0.31	< 0.0001
Stroke	19	0.18	21	0.13	0.31
HCVA	3	0.03	9	0.06	0.31
ICVA	16	0.15	12	0.07	0.08
Cardiac arrhythmia	38	0.36	73	0.45	0.26
Ventricular arrhythmia	25	0.24	48	0.30	0.39
Infection	68	0.64	116	0.71	0.47
Driveline infection	22	0.21	25	0.15	0.30
Renal dysfunction	6	0.06	18	0.11	0.15

*Denotes post hoc statistical significance

BTT, Bridge to Transplant; DT, Destination Therapy; EPPY, events per patient year; GI, gastrointestinal; HCVA, hemorrhagic cerebrovascular accident; ICVA, ischemic cerebrovascular accident; PY, patient-years.

Table 5. Reasons for Transition from DT VAD to Heart Transplantation

Reasons* for Transition from DT to Elective Transplant (n = 63)	n (%)
Improved social/compliance	26 (41.3%)
Weight loss	12 (19.0%)
Improvement in pulmonary hypertension	10 (15.9%)
Smoking/substance cessation	6 (9.5%)
Cancer/mass resolution	4 (6.3%)
Transferred to/from outside hospital	3 (4.8%)
Improved glycemic control	3 (4.8%)
Worsening aortic insufficiency	2 (3.2%)
Improved renal function	2 (3.2%)
Improved chronic obstructive pulmonary disease	1 (1.6%)
Refractory GI bleed	1 (1.6%)
Improved physical condition	1 (1.6%)
Improved cardiac function	1 (1.6%)
Donor heart available	1 (1.6%)
Reasons* for transition from DT to urgent transplant (n = 17)	**n (%)**
Pump thrombosis	5 (29.4%)
Driveline infection	5 (29.4%)
ICVA	2 (11.8%)
Hemolysis	2 (11.8%)
Right heart failure	1 (5.9%)
Decompensated heart failure	1 (5.9%)
Aortic insufficiency	1 (5.9%)
Cardiac arrhythmia	1 (5.9%)
GI bleed	1 (5.9%)
Improved patient condition	1 (5.9%)

*Patients could have multiple reasons listed.
DT, destination therapy; GI, gastrointestinal; ICVA, ischemic cerebrovascular accident; VAD, ventricular assist device.

continues to improve. With recent data demonstrating impressive long-term data that is approaching survival and morbidity figures comparable to heart transplant, this cross-over may become limited.[7,12,14] But, until adverse events with mechanical circulatory support are further minimized, transplant will likely continue to prevail as the treatment of choice for patients and providers. As such, it is critical to understand the ability of initial contraindications transplant to be corrected. Given the ability of VAD therapy to successfully support terminal heart failure patients to transplant, we will likely continue to see a cross-over from DT to BTT strategies as we have demonstrated.

Limitations

This study has important limitations to acknowledge. Patients from different cohorts were compared and the analysis was retrospective and limited in power. Unmeasured variables may have driven preoperative DT versus BTT categorization. Local payor mix can heavily influence DT and BTT categorization for VAD, especially when listing is a requirement for VAD BTT-therapy. Additionally, detailed psychosocial data, nutrition assessment, comorbidity documentation, financial security were not available, and all of these factors plan an important role in BTT candidacy. Finally, posttransplant outcomes were not collected in either the Endurance or Endurance Supplemental trials, limiting the analysis for all transplanted patients to the time period before transplantation.

Conclusion

In this post hoc analysis of the ENDURANCE and ENDURANCE Supplemental Trials, at least 1 in 10 patients achieved transplant eligibility with subsequent heart transplant within approximately 3 years of HVAD support. Most transplants were elective, occurring after modification of behavioral or obesity exclusions. DT patients should be regularly reassessed for transplant eligibility and efforts to remediate modifiable contraindications should be ongoing after HVAD implant. DT centers should continue to work with transplant programs to ensure mechanisms are in place to identify VAD patients who become eligible for transplant.

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