Title

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REGIONAL DIFFERENCES IN UTILIZATION AND OUTCOMES OF LEFT VENTRICULAR ASSIST DEVICES: INSIGHTS FROM THE INTERMACS REGISTRY

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Abstract

Background—We sought to examine whether characteristics, implant strategy, and outcomes in patients who receive continuous-flow left ventricular assist devices (CF-LVAD) differ across geographic regions in the United States (US).

Methods—A total of 7,404 CF-LVAD patients enrolled in the INTERMACS from 134 participating institutions were analyzed from four distinct regions: Northeast (n=2605, 35%), Midwest (n=2210, 30%), West (n=973, 13%) and South (n=1616, 22%).

Results—At baseline, patients in the Northeast and South were more likely to have INTERMACS risk profiles 1 and 2. Bridge to transplant (BTT) strategy was more common in the Northeast (Northeast=31.7%; West=18.5%; South=26.9%; Midwest=25.5%; p<0.0001). In contrast, destination therapy (DT) was more likely in the South (South=40.6%; Northeast=32.3%; Midwest=27.3%; West=27.3%, p<0.0001). While all regions showed a high one year survival rate, some regional differences in long term mortality were observed. Notably, South had a significantly lower survival beyond 1 year after LVAD implant. However, when stratified by device strategy, no significant differences in survival for BTT or DT patients were found among

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Dr. Ventura is a consultant to Thoratec and Otsuka; Dr. Naftel is a consultant to Thoratec and Heartware. The remaining authors report no conflicts of interest.

regions. Finally, with the exception of right ventricular failure that was more common in the South region, no other significant differences in causes of death were observed among regions.

Conclusions—Regional differences in clinical profile and LVAD strategy exist in the US. Despite an overall high survival rate at 1 year, differences in mortality among regions were noted. The lower survival rate in the South may be attributed to patient characteristics and higher use of LVAD as DT.

Background

With a limited number of heart donors, left ventricular assist devices (LVAD) are increasingly used in patients with advanced heart failure either as bridge to transplantation (BTT) or destination therapy (DT).[1–10] Current data from the United Network for Organ Sharing (UNOS) suggest regional disparities in waiting times for patients awaiting heart transplantation in the United States.[11–13] Although this may theoretically impact the utilization of LVAD particularly as BTT strategy, no studies have been performed to carefully evaluate this issue. Furthermore, there have been no reports on potential differences in LVAD use as DT across geographic regions in the US. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), a National Heart, Lung and Blood Institute (NHLBI)–sponsored database, has collected data on over 6,000 patients supported with LVAD and is currently the largest registry for mechanical circulatory support (MCS) in the US.[14] Examining data from this registry may provide important insights into regional variations in current patterns of LVAD use and outcomes in the US. Our hypothesis is that significant variations in LVAD use and outcomes exist among US regions and this study aims to: (1) describe demographic and clinical characteristics among LVAD patients enrolled in the INTERMACS registry from four distinct geographic regions: Northeast, Midwest, South and West; (2) compare device strategy (BTT vs. DT) among regions; and (3) explore regional differences in outcomes among patient receiving continuous flow (CF)-LVAD.

Methods

Data Sources

The primary data source for this study was the INTERMACS registry, an ongoing national registry for patients implanted with a Food and Drug Administration–approved MCS device designed to support patients for long periods. Details and objectives of this database have previously been described.[15] In summary, the registry was launched in 2005 with the collaborative effort the National Heart, Lung, and Blood Institute, the Food and Drug Administration, and the Centers for Medicare and Medicaid Services and has been maintained by the University of Alabama INTERMACS Data Coordinating Center since its creation. Data including patient characteristics, medical history, medications, laboratory data, INTERMACS profile, device type and patient outcomes are collected using an interactive, internet-based system to a secure server provided by the United Network for Organ Sharing. Data analysis was done at The University of Alabama, which serves as the data analysis center and has institutional review board approval for analyzing the aggregate de-identified data for research purposes.

Study Population

In this study, we selected patients who received CF-LVAD only. Between June 2006 and March 2013, there were 8,609 adult patients (age ≥ 19 years at implant) who received a heart device from 134 hospitals participating in the INTERMACS registry. After excluding pediatric patients (N=79), patients with pulsatile flow devices (N=1,127), the final study population comprised 7,404 patients from 4 geographic regions.

Definitions of Variables and Outcomes

Using the UNOS regions the following 4 geographic regions were defined; Northeast (UNOS regions 1,2,9,11), Midwest (10,7,8), South (regions 3,4) and West (regions 5,6). The rationale for choosing a UNOS based distribution was that it would allow us to align with the UNOS data. BTT strategy was used for patients listed for cardiac transplantation at the time of LVAD implant; bridge to candidacy (BTC) for patients who were considered eligible for heart transplant but not listed at the time of implantation and DT as a permanent therapy for patients who were not eligible for transplant. The primary outcome was all-cause mortality by region (overall and by device strategy) with data censored at transplantation or device removal after recovery of myocardial function. Furthermore, regional mortality was compared during the early or late/constant phases if occurred before or after 3 months from implantation respectively. The mean follow-up for this study was 12.74 months. The following causes of death were identified: right heart failure, major bleeding, cardiac arrhythmia, hemolysis, end stage cardiomyopathy, major infection, device malfunction, hepatic dysfunction, renal dysfunction, neurological dysfunction, other/unknown. The definitions of these adverse events can be found on the INTERMACS website http://www.intermacs.org.

Statistical Analysis

Baseline patient characteristics were compared among regions. Mean values with standard deviations (SDs) were used to describe continuous variables and numbers (percentages) were reported for categorical variables. Chi-square tests were used for categorical variables and two independent sample t-test or one-way ANOVA Wilcoxon rank-sum tests for continuous variables. Actuarial survival while on MCS was calculated from the date of LVAD implant to death and patients were censored at the time of cardiac transplantation, LVAD explantation. Time related event data were analyzed using Kaplan-Meier methodology and the effect of survival by geographical region were made both univariately and multivariately by a parametric hazard regression analysis. The adjusted effect of these variables were assessed after adjustment for the following pre-implant parameters; age, gender, race/ethnicity, college education, body mass index, smoking, alcohol use, INTERMACS profile, previous cancer, chronic obstructive pulmonary disease, diabetes, cerebrovascular disease, peripheral vascular disease, coronary artery disease, history of coronary artery bypass graft, history of valve surgery, ascites, implantable cardiac defibrillator, serum sodium, albumin, total bilirubin, blood urea nitrogen, creatinine, international normalized ratio, alanine aminotransferase, aspartate aminotransferase, cholesterol, white blood cell count, use of intra-aortic balloon pump, left ventricular ejection fraction<20%, left ventricular end diastolic diameter, severe right ventricular dysfunction,

biventricular assist device use, concomitant surgery, inotrope use, and pre-implant invasive hemodynamics including cardiac output, cardiac index, right atrial pressure, pulmonary capillary wedge pressure, pulmonary vascular resistance. These significant pre-implant variables were selected based on prior studies.[16–18]

All tests were 2 sided, and P values <0.05 were considered statistically significant. All analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

Results

Patient Characteristics

A total of 7,404 CF-LVAD patients from 134 participating institutions: Northeast (n=2,605, 35%), Midwest (n=2,210, 30%), West (n=973, 13%) and South (n=1,616, 22%) were included in the study. Patient characteristics are summarized in Table 1. At baseline, there were no significant regional differences with regard to patients' age, gender or body mass index (BMI). Northeast had more diabetic patients when compared to other regions. Also, patients from the Northeast and South were more likely to have INTERMACS risk profiles 1 and 2 when compared to those of Midwest and West. South had more black patients while West had more Hispanics. Similarly, patients in the South and West were more likely to be on dialysis. South had a higher proportion of patients with blood type O when compared to other regions. BTT strategy was more common in the Northeast (Northeast=31.7%; West=18.5%; South=26.9%; Midwest=25.5%; p<0.0001). In contrast, DT was more likely in the South (South=40.6%; Northeast=32.3%; Midwest=27.3%; West=27.3%, p<0.0001). A higher proportion of patients with INTERMACS profile 1 in the Northeast received short term MCS prior to LVAD implant when compared to other regions. Additionally, patients in the Northeast were more likely to receive biventricular assist device (BIVAD) or extracorporeal membrane oxygenation (ECMO) when compared to other regions.

Hospital Characteristics

This cohort included a total of 134 participating hospitals with a large number being in the Northeast (Northeast=53; Midwest=33; West=23, South=25). The majority of LVAD implanting centers were cardiac transplant centers. While Northeast had more non-transplant LVAD implanting centers, South had the highest number of DT certified centers. (Table 1)

Outcomes

Overall Mortality by Region

There were a total of 1,653 deaths (22.3%) in the study group. Unadjusted analysis showed that South had a lower survival when compared to other regions. (Figure 1). Figures 2 and 3 highlight the competing outcomes in the overall cohort and among regions. Mortality at 1 year was significantly higher in the South region than other regions. Furthermore, these regional differences in survival persisted at 2 years (South= 65%, Northeast=72%, Midwest=71%, West=70%, adjusted p=0.001). In addition, LVAD patients in the South were less likely to be transplanted at 1 year (South= 18%, Northeast=23%, Midwest=23%,

West=21%, p=0.001). In contrast, rates of myocardial recovery were low (1%) with no significant difference among regions. (Figure 2)

Mortality Among Regions by Device Strategy

Survival curves by device strategy in the overall cohort and by regions are shown in Figures 3 and 4. The actuarial survival was lower among DT patients than BTT or BTC patients (survival at 1 year: DT=75.3% vs. BTT=85.5%; BTC=81.7%, p<.0001, Figure 3). This finding was consistent across regions (Figure 4). Tables 2,3 show adjusted HR for mortality (during both the early high risk phase and late constant phase) among regions (using South as the reference group) categorized by device strategy. Some subtle regional differences were noted during the high risk (early phase) and long-term period (constant phase). Notably, in the BTT group, the lower mortality in the Northeast when compared to the South was only significant during the early phase (Table 2: Northeast vs. South; Early phase: adjusted HR=0.377, 95% CI=0.1707–0.8339, p=0.02; Constant phase: adjusted HR=0.817, 95 % CI: 0.5765–1.1588, p=0.26). In the DT group however, while a lower mortality was noted in the early phase in Midwest and West, the Northeast did not show any statistically significant differences in mortality during both the early and late phases when compared to South (Table 2). Similar to the BTT group, in the BTC group (Table 3) a significant lower early mortality in the Northeast, Midwest and West regions was noted when compared to the South.

Causes of Death

With regards to adverse events (Table 4), Infection and neurologic dysfunction were the most common etiologies with similar distribution among regions. With the exception of right ventricular failure (RVF) that was more common in the South region (South= 7.9%, Northeast=6.1%, Midwest=3.5%, West=2.5%, adjusted p=0.01), no other significant differences in causes of death were observed among regions.

Discussion

Regional differences in utilization and outcomes of LVAD in the US have not been previously studied. By our own assessment, our study is the first to explore this issue and offer important findings based on the INTERMACS database. First, at the time of LVAD implantation, patients from the Northeast and South were more likely to have INTERMACS risk profiles 1 and 2 compared with those from the Midwest and West. Second, BTT strategy was more common in the Northeast whereas DT was more common in the South. Third, despite high overall one-year survival rates across regions, patients from the South had a significantly lower survival after LVAD surgery.

Consistent with prior studies among LVAD patients,[9,19] our study population was composed predominantly of middle age, white males with no regional variation in age or gender distribution. In regard to minorities, the largest Hispanic and black populations came from the West and South, respectively.

In addition to previous INTERMACS data[9] showing that over 50% of patients had INTERMACS profile 1 and 2 at the time of device implant,[20, 21] we observed that a larger

proportion of these sicker patients were from the Northeast and South regions. Possible explanations for this finding include the higher number of LVAD implanting centers in the Northeast, the higher proportion of DT patients in the South and a higher incidence of RV failure in both of these regions. Interestingly when we compared pre-implant variables between combined regions Midwest/West vs. Northeast/South, we found that with few exceptions, no significant differences were present at baseline. (online supplemental material)

Advances in device technology and durability, along with improvement in patient management, have led to increased survival of patients on MCS. Since the early results from the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial showing one-year survival of 52% among patient who received first generation pumps,[6] patient outcomes have remarkably increased with contemporary estimates of one-year survival at 86%.[19] While we noted similar mortality endpoints in our overall study population, we found important regional differences in outcomes. Notably, patients from the South had significantly lower survival rate when compared to other regions. A number of factors may explain this observation. First, it appears that the higher mortality observed in the South may be associated with higher use of DT strategy. Prior data[22,23] support that DT patients are usually sicker and have higher mortality. Several socioeconomic and social factors may potentially impact higher DT rates in this region. For instance, higher prevalence of tobacco use and obesity may constitute a larger burden of relative contraindications for transplant and BTT listing.[24] In contrast, a number of centers may consider active or recent tobacco use acceptable for DT status. Additionally, centers with shorter transplant waiting times (i.e. South region) may opt to place a patient on an initial DT strategy until certain co-morbid factors (e.g. smoking) are resolved. Second, the relatively higher proportion of patients with INTERMACS profiles 1 and 2 in the South may explain the lower survival rates. This finding is consistent with the established association between INTERMACS profile risk and mortality.[25] Interestingly enough, we found that despite a large number of INTERMACS 1 and 2 patients in the Northeast, mortality in this region did not exceed those of others. This paradoxical finding may be related to the higher proportion of transplanted patients (i.e. BTT) in this region and the higher proportion of INTERMACS 1 patients receiving short-term mechanical circulatory support prior to LVAD implant when compared to other regions. Another possible factor, not examined in our study, that may explain regional variations in outcomes relates to the LVAD experience of implanting centers. This is particularly relevant as a significant correlation has been shown between center experience and outcome particularly in DT patients.[26] Also, variables such as the use of preoperative risk score, and other factors, such as candidate selection bias which have been shown to be an important determinant of outcome in LVAD patients was not systematically examined in our study.[26]

Adverse events in the early post-operative period have been linked to nearly 20% of overall mortality among LVAD patients.[7] Consistent with this observation, our study found that regardless of device strategy, regional differences in mortality were only significant in the early phase. Intriguingly, some of these findings persisted even after adjusting for patient characteristics. Among BTT patients, only the Northeast showed better outcome in the early phase when compared to the South. While in the BTC cohort, a lower early mortality was

noted in all regions when compared to the South, DT Patients in the Midwest and West but not in the Northeast had lower early mortality when compared to the South.

With the exception of RVF, our study showed no significant differences in causes of death among regions. Examining RVF-related deaths is challenging due to hospital-level variability on how to manage LVAD-associated RVF. To illustrate, certain centers may have lower thresholds of placing an RVAD intra-operatively rather than implanting an RVAD as a rescue strategy for post-operative RVF. This mode of management may correlate with improved mortality. Other centers, in contrast, may more likely favor medical therapy over RVAD surgery and consequently experience poorer outcomes. This strategy is particularly relevant among centers with high DT volumes since they do not have an option of transplant should RVF be unrecoverable.

Some limitations inherent to registry-based studies need to be mentioned. First, because of the retrospective nature of our study there is potential for bias. Data were collected using a medical chart review and dependent on the accuracy and completeness of documentation and abstraction and reporting to INTERMACS. Second, residual unmeasured confounding variables may also explain some of these findings. Third, although this study is first to demonstrate regional variation in use and outcomes of LVAD patients, causes of these important regional differences remain unclear and need to be further elucidated in future studies. Fourth, our analysis did not adjust for LVAD volume and experience of implanting centers. However, analysis of center volume in a voluntary registry such as INTERMACS is fraught with inherent confounders. For example, centers that joined the registry at a later date may be underrepresented. Also, patients that do not consent for enrollment will not be included (decreasing the perceived center volume). Moreover, large volume centers that enroll large number of patients in clinical trials (not represented in the registry) will be falsely identified as low volume centers. Data on center experience are not available in the INTERMACS registry. Importantly, the data presented highlights a significant deficit in the current knowledge regarding the frequency, duration and type of short-term MCS (e.g. IABP, Impella, Tandem heart) utilized as a bridge-to-bridge at the national level. The use of a temporary short term devices and its affects on post LVAD outcome remains unclear. Finally, at the local level, surgeon specific data are paramount to better understand these observed differences in outcomes among regions to potentially improve overall patient outcome. As we move forward, perhaps combining INTERMACS data with other MCS databases such as the Society of Thoracic Surgeons (STS) database which for instance include data on surgeon-specific volumes and data on both FDA-approved commercially-available devices and investigational devices may fill this important knowledge gap.

In summary, regional differences in clinical profile and LVAD strategy exist in the US. Despite an overall high survival rate at 1 year, important regional differences in overall mortality were noted. Although the lower survival rate in the South may be attributed to patient characteristics and higher use of LVAD as DT, it is important to note that further research is needed as some other potential factors not included in this analysis may also explain these observed regional differences in outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013; 62(16):e147–e239. [PubMed: 23747642]
2. Peura JL, Colvin-Adams M, Francis GS, et al. Recommendations for the use of mechanical circulatory support: device strategies and patient selection. Circulation. 2012; 126:2648–67. [PubMed: 23109468]
3. Kirklin JK, Naftel DC. Mechanical circulatory support: registering a therapy in evolution. Circ Heart Fail. 2008; 1:200–5. [PubMed: 19808290]
4. Frazier OH, Rose EA, McCarthy P, et al. Improved mortality and rehabilitation of transplant candidates treated with a long-term implantable left ventricular assist system. Ann Surg. 1995; 222:327–36. [PubMed: 7677462]
5. 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. 2001; 122:1186–95. [PubMed: 11726895]
6. Rose EA, Gelijns AC, Moskowitz AJ, et al. for the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term mechanical left ventricular assistance for end-stage heart failure. N Engl J Med. 2001; 345:1435–43. [PubMed: 11794191]
7. Miller LW, Pagani FD, Russell SD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med. 2007; 357:885–96. [PubMed: 17761592]
8. Pagani FD, Miller LW, Russell SD, et al. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol. 2009; 54:312–21. [PubMed: 19608028]
9. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med. 2009; 361:2241–51. [PubMed: 19920051]
10. Fang JC. Rise of the machines: left ventricular assist devices as permanent therapy for advanced heart failure. N Engl J Med. 2009; 361:2282–5. [PubMed: 19920052]
11. Kauffmann MH, McBride MA, Shield CF, Daily OP, Wolf JS, Kirklin JK. Determinants of waiting time for heart transplants in the United States. J Heart Lung Transplant. 1999; 18:414–9. [PubMed: 10363684]
12. H.R.a.S.A. U.S. Department of Health and Human Services, Healthcare Systems Bureau, Division of Transplantation. 2009 Annual Report of the US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1999–2008. Rockville, MD: 2009.
13. Schulze PC, Kitada S, Clerkin K, Jin Z, Mancini DM. Regional differences in recipient waitlist time and pre- and post-transplant mortality after the 2006 United Network for Organ Sharing policy changes in the donor heart allocation algorithm. J Am Coll Cardiol HF. 2014; 2:166–77.

14. Kirklin JK, Naftel DC, Kormos RL, et al. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. J Heart Lung Transplant. 2013; 32:141–56. [PubMed: 23352390]
15. Kirklin JK, Naftel DC, Warner Stevenson L, et al. INTERMACS database for durable devices for circulatory support: first annual report. J Heart Lung Transplant. 2008; 27:1065–72. [PubMed: 18926395]
16. Alba AC, Rao V, Ivanov J, Ross HJ, Delgado DH. Usefulness of the INTERMACS scale to predict outcomes after mechanical assist device implantation. J Heart Lung Transplant. 2009; 28:827–33. [PubMed: 19632580]
17. Holman WL, Kormos RL, Naftel DC, et al. Predictors of death and transplant in patients with a mechanical circulatory support device: a multi-institutional study. J Heart Lung Transplant. 2009; 28:44–50. [PubMed: 19134530]
18. Matthews JC, Pagani FD, Haft JW, Koelling TM, Naftel DC, Aaronson KD. Model for end-stage liver disease score predicts left ventricular assist device operative transfusion requirements, morbidity, and mortality. Circulation. 2010; 121:214–20. [PubMed: 20048215]
19. Aaronson KD, Slaughter MS, Miller LW, et al. Use of an Intrapericardial, Continuous Flow, Centrifugal Pump in Patients Awaiting Heart Transplantation. Circulation. 2012; 125:3191–200. [PubMed: 22619284]
20. Holman WL, Pae WE, Teutenberg JJ, et al. INTERMACS: interval analysis of registry data. J Am Coll Surg. 2009; 208:755–61. [PubMed: 19476831]
21. Miller LW, Guglin M. Patient Selection for Ventricular Assist Devices A Moving Target. J Am Coll Cardiol. 2013; 61:1209–21. [PubMed: 23290542]
22. Park SJ, Tector A, Piccioni W, et al. Left ventricular assist devices as destination therapy: a new look at survival. J Thorac Cardiovasc Surg. 2005; 129:9–17. [PubMed: 15632819]
23. Lietz K, Long JW, Kfoury AG, et al. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. Circulation. 2007; 116:497–05. [PubMed: 17638928]
24. Boyle AJ, Ascheim DD, Russo MJ, et al. Clinical outcomes for continuous-flow left ventricular assist device patients stratified by pre-operative INTERMACS classification. J Heart Lung Transplant. 2011; 30:402–7. [PubMed: 21168346]
25. Lietz K, Long JW, Kfoury AG, et al. Impact of center volume on outcomes of left ventricular assist device implantation as destination therapy: analysis of the Thoratec HeartMate registry, 1998 to 2005. Circ Heart Fail. 2009; 2:3–10. [PubMed: 19808309]
26. El-Banayosy A, Arusoglu L, Kizner L, Fey O, Minami K, Korfer R. Complications of circulatory assist. Perfusion. 2000; 15:327–31. [PubMed: 10926415]
27. Van Meter CH Jr. Right heart failure: best treated by avoidance. Ann Thorac Surg. 2001; 71(suppl):S220–2. [PubMed: 11265866]

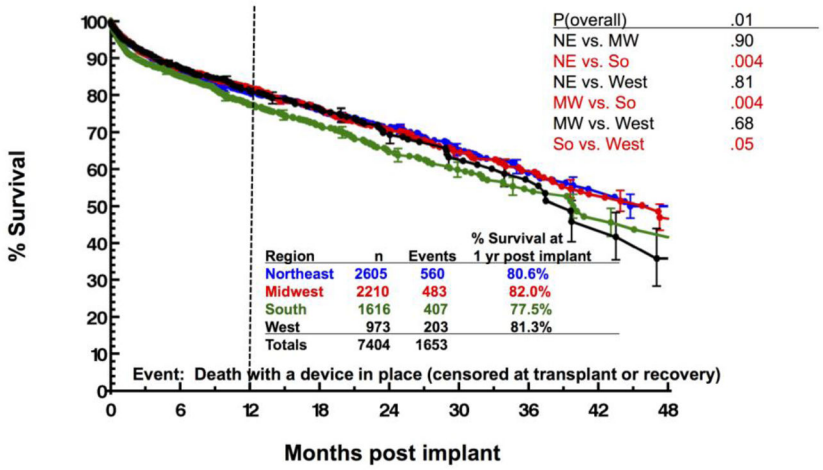

Figure 1.
Survival after implant by geographic region

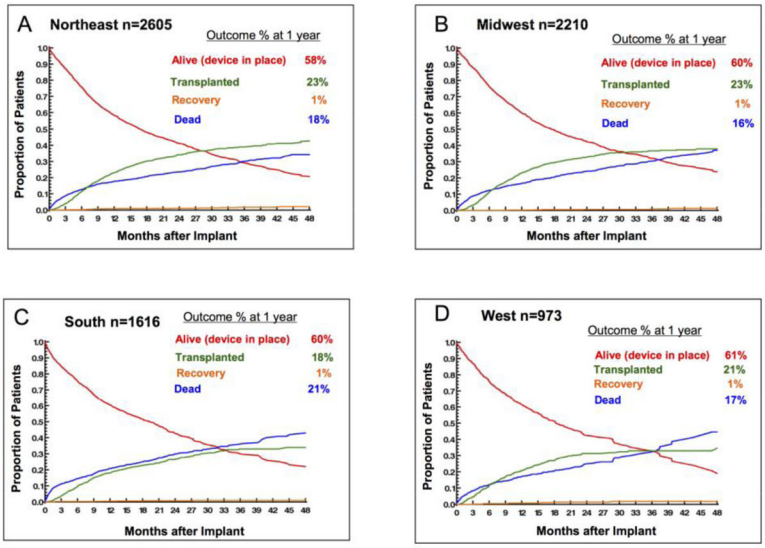

Figure 2.

Competing outcomes by region: (A) Northeast; (B) Midwest; (C) South and (D) West

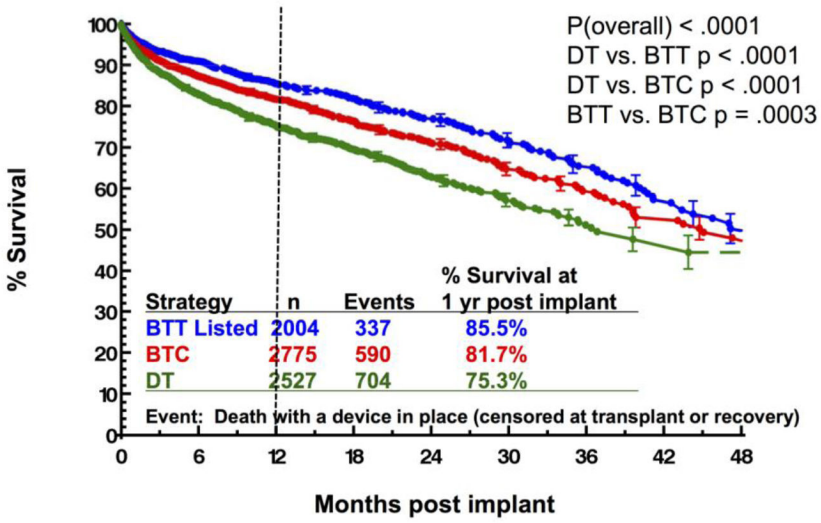

Figure 3.
Overall survival by device strategy

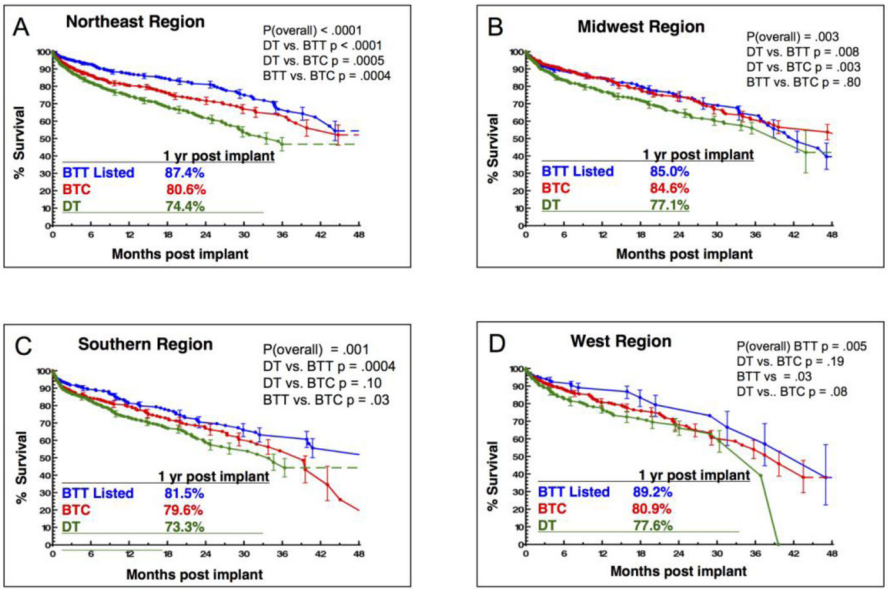

Figure 4.

Overall regional survival by device strategy, (A) Northeast; (B) Midwest; (C) South and (D) West

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Table 1

Baseline Characteristics by Geographic Region

Pre-Implant Characteristic	Total (n=7404)	Northeast (n=2605)	Midwest (n=2210)	West (n=973)	South (n=1616)	P-Value
Age at implant (years), mean (±SD)	56.7 (±12.9)*	56.7 (±12.9)	56.5 (±12.7)	57.8 (±18.7)	56.4 (±12.7)	.04
Male, %	79.1%	77.7%	79.0%	82.0%	79.5%	.04
Ethnicity						
Whites %	70.0%	65.8%	75.3%	73.9%	67.3%	< .0001
Hispanics %	6.3%	5.5%	2.6%	11.6%	9.3%	< .0001
Blacks %	22.2%	25.9%	20.1%	8.8%	27.2%	< .0001
Other	6.4%	6.7%	3.5%	14.7%	5.1%	< .0001
Medical History						
Ischemic (%)	48.0%	47.5%	48.5%	48.2%	48.0%	.93
Non-ischemic (%)	51.0%	51.5%	50.4%	50.2%	51.4%	.80
Congenital diagnosis (%)	0.5%	0.42%	0.68%	0.72%	0.19%	.11
Diabetes %	27.1%	29.2%	27.2%	24.0%	25.6%	.005
CVA/TIA %	5.4%	5.5%	5.6%	5.3%	5.2%	.96
Dialysis %	7.9%	1.0%	1.2%	3.1%	2.0%	< .0001
ICD %	81.5%	79.3%	81.2%	82.2%	85.1%	< .0001
CABG %	23.6%	22.1%	22.9%	24.6%	26.3%	.01
Valve Surgery %	7.5%	7.8%	7.7%	8.2%	6.3%	.19
ECMO%	2.0%	3.0%	2.0%	1.2%	1.1%	< .0001
IABP (%)	28.6%	26.5%	34.7%	21.6%	31.9%	< .0001
Mechanical ventilation (%)	6.6%	7.3%	5.6%	7.0%	6.5%	.13
BMI (Mean) **(±SD)**	28.6 (±6.7)	28.6 (±6.9)	28.6 (±6.5)	27.9 (±6.4)	28.9 (±6.6)	.004
BSA (Mean) **(±SD)**	2.08 (± .30)	2.07 (± .30)	2.08 (± .30)	2.06 (± .30)	2.09 (± .30)	.003
LABS (mean) (±SD)						
Sodium	134.71 (±4.85)	134.9 (±4.68)	134.8 (±4.80)	134.2 (±5.15)	134.7 (±4.99)	.004

Pre-Implant Characteristic	Total (n=7404)	Northeast (n=2605)	Midwest (n=2210)	West (n=973)	South (n=1616)	P-Value
Creatinine	1.44 (± .76)	1.4 (± .78)	1.4 (± .73)	1.4 (± .80)	1.4 (± .74)	.99
INR	1.34 (± .47)	1.4 (± .50)	1.3 (± .42)	1.4 (± .49)	1.3 (± .43)	.0002
Total Bilirubin	1.38 (±1.51)	1.4 (±1.22)	1.3 (±1.17)	1.4 (±2.23)	1.4 (±1.74)	.13
SGOT/AST	67.51 (±275.8)	72.2 (±330.7)	66.9 (±242.1)	67.6 (±293.3)	60.9 (±202.8)	.67
SGPT/ALT	77.02 (±254.1)	75.6 (±284.3)	82.7 (±251.4)	77.8 (±277.1)	71.3 (±181.6)	.62
Hemoglobin	11.38 (±1.99)	11.3 (±1.99)	11.4 (±1.96)	11.6 (±2.02)	11.3 (±2.02)	< .0001
WBC	8.56 (±4.22)	8.8 (±4.19)	8.4 (±4.08)	8.4 (±3.68)	8.7 (±4.73)	.005
Device Type						
LVAD %	97.4%	96.2%	98.4%	95.7%	99.0%	< .0001
BI-VAD %	2.6%	3.8%	1.6%	4.3%	1.1%	< .0001
INTERMACS LEVEL						
1. Critical cardiogenic shock	14.9%	17.4%	14.3%	9.9%	14.9%	< .0001
2. Progressive decline	39.8%	42.9%	37.4%	34.8%	41.2%	< .0001
3. Stable but inotrope dependent	26.5%	25.1%	23.2%	32.9%	29.2%	< .0001
4. Recurrent advanced HF	13.4%	10.5%	18.3%	15.5%	10.1%	< .0001
5. Exertion intolerant	3.0%	2.2%	4.0%	3.5%	2.5%	< .0001
6. Exertion limited	1.6%	1.3%	2.1%	2.7%	1.0%	< .0001
7. Advanced NYHA III	1.0%	0.7%	0.6%	0.7%	1.6%	.004
Pre-Implant Device Strategy						
Bridge to transplant (currently listed)	27.1%	31.7%	25.5%	18.5%	26.9%	< .0001
Bridge to candidacy						
• Listing likely	24.1%	21.3%	26.7%	34.6%	18.5%	< .0001
• Listing moderately likely	10.2%	10.2%	8.9%	13.3%	9.9%	.003
• Listing unlikely	3.3%	3.0%	3.2%	5.3%	2.5%	.0008
Destination Therapy (permanent device)	34.1%	32.3%	34.5%	27.3%	40.6%	< .0001
Bridge to recovery	1.0%	0.7%	0.4%	0.3%	0.7%	.29
Rescue therapy	0.3%	0.4%	0.2%	0.1%	0.4%	.38
Other	1.0%	0.4%	0.7%	0.6%	0.5%	.54
Number of patients with LVEF<20 %, (n)	68.08 (n=6665)	67.4% (n=2362)	68.7% (n=1951)	61.4% (n=898)	71.9% (n=1454)	< .0001

Pre-Implant Characteristic	Total (n=7404)	Northeast (n=2605)	Midwest (n=2210)	West (n=973)	South (n=1616)	P-Value
Severe RHF	2.6%	3.8%	1.6%	4.3%	1.1%	< .0001
Blood type O %, (n)	48.5% (n=7287)	50.4% (n=2528)	44.8% (n=2191)	46.1% (n=969)	51.8% (n=1599)	< .0001
Center Characteristics*						
Centers (Total)	134	53	33	23	25	
Transplant center %, (n)	90% (n=120)	87%, (n=46)	91%, (n=30)	91%, (n=21)	92%, (n=23)	
Not a Transplant Center %, (n)	10%, (n=14)	13%, (n=7)	9%, (n=3)	9%, (n=2)	8% (n=2)	
DT Certified Center %, (n)	89%, (n=119)	89%, (n=47)	85%, (n=28)	87%, (n=20)	96% (n=24)	

* Region Percentages are based on hospitals that contributed data to this cohort.

INTERMACS collects information on whether the center is a DT center (based on DT certification posted by CMS 1/10/2014) and whether the center is or is not a transplant center (includes all organ transplantation).

Tables 2

Unadjusted and adjusted[†] Hazard Ratios (HR) with 95% confidence intervals (CI) for BTT and DT: by Geographic Region (using South as reference group)

Geographic Regions	Bridge to Transplant: Patient Listed		Destination Therapy	
	Early	Constant	Early	Constant
	HR, p-value	HR, p-value	HR, p-value	HR, p-value
NE v So				
Unadjusted	0.28 (0.12–0.67), P=0.004	0.74 (0.51–1.05), p=0.1	0.87 (0.56–1.35), p=0.55	0.97 (0.74–1.25), p=0.82
Adjusted	0.37 (0.17–0.83), P=0.02	0.81 (0.57–1.15), p=0.26	0.65 (0.41–1.03), p=0.07	0.97 (0.75–1.26), p=0.87
MW v So				
Unadjusted	0.89 (0.45–1.74), p=0.74	1.01 (0.69–1.46), p=0.97	0.69 (0.43–1.09), p=0.12	0.81 (0.61–1.06), p=0.13
Adjusted	0.60 (0.29–1.22), p=0.16	1.06 (0.73–1.51), p=0.76	0.51 (0.31–0.83), p=0.01	0.82 ((0.63–1.07), p=0.16
West v So				
Unadjusted	0.59 (0.23–1.51), p= 0.28	0.76 (0.42–1.35), p=0.35	0.73 (0.40–1.32), p=0.30	0.82(0.57–1.18), p=0.30
Adjusted	0.52 (0.19–1.39), p=0.19	0.85 (0.49–1.49), p=0.59	0.43 (0.22–0.83), p=0.01	0.71 (0.50–1.00), p=0.05

BTT: Bridge to transplant; **DT: Destination therapy; NE:** Northeast; **S:** South; **MW:** Midwest; **W:** West

[†]Variables in the model: age, gender, race/ethnicity, college education, body mass index, smoking, alcohol use, INTERMACS profile, previous cancer, chronic obstructive pulmonary disease, diabetes, cerebrovascular disease, peripheral vascular disease, coronary artery disease, history of coronary artery bypass graft, history of valve surgery, ascites, implantable cardiac defibrillator, serum sodium, albumin, total bilirubin, blood urea nitrogen, creatinine, international normalized ratio, alanine aminotransferase, aspartate aminotransferase, cholesterol, white blood cell count, use of intra-aortic balloon pump, left ventricular ejection fraction<20%, left ventricular end diastolic diameter, severe right ventricular dysfunction, biventricular assist device use, concomitant surgery, inotrope use, and pre-implant invasive hemodynamics including cardiac output, cardiac index, right atrial pressure, pulmonary capillary wedge pressure, pulmonary vascular resistance.

Tables 3

Unadjusted and adjusted[†] HR with 95 % CI for BTC: by Geographic Region (using South as reference group)

Geographic Regions	Bridge to Candidacy			
	Early		Constant	
	HR	p-value	HR	p-value
NE v So				
Unadjusted	0.66 (0.40–1.08)	0.10	0.78 (0.56–1.09)	0.15
Adjusted	0.54 (0.33–0.89)	0.02	0.79 (0.56–1.11)	0.18
MW v So				
Unadjusted	0.37 (0.20–0.67)	0.001	0.72(0.52–1.00)	0.06
Adjusted	0.48 (0.27–0.84)	0.01	0.76 (0.55–1.05)	0.10
West v So				
Unadjusted	0.54 (0.30–0.97)	0.04	0.90 (0.64–1.27)	0.58
Adjusted	0.41 (0.22–0.76)	0.005	0.95 (0.67–0.95)	0.79

BTC: Bridge to candidacy; NE: Northeast; **S:** South; **MW:** Midwest; **W:** West

[†]Variables in the model: age, gender, race/ethnicity, college education, body mass index, smoking, alcohol use, INTERMACS profile, previous cancer, chronic obstructive pulmonary disease, diabetes, cerebrovascular disease, peripheral vascular disease, coronary artery disease, history of coronary artery bypass graft, history of valve surgery, ascites, implantable cardiac defibrillator, serum sodium, albumin, total bilirubin, blood urea nitrogen, creatinine, international normalized ratio, alanine aminotransferase, aspartate aminotransferase, cholesterol, white blood cell count, use of intra-aortic balloon pump, left ventricular ejection fraction<20%, left ventricular end diastolic diameter, severe right ventricular dysfunction, biventricular assist device use, concomitant surgery, inotrope use, and pre-implant invasive hemodynamics including cardiac output, cardiac index, right atrial pressure, pulmonary capillary wedge pressure, pulmonary vascular resistance.

Table 4

Causes of Death by Geographic Region (n=total deaths/total patients)

Causes of Death %	Total (n=1653)	Northeast (n=560)	Midwest (n=483)	West (n=203)	South (n=407)	P Value
Right Heart Failure	5.3%	6.1%	3.5%	2.5%	7.9%	.01
Major Bleeding	4.2%	5.0%	3.7%	5.4%	3.0%	.32
Cardiac Arrhythmia	3.0%	3.0%	2.5%	3.9%	3.2%	.78
Hemolysis	0.5%	0.7%	0.6%	0.5%	0.3%	.76
End Stage	1.8%	1.6%	1.2%	3.0%	2.2%	.41
Cardiomyopathy	10.4%	11.8%	11.4%	7.4%	8.9%	.20
Major Infection	3.2%	2.9%	3.7%	4.9%	2.2%	.28
Device Malfunction	1.2%	0.9%	1.7%	0.5%	1.2%	.53
Hepatic	1.6%	1.1%	1.9%	0.5%	2.7%	.12
Dysfunction	18.3%	16.8%	18.6%	19.2%	19.4%	.72
Renal Dysfunction	47.7%	47.7%	47.6%	49.8%	46.9%	.93
Neurological	2.7%	2.5%	3.5%	2.5%	2.2%	.63
Dysfunction						
Other						
Unknown						

* overall p-value = .23