The Paradoxical Relationship Between Donor Distance and Survival After Heart Transplantation

Todd C. Crawford, MD, J. Trent Magruder, MD, Joshua C. Grimm, MD, Clinton D. Kemp, MD, Alejandro Suarez-Pierre, MD, Kenton J. Zehr, MD, Kaushik Mandal, MD, Glenn J. Whitman, MD, John V. Conte, MD, Robert S. Higgins, MD, Duke E. Cameron, MD, and Christopher M. Sciortino, MD, PhD

Division of Cardiac Surgery, Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

Background. **Concerns over prolonged allograft ischemia have limited the widespread adoption of long-distance organ procurement in heart transplantation (HT). We sought to assess whether donor distance from the center of transplantation independently affects mortality.**

Methods. **We queried the United Network for Organ Sharing (UNOS) database for adults undergoing isolated HT from 2005 to 2012. Risk-adjusted Cox proportional hazards models were constructed for the primary outcomes of 30-day and 1-year mortality, and the independent impact of donor distance from transplantation center at the time of procurement was assessed.**

Results. **We included 14,588 heart transplant recipients. The mean distance from location of the donor heart to transplantation center was 184.4 ± 214.6 miles; 1,214 HTs (8.3%) occurred at the same location as the donor heart. Ischemic times were inversely related to the distance from the site of donor procurement to recipient transplantation. After risk adjustment, longer donor distances (in miles) were associated with a significantly lower risk of mortality at both 30 days (hazard ratio [HR] 0.9993, 95% confidence interval [CI]: 0.9988 to 0.9998, $p < 0.01$) and 1 year (HR 0.9994, 95% CI: 0.9989 to 0.9999, $p = 0.015$). Risk-adjusted hazards for mortality were significantly reduced in recipients receiving hearts from more than 25 miles away. The hazard reduction was greatest in recipients receiving donor hearts from more than 500 miles away (1-year HR 0.64, $p < 0.01$; 30-day HR 0.47, $p < 0.01$).**

Conclusions. **Longer distances between donor location and center of heart transplantation are associated with a reduced hazard for survival at 30 days and 1 year, despite greater ischemic times. Future studies are necessary to elucidate the protective factors surrounding long-distance heart donation.**

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End-stage heart failure represents the final common pathway of several different cardiomyopathic disorders. Despite the emergence of multiple methods of temporary or long-term mechanical circulatory support, heart transplantation remains the only curative therapy. As with other solid organs, heart transplantation is constrained by a scarcity of suitable donors, limiting the availability of this potentially life-saving intervention. Further exacerbating the supply–demand mismatch are historic concerns over the duration of ischemic time and its detrimental influence on survival [1–4], thus restricting the widespread incorporation of long-distance donors into the supply chain. In the current era of transplantation, donor distances from the center of heart recipient transplantation, which are positively correlated with ischemic time, vary widely depending on the region the transplantation occurs in.

As early as the late 1970s, single institutions began exploring long-distance organ procurement as a means of expanding the donor pool [5]. Early results demonstrated equivalent mortality among short-distance and long-distance donors [6, 7]. Similar findings have been corroborated in subsequent studies in which allograft ischemic time has extended beyond 300 minutes without compromising graft function or survival [8–10]. More recently, Atik and colleagues [11] demonstrated that the addition of long-distance heart procurements could expand the viable donor pool and reduce wait list mortality without compromising 30-day or 1-year survival. Although previous literature has demonstrated a detrimental effect of longer ischemic times on mortality after heart transplantation, the survival impact of the donor location relative to recipient location has not been previously elucidated.

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Address correspondence to Dr Sciortino, Division of Cardiac Surgery, Department of Surgery, Johns Hopkins University School of Medicine, 1800 Orleans St, Zayed Tower 7107, Baltimore, MD 21287; email: csciort2@jhmi.edu.

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We sought to investigate the impact of the donor distance (in miles) from the recipient transplantation center on 30-day and 1-year survivals, hypothesizing that recipients who received a transplant at the same location as the donor would experience superior survival in comparison with patients who receive donor hearts further from the center of transplantation.

Patients and Methods

Patient Selection

The United Network for Organ Sharing (UNOS) data file is a de-identified database that is available for research purposes. We received institutional review board approval to retrospectively study outcomes after heart transplantation. All adult recipients (≥18 years of age) in the UNOS database who underwent isolated orthotopic heart transplantation from 2005 to 2012 were included in this study.

Donor Distance Cohorts

The donor distance (ie, procurement location in relation to recipient transplantation location) was broken down into seven strata in an attempt to capture local, regional, and cross-state disparities in donor characteristics. We were particularly interested in comparing donors from communities in which a transplantation center was located against donors distant from the transplanting center. Accordingly, we created the following distance strata: identical donor and transplantation location, donor location 0 to 10 miles from transplantation location, 10 to 25 miles, 25 to 100 miles, 100 to 300 miles, 300 to 500 miles, and more than 500 miles.

Outcomes

The primary outcomes were death within 30 days and death within 1 year of transplantation.

Statistical Analysis

All statistical analysis was performed using STATA 12.0 (StataCorp, College Station, TX). Normally distributed variables were listed as mean ± SD, and nonparametric variables were listed as median (interquartile range). Descriptive analysis was performed using Student's t tests or Wilcoxon rank-sum testing for continuous variables. Categorical variables are listed as number (%) and compared using χ^2 tests. Significance was defined as a p value less than 0.05 for all tests.

We first assessed the unadjusted impact of donor distance from the center of heart transplantation on our primary outcomes of 30-day and 1-year mortality by the method of Kaplan and Meier. Cox proportional hazards modeling was then performed. We tested patient and donor risk factors first as univariables. Covariates that demonstrated an association with the outcome of interest ($p < 0.20$) were added manually forward into a multivariable regression model. Likelihood ratio testing and Akaike information criteria were used to construct the most parsimonious model. We performed an effect–size determination calculation to determine the minimum hazard ratio (HR) for mortality that could be detected given our sample size, assuming a standard power of 0.80 and alpha of 0.05. This was determined to be 0.90.

Results

Over the study period, 14,588 patients underwent isolated heart transplantation. The mean recipient age was 52 ± 13 years, and average donor age was 31 ± 12 years. Median distance from the location of donor procurement to the recipient transplantation site was 101 miles (interquartile range, 14 to 304 miles) with a range of 0 to 2,109 miles. However, significant UNOS regional variation was observed for donor distance, with region 1 having the shortest average donor distance of 135 ± 159 miles and region 6 having the longest average donor distance at 308 ± 353 miles, a two-fold greater distance than region 1.

A breakdown of patients who received a transplant based on distance from the donor is detailed as follows: procurement site same as recipient site, 1,214 patients (8.3%); 0 to 10 miles, 1,993 patients (13.7%); 10 to 25 miles, 1,214 patients (8.3%); 25 to 100 miles, 2,823 patients (19.4%); 100 to 300 miles, 3,623 patients (24.8%); 300 to 500 miles, 2,792 patients (19.1%); and more than 500 miles, 929 patients (6.4%). Average ischemic time was 3.3 ± 1.1 hours and also varied by region (Table 1); 3,440 patients (23.6%) had an ischemic time more than 4 hours, and 562 patients (3.9%) had an ischemic time more than 6 hours. Average ischemic time was positively correlated with the donor distance from the site of recipient transplantation and varied significantly among different distance strata (analysis of variance $p < 0.01$).

A review of recipient and donor characteristics based on donor distance from the site of transplantation revealed significant differences among donor distance strata (Table 2). Recipient age, sex, race, and body mass index differed significantly across cohorts ($p < 0.01$ for

Table 1. Comparison of Donor Distances From Transplantation Center and Ischemic Times Across UNOS Regions

UNOS Region	Average Donor Distance (miles)	Average Ischemia Time (hours)	Total Transplantations Over Study Period
1	135 ± 159	3.2 ± 0.9	599
2	174 ± 217	3.2 ± 1.0	2,019
3	184 ± 232	3.4 ± 1.2	1,833
4	182 ± 190	3.2 ± 1.0	1,459
5	163 ± 189	3.4 ± 1.0	2,238
6	308 ± 353	3.9 ± 1.3	404
7	203 ± 229	3.3 ± 1.1	1,340
8	184 ± 206	3.1 ± 1.1	880
9	227 ± 255	3.3 ± 1.1	982
10	175 ± 199	3.0 ± 0.9	1,200
11	182 ± 174	3.1 ± 0.9	1,610

UNOS = United Network for Organ Sharing.