Survival After Heart Transplantation Is Not Diminished Among Recipients With Uncomplicated Diabetes Mellitus
An Analysis of the United Network of Organ Sharing Database

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Background—This study compares posttransplantation outcomes of survival and morbidity among recipients with and without diabetes mellitus (DM).

Methods and Results—The United Network of Organ Sharing (UNOS) provided deidentified patient-level data. Primary analysis focused on 20,412 first-time heart transplant recipients aged ≥18 years who underwent transplantation between January 1, 1995, and December 31, 2005. To determine severity of DM, DM recipients were stratified by their aggregate number of diabetes-related complications (DRCs), including pretransplantation history of renal failure (serum creatinine ≥2.5 mg/dL), peripheral vascular disease, cerebrovascular accident, and severe obesity (body mass index ≥35 kg/m²). Kaplan-Meier analysis was performed to compare time to event. Although posttransplantation survival was significantly better (P<0.001) among patients without DM (median survival 10.1 years) than among those with DM (9.0 years), survival did not differ (P=0.08) between those without DM (10.1 years) and those with uncomplicated DM (0 DRCs; 9.3 years). Among those with DM, survival was worse with each additional DRC: 0 DRC, 9.3 years; 1 DRC, 6.7 years; and ≥2 DRCs, 3.6 years. Although acute rejection and transplant coronary artery disease–free survival did not differ between groups, renal failure and severe infection-free survival were worse in those with DM and were inversely related to the number of DRCs.

Conclusions—Posttransplantation survival among patients with uncomplicated DM was not significantly different than that among nondiabetics. However, when stratified by disease severity, recipients with more severe diabetes had significantly worse survival than nondiabetics. Therefore, although DM alone should not be a contraindication to heart transplantation, given the critical shortage of transplantable organs, maximal benefit may be achieved by exploring alternative treatment options in patients with severe DM. These include use of high-risk transplant lists and destination therapy.

Key Words: transplantation ■ diabetes mellitus ■ risk factors ■ heart failure ■ outcomes

Diabetes mellitus is a significant risk factor for developing cardiac disease, including heart failure. In fact, compared with nondiabetics, diabetic patients are twice as likely to develop heart failure,¹ and in recent years, an increasing percentage of heart failure has been attributed to diabetes.² As a result, many diabetics will progress to end-stage heart failure.

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Heart transplantation remains the “gold standard” for the treatment of end-stage heart failure; however, because of a number of concerns, transplantation in diabetic patients remains controversial. First, diabetics face an increased risk of pretransplantation renal failure (PRF),³,⁴ peripheral vascular disease (PVD),⁵ and cerebrovascular accidents (CVAs).⁶ In addition, the hyperglycemic effect of immunosuppressant steroid therapy further complicates the posttransplantation management of their disease. Moreover, there is concern for a multiple-hit phenomenon in which the use of nephrotoxic immunosuppressant drugs further increases the likelihood of renal disease in patients already at risk. Finally, although still unproven, a higher incidence of posttransplantation infection,⁷ rejection,⁸ and transplant coronary artery disease (TCAD)⁹,¹⁰ is hypothesized. Given these concerns, diabetes is a relative contraindication to heart transplantation at some
centers, and diabetes complicated by end-organ damage is frequently suggested as an indication for long-term support with a ventricular assist device as an alternative to transplantation, in a treatment strategy known as destination therapy.

Previous studies including studies from our institution, examining posttransplantation survival among diabetic recipients found no significant difference in survival among diabetics compared with nondiabetics. However, by demonstrating a trend toward worse survival among diabetic recipients, these single-center studies, which were limited in size and duration of follow-up, did not end the debate about the effect of diabetes on posttransplantation survival. In the face of a critical scarcity of transplantable organs, it is important to understand the risks and benefits associated with providing transplants to this growing population of heart failure patients. Therefore, we chose to analyze the United Network for Organ Sharing (UNOS) database to provide the first review of the national experience with diabetes mellitus and heart transplantation.

The purpose of the present study was to assess (1) the long-term survival of diabetic recipients after heart transplantation and (2) transplant-related morbidity, including posttransplantation renal failure (RF), infection, rejection, and TCAD. Because diabetes occurs across a broad spectrum of severity, diabetic recipients were stratified on the basis of disease severity by methods similar to those used in previous studies of diabetic cardiac surgery patients. Specifically, diabetic recipients were grouped on the basis of disease severity as defined by their number of diabetes-related complications (DRCs), including pretransplantation history of PVD, PRF, CVA, and severe obesity (body mass index [BMI] ≥35 kg/m²).

Methods

Data Collection

Use of these data is consistent with the regulations of our university’s Institutional Review Board. UNOS provided deidentified patient-level data from the Thoracic Registry (data source #021606-4). These data included all heart transplant recipients and donors in the United States and reported to the Organ Procurement and Transplantation Network between October 1, 1987, and February 27, 2006. Data entry by all US transplant centers has been mandatory since the passage of the National Transplantation Act of 1984. There is 1 record per waiting list registration/transplantation event, and each record includes the most recent follow-up information (including patient and graft survival) reported to the Organ Procurement and Transplantation Network as of the date the file was created. To ensure the confidentiality of centers and patients, the dataset does not include any patient or transplant center identifiers except for a unique patient identification number. All dates are offset by a random number of days between −180 and 180. The offset number is patient specific and applied to entered data for a given patient; therefore, it does not affect calculations related to time between events.

Follow-up data are represented as 1 record per follow-up per transplantation event. Some patients have multiple records in a given year, whereas others have only 1 record. Patients lost to follow-up were censored at the time of last known follow-up.

Study Population

The study considered patients aged 18 years and older undergoing first-time heart transplantation between January 1, 1995, and December 31, 2005 (n = 21,348). Of these, patients with a previous heart transplant (n = 556, 2.60%) and those undergoing a multivisceral transplantation (n = 380, 1.78%) were excluded. Patients were monitored from the date of transplantation to February 27, 2006, which was the last day of follow-up provided by UNOS. Mean patient follow-up period was 3.76 ± 3.05 years.

Diabetes-Related Complications

DRCs included pretransplantation history of CVA, PVD, PRF, and severe obesity (BMI ≥35 kg/m²). Information on demographics and past medical history was collected by the listing centers at the time of listing for transplantation. PRF was defined as creatinine ≥2.5 mg/dL at the time of listing or transplantation or prior history of dialysis at the time of listing or during the waiting period, as recorded by the listing centers. Severe obesity was defined as BMI ≥35 kg/m² at the time of listing. For each patient with diabetes, the number of DRCs was aggregated; uncomplicated diabetes was defined by the absence of pretransplantation PVD, PRF, and CVA, with a BMI <35 kg/m².

Outcomes Measures

The primary outcomes measure was median posttransplantation survival (MPS) in years. Other outcomes of interest included TCAD-free survival (TCAD-FS), posttransplantation renal failure–free survival (RF-FS), acute rejection–free survival (AR-FS), and severe infection–free survival (SI-FS). RF was defined as posttransplantation creatinine ≥2.5 mg/dL or need for dialysis. SI was defined as the need for hospitalization due to infection, and AR was defined as an episode of acute rejection that required medical treatment. In addition, cause of death was grouped into 1 of 5 categories (infection, cerebrovascular, cardiovascular, renal failure, and rejection). Finally, functional status was analyzed. Functional status was scored on a scale ranging from 1 to 3, in which an individual is categorized as performing activities of daily living with no assistance (1), some assistance (2), or total assistance (3).

Data Analysis

Continuous variables were reported as mean ± SD and compared with the Student t test. To compare categorical variables, the χ² test was used. The conventional probability value of 0.05 or less was used to determine the level of statistical significance. All reported probability values are 2 sided.

Survival and Other Time-to-Event Analysis

Kaplan-Meier analysis with log-rank test was used for time-to-event analysis for actuarial survival, as well as TCAD-FS, RF-FS, AR-FS, and SI-FS. For survival analysis, the outcome of interest was death (n = 5,335, 27.4%) or retransplantation (n = 191, 0.98%); other patients, including those lost to follow-up (n = 734, 3.76%) or alive at last follow-up (13,259, n = 67.9%), were censored on the day of last known follow-up. For other time-to-event analyses, including analysis to examine TCAD-FS, RF-FS, AR-FS, and SI-FS, patients were censored at the time of death, retransplantation, or last known follow-up. Median time to event was the period of follow-up in years when 50% of uncensored patients experienced the event of interest (RF, infection, rejection, or TCAD). Survival is actuarial survival and is expressed as median survival in terms of years, where more years mean better survival.

Multivariable Cox proportional hazards regression was also performed (backward, remove P > 0.15) to assess the simultaneous effect of multiple variables on survival after heart transplantation, including history of hypertension, history of diabetes, donor age, recipient age, ischemic origin of heart failure, ischemic time, and UNOS status at the time of transplantation 1/1A/1B. The hazard ratio and 95% CI were reported for each factor. All data were analyzed with a statistical software package, Stata 9 (Stata Corp, College Station, Tex).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.
Results

Study Population
The study population comprised 20,412 heart transplant recipients. Analysis included 75,997.9 years at risk; median survival for all recipients was 9.9 years. Among recipients, 15,826 (77.5%) were nondiabetic, and 3687 (18.1%) had diabetes; 899 (4.4%) recipients were dropped from analysis because data on diabetic status were omitted. Demographic and clinical characteristics of the study patients are summarized in Table 1.

Diabetes-Related Complications
Compared with nondiabetics, a history of CVA (n=881, 5.6% versus 266, 7.2%; P<0.001), PRF (884, 5.6% versus 285, 7.7%; P<0.001), PVD (439, 2.8% versus 255, 6.9%; P<0.001), and severe obesity (508, 3.2% versus 215, 5.8%; P<0.001) occurred more frequently among diabetics (Table 1). Among the diabetic group, 2805 (76.1%) did not have any DRCs, whereas 766 (20.8%) and 116 (3.2%) had 1 and 2 DRCs, respectively. Diabetics had significantly worse survival than nondiabetics with the same pretransplantation condition: CVA (8.6 versus 9.6 years, P<0.05), PRF (3.4 versus 6.8 years, P=0.01), PVD (6.0 versus 8.5 years, P=0.02), or BMI ≥35 kg/m² (5.7 versus 8.6 years, P=0.02; Figure 1).

Survival
As shown in Figure 2a and Table 2, median survival among nondiabetic patients (10.1 years) was significantly better (P<0.001) than among diabetic patients (9.0 years). In the multivariable Cox proportional hazards regression, history of diabetes (P<0.001), increasing donor age (P<0.001), increasing recipient age (P=0.009), increasing ischemic time

### Table 1. Patient Characteristics for All Heart Transplant Recipients Aged 18 Years and Over (1995–2005)

<table>
<thead>
<tr>
<th></th>
<th>Nondiabetics</th>
<th>Diabetics</th>
<th>Total</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart transplant recipients, n (%)</td>
<td>15,826 (81.10)</td>
<td>3687 (18.90)</td>
<td>19,513 (100)</td>
<td></td>
</tr>
<tr>
<td>Mean age, y</td>
<td>51.2±12.1</td>
<td>55.8±7.89</td>
<td>52.1±11.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>11,990 (75.76)</td>
<td>2942 (79.79)</td>
<td>14,932 (76.52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.8±4.7</td>
<td>27.7±4.6</td>
<td>26.1±4.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>12,421 (78.48%)</td>
<td>2870 (77.84%)</td>
<td>15,291 (78.36%)</td>
<td>0.373</td>
</tr>
<tr>
<td>Black</td>
<td>2122 (13.41%)</td>
<td>463 (12.56%)</td>
<td>2585 (13.25%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hispanic</td>
<td>865 (5.47%)</td>
<td>255 (6.92%)</td>
<td>1120 (5.74%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Asian</td>
<td>277 (1.75%)</td>
<td>64 (1.74%)</td>
<td>341 (1.75%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Other</td>
<td>141 (0.89%)</td>
<td>35 (0.95%)</td>
<td>176 (0.90%)</td>
<td>0.951</td>
</tr>
<tr>
<td>Blood type, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>6859 (43.34%)</td>
<td>1676 (45.46%)</td>
<td>8535 (43.74%)</td>
<td>0.02</td>
</tr>
<tr>
<td>B</td>
<td>1984 (12.54%)</td>
<td>473 (12.83%)</td>
<td>2457 (12.59%)</td>
<td>0.812</td>
</tr>
<tr>
<td>AB</td>
<td>778 (4.92%)</td>
<td>171 (4.64%)</td>
<td>949 (4.86%)</td>
<td>0.563</td>
</tr>
<tr>
<td>0</td>
<td>5747 (36.31%)</td>
<td>1252 (33.96%)</td>
<td>6999 (35.87%)</td>
<td>0.021</td>
</tr>
<tr>
<td>Cause of heart failure, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>7267 (45.92%)</td>
<td>2409 (65.34%)</td>
<td>9676 (49.59%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dilated</td>
<td>7069 (44.67%)</td>
<td>1147 (31.11%)</td>
<td>8216 (42.11%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>1490 (9.41%)</td>
<td>131 (3.55%)</td>
<td>1621 (8.31%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Status at transplantation, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11,312 (71.48%)</td>
<td>2687 (72.88%)</td>
<td>13,999 (71.74%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4514 (28.52%)</td>
<td>1000 (27.12%)</td>
<td>5514 (28.26%)</td>
<td>0.089</td>
</tr>
<tr>
<td>Life support at transplantation, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD</td>
<td>2777 (17.55%)</td>
<td>646 (17.52%)</td>
<td>3423 (17.54%)</td>
<td>0.97</td>
</tr>
<tr>
<td>IABP</td>
<td>805 (5.09%)</td>
<td>229 (6.21%)</td>
<td>1034 (5.30%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Intubated</td>
<td>465 (2.94%)</td>
<td>95 (2.58%)</td>
<td>560 (2.87%)</td>
<td>0.235</td>
</tr>
<tr>
<td>Ischemic time, h</td>
<td>3.04±1.02</td>
<td>3.09±1.04</td>
<td>3.05±1.02</td>
<td>0.15</td>
</tr>
<tr>
<td>Donor age, y</td>
<td>31.0±12.8</td>
<td>32.1±12.7</td>
<td>31.2±12.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pretransplantation history, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVA</td>
<td>881 (5.57%)</td>
<td>266 (7.21%)</td>
<td>1147 (5.88%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RF</td>
<td>884 (5.59%)</td>
<td>285 (7.73%)</td>
<td>1169 (5.99%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PVD</td>
<td>439 (2.77%)</td>
<td>255 (6.92%)</td>
<td>694 (3.56%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe obesity (BMI ≥35)</td>
<td>508 (3.21%)</td>
<td>215 (5.83%)</td>
<td>723 (3.71%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
(P<0.001), ischemic cause of heart failure (P<0.001), and UNOS status 1/1A/1B at transplantation (P<0.001) were associated with worse survival. However, as shown in Figure 2b, median survival did not differ significantly (P=0.080) between nondiabetics (10.1 years) and those patients with uncomplicated diabetes (9.3 years). This relationship persisted in the multivariate model (P=0.276). Figure 2b also demonstrates that diabetic transplant recipients with 1 DRC (6.7 years) or ≥2 DRCs (3.6 years) had much worse survival than nondiabetic recipients, with survival worsening with each additional DRC.

**Posttransplantation Infection**
SI-FS was significantly better (P<0.001) in nondiabetics (8.9 years) than in diabetics (5.1 years). Among diabetic recipients, SI-FS was better (P<0.001) in uncomplicated diabetics (6.0 years) than in diabetic patients with 1 DRC (3.1 years) and was worst among patients with ≥2 DRCs (2.0 years; Figure 3a).

**Posttransplantation Renal Failure**
Posttransplantation RF-FS was significantly better (P<0.001) among nondiabetics (7.2 years) than among diabetics (5.0 years). Among diabetic recipients, RF-FS was better (P<0.001) among uncomplicated diabetics (5.2 years) than among diabetic patients with 1 DRC (4.0 years), and RF-FS was worst among patients with ≥2 DRCs (2.0 years; Figure 3b).

**Posttransplantation Rejection**
AR-FS was not significantly different (P=0.36) between diabetic (3.1 years) and nondiabetic (3.7 years) recipients. When stratified groups were compared with nondiabetics, there was no significant difference in AR-FS for recipients with uncomplicated diabetes (3.3 years; P=0.86) and diabetics with 1 DRC (2.9 years; 0.22) or ≥2 DRCs (1.4 years; P=0.040; Figure 3c).

**Posttransplantation Coronary Artery Disease**
There was a statistically significant difference (P=0.035) in TCAD-FS when diabetics (8.0 years) were compared with nondiabetic (8.3 years) patients. However, when stratified groups were compared with nondiabetics, there were no significant differences in TCAD-FS for uncomplicated diabetics (8.0 years; P=0.12) or for diabetics with 1 DRC (8.0 years; 0.096) or ≥2 DRCs (6.1 years; P=0.16; Figure 3d).
When we compared nondiabetics with transplant recipients with uncomplicated diabetes, the percentage of patients who were able to perform activities of daily living with no assistance was greater in the nondiabetic group at 1 year (n/N9906, 89.8% versus n/N2150, 85.1%; P/N0.001), 3 years (n/N7532, 90.8% versus n/N1508, 84.9%; P/N0.001), and 9 years (n/N1169; 80.8% versus n/N150, 70.1%; P/N0.001) of follow-up (Table 2).

**Cause of Death**

As described in Table 3, death due to infection (P/N0.001), CVA (P/N0.004), and RF (P/N0.02) occurred more frequently in the diabetic group, with frequency increasing with the severity of diabetes.

**Discussion**

With median posttransplantation survival approaching 10 years, heart transplantation offers substantial benefits to end-stage heart failure patients. Unfortunately, because organs available for transplantation remain critically scarce, achievement of the maximal benefit from this therapy is predicated on improved patient selection. To this end, the risks and benefits associated with transplantation in various groups of heart failure patients must be better understood.

Previous studies have attempted to describe posttransplantation morbidity and mortality among diabetic patients. Although offering some insight, these studies, because of limitations in size and follow-up, were unable to draw definitive conclusions regarding the effect of...
diabetes on heart transplant recipients. The present study overcomes these limitations by including all adult heart transplant recipients in the United States since 1995. Furthermore, by stratifying patients on the basis of the severity of their diabetes, this study considers the effects of diabetes across a spectrum of severity levels.

Survival
When considered as a single group, diabetics demonstrated worse survival after heart transplantation than nondiabetics; however, when stratified by disease severity, diabetic recipients with less severe disease achieved significantly better survival than those with more severe diabetes. In fact, there was no statistically significant difference in survival between nondiabetic recipients and recipients with uncomplicated diabetes. This finding supports the belief that survival in well-selected diabetic recipients is not different from nondiabetics. Conversely, recipients with more severe diabetes did suffer a dramatic decrease in survival; among diabetics with 1 and ≥2 DRCs, median survival was 3.4 and 6.5 years less than in nondiabetic patients, respectively.

Diabetes-Related Complications
Compared with nondiabetics with the same pretransplantation condition, diabetics with a history of CVA, BMI ≥35 kg/m², PVD, and PRF had reductions in median survival of 1.0, 2.9, 2.5, and 3.4 years, respectively. This finding is important because it suggests that although these conditions, defined in the present study as DRCs, are not limited to diabetics, the underlying disease process likely differs between diabetics and nondiabetics.

Secondary End Points: Infection, Rejection, Renal Failure, and TCAD
As in previous studies,13 risk of infection in the present study was significantly worse among diabetic patients. This was true whether patients had uncomplicated or complicated diabetes; however, SI-FS was inversely related to the number of DRCs, with the recipient’s risk increasing with each additional DRC. As with infection, diabetic recipients progressed to renal failure more rapidly than nondiabetics, and again, the progression was more rapid with increasing severity of diabetes. Furthermore, the incidence rates of deaths related to infection and renal failure were greater in diabetic patients than in nondiabetics, and as expected, incidence rates increased with severity of diabetes.

With regard to rejection, some investigators have theorized that diabetics face decreased rejection, possibly secondary to a decrease in cell-mediated immune function; others have suggested that the higher incidence of infection leads to increased rates of rejection. However, as in our institution’s previous study,7 the present study found no demonstrable difference in AR-FS between the diabetic and nondiabetic recipients. When we compared median TCAD-FS among all diabetics with nondiabetics, there was a small but statistically significant difference of 105 days. Moreover, when we compared nondiabetics with recipients from any of the stratified diabetic groups, there was no statistically significant difference. On the basis of these findings, it appears that history of diabetes is not an important risk factor for the development of either rejection or TCAD.

Functional Status
Although survival remains the primary outcomes measure after transplantation, measures of quality of life should not be overlooked. Information on patients’ functional status is obtained as part of standard reporting procedures. By the UNOS classification scheme, individuals are classified as capable of performing activities of daily living with no assistance (1), some assistance (2), or total assistance (3). Consistent with other measures, patients with an increasing number of DRCs had worse functional status than other patients. Nevertheless, with >70% of patients with uncomplicated diabetes performing activities of daily living without any assistance at 9 years, uncomplicated patients demonstrated acceptable levels of functional status.

Study Limitations
Although other investigators15,16 have applied similar approaches to characterize the severity of diabetes in cardiac surgery patients, a complex multidimensional construct such as severity of diabetes cannot be fully characterized by any single measure or group of measures. In addition, important DRCs, including neuropathy and retinopathy, were not captured in the present dataset, nor were duration

TABLE 3. Incidence Rate of Death by Cause (per 100 Patient-Years) and DRCs

<table>
<thead>
<tr>
<th>Cause</th>
<th>Non-DM</th>
<th>DM</th>
<th>P</th>
<th>0 DRC</th>
<th>1 DRC</th>
<th>≥2 DRC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>1.22</td>
<td>1.71</td>
<td>&lt;0.001</td>
<td>1.48</td>
<td>0.040</td>
<td>2.24</td>
<td>0.001</td>
</tr>
<tr>
<td>CVA</td>
<td>2.51</td>
<td>3.87</td>
<td>0.004</td>
<td>3.44</td>
<td>0.064</td>
<td>5.06</td>
<td>0.011</td>
</tr>
<tr>
<td>RF</td>
<td>1.32</td>
<td>2.13</td>
<td>0.016</td>
<td>1.79</td>
<td>0.185</td>
<td>2.68</td>
<td>0.060</td>
</tr>
<tr>
<td>Rejection</td>
<td>11.40</td>
<td>10.20</td>
<td>0.184</td>
<td>9.55</td>
<td>0.055</td>
<td>12.70</td>
<td>0.487</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>10.12</td>
<td>9.70</td>
<td>0.617</td>
<td>8.97</td>
<td>0.216</td>
<td>11.90</td>
<td>0.320</td>
</tr>
</tbody>
</table>

Non-DM indicates nondiabetic recipients; DM, diabetic recipients; and cardiovascular, cardiovascular-related deaths as categorized by UNOS, including death attributed to (in order of frequency): cardiac arrest, coronary artery disease/atherosclerosis, myocardial infarction, ventricular failure, rhythm disorder, cardiogenic shock, aortic aneurysm, arterial embolism, and cardiitis.

All probability values were calculated by comparing the group of interest with nondiabetic recipients.
of diabetes or insulin requirements. Nevertheless, PRF, CVA, PVD, and obesity are known complications of diabetes and occur more frequently among those with more severe cases. Moreover, for purposes of the present analysis, severity of diabetes was characterized by discrete severity strata and DRCs only by presence or absence of disease. Information is lost with this strategy because it assumes that all patients in a given group face identical disease burden, whereas patients in different groups face different risks. However, each of these conditions occurs across a continuous spectrum of disease severity. Therefore, although patients with BMIs of 36 and 46 kg/m² were assigned the same risk, patients with higher BMIs should be expected to face greater risks. Conversely, although patients with serum creatinine of 2.6 mg/dL were classified as having chronic renal failure and those with serum creatinine of 2.4 mg/dL were not, both have significant renal dysfunction and therefore are higher-risk transplantation candidates.

Conditions termed DRCs are not caused exclusively by diabetes. For example, hypertension is an important cause of both renal failure and CVAs and certainly is a contributing factor in at least some cases. However, there was no difference in pretransplantation hypertension among recipients with or without a history of PRF (n = 2128, 11.24% versus n = 145, 10.51%; P = 0.41) or with or without a history of CVA (n = 2140, 11.17% versus n = 133, 11.65%; P = 0.62).

Time-to-event analysis for TCAD-FS, RF-FS, AR-FS, and SI-FS assumes that the event of interest is the only outcome, and therefore if death occurred before this outcome, the patients were censored. As part of future studies, we will perform analysis of competing outcomes to account for multiple possible outcomes; this analysis was omitted here because it was clinically meaningless within the context of the present study.

Finally, although the UNOS reporting system provided guidelines for defining conditions such as CVA, PVD, and rejection, definitions may vary by center. In addition, patient registries often suffer from variability in data entry. However, fields contained within this database were generally well populated, with a 95% to 99% data-entry rate for the majority of variables; moreover, both the percentage of recipients with diabetes and median, 1-year, and 5-year survival rates were similar to data reported in our institution’s review of posttransplantation survival among diabetics.?

Conclusions and Implications

Relative to nondiabetics, diabetic recipients had worse posttransplantation survival. Diabetics were also more susceptible to infection and renal failure. However, when diabetics were stratified by disease severity, recipients with less severe disease achieved better survival. Accordingly, posttransplantation survival was not significantly different between uncomplicated diabetics and nondiabetic recipients. Furthermore, relative to other diabetics, recipients with uncomplicated diabetics experienced better SI-FS and RF-FS.

Given these findings, diabetes alone should not be a contraindication to heart transplantation. Well-selected diabetic patients achieve the same survival as nondiabetic patients. Conversely, patients with complicated diabetes have significantly worse survival. Therefore, given the critical shortage of transplantable organs, maximal benefit may be achieved by exploring alternative treatment options in patients with severe diabetes. These include use of high-risk transplant lists and destination therapy.

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Disclosures

None.

References

With organs available for transplantation critically scarce, the achievement of maximal benefit from this therapy is predicated on improved patient selection. To this end, the risks and benefits associated with transplantation in various groups of heart failure patients must be better understood. Diabetes mellitus is a significant risk factor for developing cardiac disease, including heart failure, and an increasing percentage of heart failure has been attributed to diabetes. As a result, many diabetics will progress to end-stage heart failure. Heart transplantation remains the “gold standard” for the treatment of end-stage heart failure; however, because of a number of concerns, transplantation in diabetic patients remains controversial, and diabetes complicated by end-organ damage is frequently suggested as an indication for destination therapy. An analysis of the United Network for Organ Sharing database demonstrates that relative to nondiabetics, diabetic recipients had worse posttransplantation survival. However, when diabetic patients were stratified by disease severity, recipients with less severe disease achieved better survival. Accordingly, posttransplantation survival was not significantly different between recipients with uncomplicated diabetes and nondiabetic recipients. Given these findings, diabetes alone should not be a contraindication to heart transplantation. Well-selected diabetic patients achieve the same survival as nondiabetic patients. Conversely, patients with complicated diabetes have significantly worse survival. Therefore, given the critical shortage of transplantable organs, maximal benefit may be achieved by exploring alternative treatment options in individuals with severe diabetes. These include use of high-risk transplant lists and destination therapy.
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