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Survival in patients removed from the heart transplant waiting list before receiving a transplant

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BACKGROUND: Little is known about the outcomes in patients who are removed from the heart transplant (HT) waiting list before receiving a transplant. We sought to analyze outcomes in such patients in the United States (U.S.) in the current era.

METHODS: All patients aged ≥ 18 years old listed for a primary HT in the U.S. between July 2004 and September 2010 were identified. Outcomes in those removed from the list by March 2011 (survival, relisting, HT) were examined using time-to-event analyses.

RESULTS: Of 15,061 patients listed for primary HT, 10,168 (68%) received a HT, 1,393 (9%) died on the waiting list, and 1,871(12%) were removed before receiving HT. Of patients removed from the list, 560 (30%) were removed due to clinical improvement, 692 (37%) due to deterioration, and 619 (33%) due to other reasons. After removal, 30-day and 1-year survival were 99.6% and 94%, respectively, in patients removed due to improvement and 44% and 26%, respectively, in patients removed due to deterioration. Multivariable predictors of death after removal were removal due to clinical deterioration, hypertrophic or restrictive cardiomyopathy, United Network of Organ Sharing status 1A/1B at listing, and renal dysfunction. Only 27 patients (4.8%) among those removed due to improvement, 21 (3.0%) removed due to deterioration, and 46 (7.4%) removed due to other reasons were relisted.

CONCLUSIONS: One in 8 patients listed for HT in the U.S. are removed from the waiting list before receiving HT. The indication for removal (clinical deterioration vs improvement) is the strongest independent predictor of survival after removal from the list.

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Heart failure (HF) plays a causal role in > 50,000 deaths among United States (U.S.) adults every year.[1] Although advances in medical management and devices during the last 2 decades have significantly improved survival in HF patients,[2–5] 50% of patients diagnosed with end-stage HF still die within 5 years.[6,7] Heart transplant (HT) is an established therapy for end-stage HF but is available to only 2,000 patients per year in the U.S. due to limited availability of donor hearts.[8] This imbalance between demand and supply for donor hearts has led some experts to compare treating HF with transplantation to treating poverty with lottery.[9]

The scarcity of donor hearts puts enormous responsibility on transplant teams when evaluating HF patients so that HT is offered only when it is expected to substantially improve

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survival or quality of life compared with medical therapy. Furthermore, candidate selection is a dynamic process, and a number of patients initially listed for HT are subsequently de-listed because they no longer meet the listing criteria. The outcomes in patients who are removed from the waiting list before receiving a HT have received little attention. Previous reports are limited to single-center experiences[10–13] and are from an era when a much lower percentage of patients was supported on a ventricular assist device (VAD) at listing compared with the current era. Because patients may be removed from the waiting list due to clinical improvement or deterioration, characterizing outcomes in these cohorts may provide important insights into candidate selection and re-evaluation for listing.

The purpose of this study was to evaluate outcomes in patients removed from the HT waiting list before receiving HT in the current era. The specific objectives were (1) to compare baseline characteristics between patients removed from the list due to clinical deterioration and those removed due to improvement, and (2) to assess outcomes, including survival and relisting, and predictors of survival after removal from the waiting list.

Methods

Study population

We identified all patients aged ≥ 18 years listed for primary HT in the U.S. between July 1, 2004, and September 30, 2010, in the Organ Procurement and Transplant Network (OPTN) database, which includes clinical information on all listed candidates in the U.S. as submitted by transplant centers. The Health Resources and Services Administration, U.S. Department of Health and Human Services, provides oversight to the activities of the OPTN contractor, the United Network of Organ Sharing (UNOS). The Social Security Death Master File provided by the Social Security Administration, which records vital status of U.S. residents,[14] is internally linked to the OPTN database to allow assessment of survival after a candidate is removed from the waiting list and is no longer monitored by UNOS. More than 98% of deaths recorded in the Social Security Death Master File are completed within 3 months after death.[14–18]

We excluded patients who were listed for repeat HT or for multiorgan transplantation. Study patients were monitored from the time of listing until HT, death, removal from the waiting list, or the day of last observation on March 31, 2011. Patients who were removed from the list were monitored until death, relisting (and HT), or the day of last observation. The study cohort did not include those who were only temporarily inactivated.

Study design and definitions

We compared baseline characteristics and outcomes in patients who were removed from the HT waiting list due to clinical improvement, patients removed due to clinical deterioration, and those removed due to other reasons. Demographic and clinical variables were defined at the time of listing. The primary end point was death after removal from the waiting list. We also analyzed patients relisted and who received HT in each group after removal from the list.

Mechanical support was defined using the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) criteria as temporary (projected duration of use < 45 days) or durable. Durable support was assessed as mutually exclusive categories of total artificial heart, biventricular assist device (BIVAD), pulsatile left VAD (LVAD), and continuous-flow LVAD. Ventilator support, inotrope support, implantable cardiac defibrillator, and intra-aortic balloon pump were assessed as dichotomous (yes/no) variables. Listing status was defined according to UNOS definitions.[19] Patient race/ethnicity was recorded as reported by the transplant center and analyzed as white (non-Hispanic), black (non-Hispanic), Hispanic, or other. Renal function was analyzed as a categoric variable (serum creatinine > 1.5 mg/dl) and as estimated glomerular filtration rate using the Modification of Diet in Renal Disease formula.[20]

To assess center volume, we divided transplant centers into 3 categories: low-volume ($n = 65$, those with < 88 patients listed for HT during the study period), medium-volume ($n = 51$, those with 88 to 207 patients listed), and high-volume ($n = 13$, > 207 patients listed) centers. The number of patients chosen to define centers as low-, medium-, and high-volume was empiric and derived from the distribution of listed patients among 129 U.S. centers during the study period as < 50th percentile, 50th to 90th percentile, and >90th percentile, respectively.

No data were missing for the variables of age, sex, race/ethnicity, diagnosis, blood type, hemodynamic support (intra-aortic balloon pump, inotrope support, ventilator, mechanical support), dialysis, medical insurance (Medicaid), UNOS listing status, and dates of listing and removal from the waiting list. For patients with missing data on other variables, we created indicator variables to allow these patients to contribute their other variables to the analysis.

Statistical analysis

Potential outcomes among listed patients—death, HT, or removal from the list—were assessed using competing-outcomes analysis.[21,22] Baseline characteristics in patients who received HT, those who died, and those who were removed from the list, and in patients removed from the waiting list by indication, were compared using the chi-square test for categoric variables and the Kruskal-Wallis test for continuous variables. Survival after removal from the list was assessed using the Kaplan-Meier method and a log-rank test. A multivariable Cox model using forward selection was developed to evaluate the risk factors for death after removal from the list; all variables available at baseline were considered. Variables significant at the 0.10 level based on a likelihood ratio test were retained in the model. Data were analyzed using SAS 9.1 software (SAS Institute Inc, Cary, NC). All statistical tests were 2-sided, and a p-value of < 0.05 was considered statistically significant.

Results

Study population

During the study period, 15,061 patients were listed in the U.S. for their first HT. Of these, 10,168 (68%) underwent HT, 1,393 (9%) died on the waiting list, 1,871(12%) were removed from the list before receiving HT, and 1,629 (11%) were still waiting for HT on the last day of observation. Figure 1 illustrates competing outcomes in listed patients during the first year after listing. Baseline characteristics of