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MINI-FOCUS ISSUE: END-STAGE HEART FAILURE

Does Survival on the Heart Transplant Waiting List Depend on the Underlying Heart Disease?

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ABSTRACT

OBJECTIVES The aim of this study was to identify differences in survival on the basis of type of heart disease while awaiting orthotopic heart transplantation (OHT).

BACKGROUND Patients with restrictive cardiomyopathy (RCM), congenital heart disease (CHD), or hypertrophic cardiomyopathy (HCM) may be at a disadvantage while awaiting OHT because they often are poor candidates for mechanical circulatory support and/or inotropes.

METHODS The study included all adults in the Scientific Registry of Transplant Recipients database awaiting OHT from 2004 to 2014, and outcomes were evaluated on the basis of type of heart disease. The primary endpoint was time to all-cause mortality, censored at last patient follow-up and time of transplantation. Multivariate Cox proportional hazards modeling was performed to evaluate survival by type of cardiomyopathy.

RESULTS There were 14,447 patients with DCM, 823 with RCM, 11,799 with ischemic cardiomyopathy (ICM), 602 with HCM, 964 with CHD, 584 with valvular disease, and 1,528 in the "other" category (including 1,216 for retransplantation). During median follow-up of 3.7 months, 4,943 patients died (1,253 women, 3,690 men). After adjusting for possible confounding variables including age, renal function, inotropes, mechanical ventilation, and mechanical circulatory support, the adjusted hazard ratios by diagnoses relative to DCM were 1.70 for RCM (95% confidence interval [CI]: 1.43 to 2.02), 1.10 for ICM (95% CI: 1.03 to 1.18), 1.23 for HCM (95% CI: 0.98 to 1.54), 1.30 for valvular disease (95% CI: 1.07 to 1.57), 1.37 for CHD (95% CI: 1.17 to 1.61), and 1.51 for "other" diagnoses (95% CI: 1.34 to 1.69). Sex was a significant modifier of mortality for ICM, RCM, and "other" diagnoses ($p < 0.05$ for interaction).

CONCLUSIONS In the United States, patients with RCM, CHD, or prior heart transplantation had a higher risk for death while awaiting OHT than patients with DCM, ICM, HCM, or valvular heart disease. (J Am Coll Cardiol HF 2016;4:689–97)

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ABBREVIATIONS AND ACRONYMS

CHD = congenital heart disease

CI = confidence interval

DCM = dilated cardiomyopathy

ECMO = extracorporeal membrane oxygenation

HCM = hypertrophic cardiomyopathy

HR = hazard ratio

IABP = intra-aortic balloon pump

ICD = implantable cardioverter-defibrillator

ICM = ischemic cardiomyopathy

LVAD = left ventricular assist device

OHT = orthotopic heart transplantation

RCM = restrictive cardiomyopathy

SRTR = Scientific Registry of Transplant Recipients

TAH = total artificial heart

UNOS = United Network for Organ Sharing

VAD = ventricular assist device

There are few studies comparing the survival of patients with different types of heart disease. Prognosis and the optimal timing to waitlist patients with advanced heart failure for orthotopic heart transplantation (OHT) are especially important among cohorts not easily rescued with inotropes or mechanical circulatory support. Studies have shown that patients with congenital heart disease (CHD) have higher 2-month mortality on the waiting list after multivariate analysis compared with patients without CHD (1) and no survival benefit with ventricular assist device (VAD) support (2). Patients with restrictive cardiomyopathy (RCM) may also be at a disadvantage (3), because VAD support is often not possible with small ventricular cavities. In addition, there is concern that patients with hypertrophic cardiomyopathy (HCM) may have a poor prognosis and may not qualify for high-priority transplantation on the basis of the current allocation system (4). In a national study analyzing survival among patients removed from the heart transplant waiting list, HCM and RCM were among the highest predictors of death (5).

The goal of this study was to evaluate whether the type of heart disease affects mortality while awaiting OHT. Because OHT is a competing outcome, differences in rate of transplantation, United Network for Organ Sharing (UNOS) status at time of transplantation, and use of VAD support were also evaluated. The cohort included all adult patients registered on the national heart transplant waitlist between January 1, 2004, and September 3, 2014.

METHODS

SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS. We used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR database includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network, and has been described elsewhere. The Health Resources and Services Administration, U.S. Department of Health and Human Services, provides oversight for the activities of Organ Procurement and Transplantation Network and SRTR contractors. Human error in collecting data is minimized by edit checks, validation of data at the time of entry, and internal verification when there are outliers (6).

PATIENT POPULATION AND UNOS STATUS. We included all adult patients in the SRTR database placed on the waiting list for heart transplantation from January 1, 2004, to September 3, 2014. Patients <18 years of age were excluded because UNOS criteria for listing pediatric patients differed from those for adults (7).

Primary diagnosis was the principal explanatory variable and was categorized on the basis of definitions in the SRTR database: dilated cardiomyopathy (DCM), RCM (idiopathic, amyloid, endocardial fibrosis, sarcoidosis, radiation- or chemotherapy-induced heart disease, and other), ischemic cardiomyopathy (ICM), HCM, valvular heart disease, CHD, and "other" (1,216 prior heart transplantations and 312 "other" diagnoses).

UNOS status was at the time of listing for heart transplantation. UNOS status 1A (high priority) includes patients requiring intra-aortic balloon pumps (IABPs), extracorporeal membrane oxygenation (ECMO), total artificial hearts (TAHs), VADs with device complications, VADs without complications for a total of 30 days, continuous mechanical ventilation, multiple inotropes, or a single high-dose inotrope with continuous hemodynamic monitoring. UNOS status 1B is defined as a patient not meeting criteria for UNOS status 1A but still requiring continuous intravenous inotrope support or VAD support. Finally, UNOS status 2 is for all other active OHT candidates.

OUTCOME MEASURES. The primary endpoint was all-cause mortality, assessed as right-censored time to death, with follow-up censored at the time of heart transplantation. SRTR mortality data are maintained by the transplantation centers and verified with the complete Social Security Death Master File, which is recently available through a specific waiver granted to the SRTR. We also evaluated the cumulative incidence of time to transplantation on the basis of primary diagnosis, censored at the time of last patient follow-up and death.

STATISTICAL ANALYSIS. Baseline characteristics at the time of listing for OHT were stratified by type of heart disease. Continuous variables are expressed as mean ± SD. Categorical variables are expressed as number of patients with frequency (but absolute values were not provided if patient number was <10, to protect the identity of the cohort per SRTR policy). Waitlist survival analysis on the basis of type of heart disease was performed using the Kaplan-Meier method, with censoring for OHT. The primary analysis was based on intention to treat, such that deaths following removal from the waiting list were included in the primary analysis. Multivariable Cox proportional hazards models were created to compare type of