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Wait-List Outcomes for Adults With Congenital Heart Disease Listed for Heart Transplantation in the U.S.

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ABSTRACT

BACKGROUND Heart failure represents a common end-stage syndrome for many adults with congenital heart disease (ACHD). These patients, however, have been excluded from most heart transplantation research. It is not known how current criteria, derived from non-ACHD populations, used to determine priority at the time of transplant listing, impact the outcomes for ACHD patients listed for heart transplantation.

OBJECTIVES The goal of this study was to investigate outcomes of ACHD in comparison to non-ACHD patients while listed for heart transplantation.

METHODS We conducted a retrospective study using the Scientific Registry of Transplant Recipients on patients ≥18 years of age listed in the United States between 1999 and 2014. The probability of mortality or delisting due to clinical worsening was estimated using cumulative incidence functions, where transplantation was a competing event.

RESULTS Among 1,290 ACHD and 38,557 non-ACHD patients listed, 237 ACHD and 6,377 non-ACHD patients died or were delisted due to clinical worsening. Death or delisting for clinical worsening was more likely for ACHD patients initially listed as status 1A (24% ACHD vs. 17% non-ACHD after 180 days; $p < 0.001$). There were no significant differences between ACHD and non-ACHD patients listed as status 1B or 2. In multivariable analysis, factors associated with death or delisting due to clinical worsening within 1 year in ACHD included: estimated glomerular filtration rate <60 ml/min/1.73 m^2 (hazard ratio [HR]: 1.4; 95% confidence interval [CI]: 1.0 to 1.9; $p = 0.043$); albumin <3.2 g/dl (HR: 2.0; 95% CI: 1.3 to 2.9; $p < 0.001$); and hospitalization at the time of listing, whether in the intensive care unit (HR: 2.3; 95% CI: 1.6 to 3.5; $p < 0.001$) or not (HR: 1.9; 95% CI: 1.2 to 3.0; $p = 0.006$) relative to outpatients.

CONCLUSIONS Wait-list mortality or delisting due to worsening clinical status is disproportionately common for ACHD patients listed as status 1A. An allocation system that takes into account the distinctive aspects of ACHD patients may help better care for this growing population. (J Am Coll Cardiol 2016;68:908–17) © 2016 by the American College of Cardiology Foundation.

Advances in surgical and medical care have led to a dramatic increase in survivorship of children born with congenital heart disease (CHD) (1,2). As a consequence, most patients living with CHD are now adults (3). This growing population of adults with congenital heart disease (ACHD) is faced with an increasing burden of chronic diseases, including heart failure (HF) (4). The magnitude of this issue is reflected in the almost doubling of hospitalizations for ACHD with HF between 1998 and

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2005 (5). As mortality in survivors of CHD shifts into adulthood, HF is emerging as a leading cause of death (6).

The presentation of HF in ACHD patients is diverse and often atypical, owing to the heterogeneity of the underlying cardiac defects and subsequent surgical and transcatheter interventions. Consistent definition, identification, and prognostic evaluation of HF in this population is challenging (4,7). Furthermore, landmark clinical trials in HF have excluded patients with CHD, resulting in uncertainty in evaluating mortality benefit from medical or device therapies (4,8,9). ACHD patients who undergo transplantation experience higher mortality in the immediate postoperative period, but those who remain alive enjoy significantly better long-term survival compared with non-ACHD patients (10–12).

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Because the criteria for determining priority status for listing for heart transplantation are derived from evidence in the non-ACHD population, these criteria could misclassify prognosis for the ACHD population and may therefore not reflect the relative benefit of transplant versus alternative therapies. Previous studies suggest similar overall wait-list mortality for ACHD and non-ACHD patients listed for heart transplantation despite a higher likelihood of transplantation in the non-ACHD population (13,14). Untested clinical factors potentially germane to this question may account for the incongruity, such as divergent initial listing status and incomplete characterization of those delisted due to worsening clinical status precluding transplant. The 1-year probability of survival after delisting due to worsening is 26% for all patients; those with CHD had a 40% greater likelihood of death after delisting compared with non-ACHD patients, which translates into approximately 16% survival at 1 year after delisting (15).

Using a national database, we investigated outcomes of ACHD compared with non-ACHD patients while listed for heart transplantation, as well as correlates of mortality or delisting due to worsening of clinical status in ACHD patients.

METHODS

STUDY SAMPLE. The Scientific Registry for Transplant Recipients is a multicenter cohort database that continuously receives data from the Organ Procurement and Transplantation Network. This network gathers information on all patients listed for solid organ transplantation in the United States via reports from the transplanting centers (16). The present study included 1,649 ACHD and 60,667 non-ACHD patients ≥18 years of age listed for first orthotopic heart transplantation between April 1, 1986, and June 2, 2014. Due to observed significant improvement in survival over time, the analysis was restricted to the current era, defined as initial listing after January 19, 1999, on the basis of when a 3-tiered (1A, 1B, and 2) priority listing status was introduced. Patients listed for multiple organs or for repeat transplantation were excluded from this analysis.

ABBREVIATIONS AND ACRONYMS

ACHD = adult congenital heart disease

CHD = congenital heart disease

eGFR = estimated glomerular filtration rate

HF = heart failure

ICU = intensive care unit

MCS = mechanical circulatory support

The Institutional Review Board of the University of Iowa approved the study. The data reported were supplied by the Minneapolis Medical Research Foundation as the contractor for the Scientific Registry for Transplant Recipients.

CLINICAL ENDPOINTS AND VARIABLE DEFINITIONS. Our primary hypothesis was that ACHD patients listed for heart transplantation experience higher mortality or delisting due to worsening of clinical status than patients without CHD. In addition, we aimed to assess predictors of death or worsening clinical status for ACHD patients while listed for heart transplantation. Patients were followed up from the time of listing until 1 of the following outcomes occurred: death, transplant, delisting due to worsening, or delisting due to improvement. Patients were considered to experience the primary outcome if they died or were delisted due to worsening of clinical status. Listing status was defined as the initial listing status, irrespective of status changes during the observation period.

Race/ethnicity categories were reported by the transplanting center as black or African American, white, multiracial, American Indian or Alaska Native, Asian, Hispanic/Latino, Native Hawaiian, or other Pacific Islander. For this study, race was dichotomized as white versus nonwhite. Estimated glomerular filtration rate (eGFR) was calculated by using the Modification of Diet in Renal Disease formula (17). Activities of daily living included walking around the home, getting out of bed or a chair, eating, dressing, bathing or showering, or using the toilet. Mechanical circulatory support (MCS) included an intra-aortic balloon pump, ventricular assist device, total artificial heart, and extracorporeal membrane oxygenation. Pulmonary vascular resistance (in Wood units) was calculated as: mean pulmonary artery pressure − pulmonary capillary wedge pressure/cardiac output.

STATISTICAL ANALYSIS. Summary statistics were reported for quantitative variables as medians (interquartile ranges) and for qualitative variables as