

Decline of Increased Risk Donor Offers on Waitlist Survival in Heart Transplantation

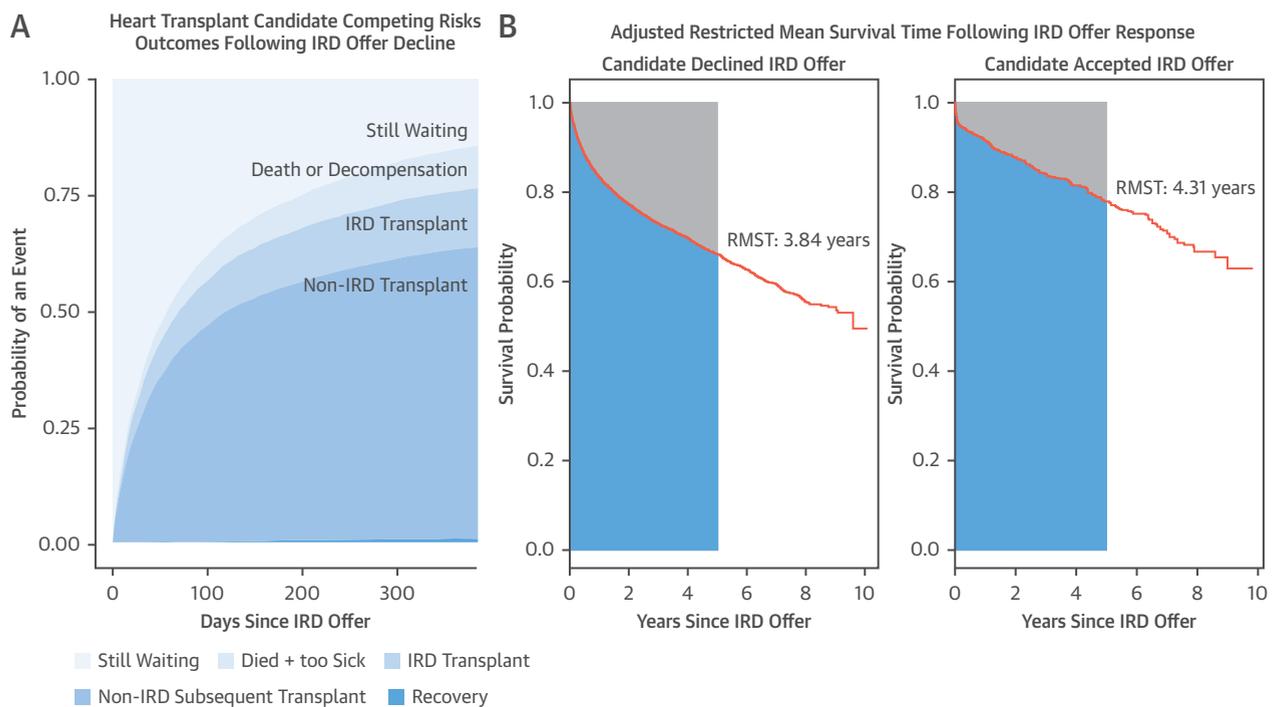


Cardiac transplantation (HTX) is the gold standard and is an increasingly utilized therapy for patients with end-stage heart failure (1). Strategies to reduce the risk of waitlist mortality remain urgently needed. The Public Health Service defines increased risk donors (IRDs) as donors who carry an increased risk for inadvertent window-period disease transmission to a transplant recipient, specifically human immunodeficiency virus, hepatitis B virus, and hepatitis C virus (2). IRDs represent an increasing fraction of the donor pool, to 19.5% in 2015 (3). Outcomes regarding the use of IRD allografts remain scarce in HTX. Single-center data have not identified adverse long-term outcomes or an increased rate of disease transmission (4). However, the comparison between standard and IRD

allografts is fundamentally incorrect from the perspective of the waitlist candidate, as the decline of an IRD offer is associated not with an immediate non-IRD alternative offer, but instead with the prospect of additional waitlist time of uncertain duration before a suitable offer becomes available. To ascertain the effect of the decline of IRD organ offers to HTX candidates, we performed a retrospective registry analysis to examine competing-risks outcomes for candidates that declined IRD organ offers.

Following institutional review board approval, we performed a retrospective cohort analysis using United Network of Organ Sharing data for adult isolated HTX candidates who received an offer for an IRD allograft from 2007 to 2017. To measure the risks of competing outcomes following IRD offer decline, we followed candidates who declined an IRD offer from the time of response until eventual IRD or non-IRD HTX, death or decompensation precluding HTX, or administrative censoring. To determine the survival benefit associated with acceptance of the IRD offer, we identified candidates who accepted the IRD offer, and compared

FIGURE 1 Outcomes for Heart Transplant Candidates Following Receipt of an Increased Risk Donor Offer



(A) Competing risks outcomes for heart transplant candidates following decline of increased risk donor (IRD) offer. Time 0 represents the time of offer. **(B)** Analysis of adjusted restricted mean survival time (RMST) (blue).

them with matched candidates who had declined those IRD offers. Because those candidates who accepted the IRD offer faced an immediate hazard of perioperative mortality associated with HTX, and those who declined the offer do not, the proportional hazards assumption is violated. As such, we used a Cox model stratified on offer acceptance versus decline, and estimated survival time using Cox-adjusted survival and restricted mean survival time (RMST). Each model adjusted for age, sex, serum creatinine, diagnosis group, need for ventilator, and waitlist status.

A total of 2,602 IRD allografts were offered to 10,851 candidates. Of those who declined the IRD offer, 58.0% underwent non-IRD HTX, 12.4% underwent later IRD HTX, 7.9% were removed from the waitlist due to death or decompensation, and 21.1% were still awaiting HTX at 1 year post-offer (Figure 1A). Stratified Cox-adjusted estimates of survival at 1 year from IRD offer were 92.1% for those who accepted and 83.1% for those who declined, a benefit that persisted through 5 years post-offer. The adjusted RMST model again favored acceptance, with RMST of 4.31 years for the accept group versus 3.84 years for the decline group ($p < 0.001$) (Figure 1B).

In this retrospective analysis of registry data, we find that acceptance of an IRD offer is associated with a significant and clinically meaningful survival benefit. This survival benefit associated with IRD offer acceptance should inform decision making for centers and candidates as they consider the use of IRD allografts in HTX. Several limitations bear review in consideration of this analysis, including the potential for unmeasured confounders, particularly with respect to uncertainty in the reasons for organ offer decline, as well as data regarding post-transplant serologic conversion. These data should be incorporated into discussions between candidates and listing centers to promote better understanding of the risks and benefits of IRD allografts (5). The nature of this offer-based experimental design permits a superior approximation of the decisions faced by centers and candidates at the time of IRD offer. Increased utilization of IRD offers represents a rare opportunity to decrease waitlist mortality in cardiac transplantation.

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Stroke Risk Stratification for Atrial Fibrillation Patients With Hypertrophic Cardiomyopathy



Stroke prevention is the principal management priority in patients with nonvalvular atrial fibrillation (AF) given its association with a 5-fold increase in stroke risk (1). Of note, AF is the most common arrhythmia in hypertrophic cardiomyopathy (HCM) (2), and patients with HCM have a 4-fold to 6-fold greater likelihood of AF development compared with the general population (2,3). Therefore, major guidelines recommend lifelong oral anticoagulant (OAC) therapy to prevent stroke in HCM patients