HEART FAILURE AND TRANSPLANTATION
# Journal Watch
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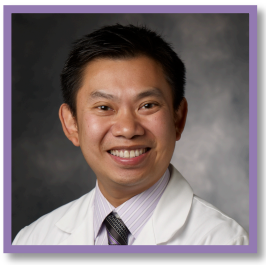

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## REVIEWS:

**Burchill, L; et al. "Impact of adult congenital heart disease on survival and mortality after Heart Transplantation."** ***J Heart Lung Transplant*** **2014;33:1157-1163**

This analysis of the ISHLT registry describes overall survival, cause of death, and predictors of early (<1 year), mid-term (1 to 5 years) and late (>5 years) mortality among patients with adult congenital heart disease (ACHD) who underwent heart transplantation. Outcomes of patients transplanted for ACHD were compared to heart transplants performed for alternative etiologies ("controls"). Of the 85,647 adults who underwent heart transplantation from 1985 to 2010, 2.2% (1,851) were transplanted for ACHD. Overall survival was evaluated at 1, 5, 10 and 15 years. Predictors of mortality were examined in a contemporary cohort of patients transplanted between January 2004 and December 2010, and multivariable analyses of 1-year and 5-year mortality risk factors were assessed.

Compared to controls, ACHD patients were younger (32 years vs. 53 years, $p<0.001$) and more likely to be female. Pre-transplant, these patients also had a significantly lower prevalence of diabetes, renal dysfunction and hypertension in addition to having a lower BMI. These patients had lower rates of intra-aortic balloon pump and ventricular assist device placement prior to transplantation, but were found to have higher rates of allosensitization (defined as panel-reactive antibody >10%) and mechanical ventilation.

Survival at 1 and 5 years was lower in patients with ACHD compared to controls, 77% and 67% vs. 83% and 70% respectively. Higher survival was noted at the 10-year mark and most notably at the 15-year mark in ACHD patients, 57% and 53% compared with 53% and 37% in controls. The most common causes of death in the first year for all adult transplant recipients were graft failure (29%), infection (22%), multi-organ failure (12%) and acute rejection (10%). Infection was the most common cause of first year death in the control population (22%), and ACHD patients had significantly lower rates of infection as a cause of death (12%). ACHD patients were found to have significantly higher rates of technical issues as the primary cause of death compared to the control population (10% vs. 4%). The most common causes of mid-term mortality for both groups were graft failure, cardiac allograft vasculopathy (CAV), malignancy and infection. Compared to controls, ACHD patients had a significantly lower rate of malignancy-related death during the mid-term period. The most common causes of late mortality were malignancy and CAV and there were no significant differences in these rates between groups.

Multivariable analysis revealed that independent predictors of early mortality included: age, female gender, renal function, BMI and CMV+ donor status. The authors found that age had a non-linear relationship with death. Patients aged 25-30 years had the highest hazard ratio for death, and this declined through age 50. The only independent risk factor for mortality at 5 years in ACHD patients was cardiac re-transplantation, which occurred significantly more frequently compared to controls (6.9% vs. 2.8%). Cardiac re-transplantation was

not associated with negative outcomes early after transplant, but it was associated with a 2.75-fold increase in the hazard ratio for death within 5 years.

This observational study is the largest to evaluate outcomes in ACHD and confirms the high early post-transplant mortality observed in previous studies. The first year after transplant poses the highest risk for all patients, and this study further illustrates the additional risk conferred by ACHD. In these patients, death in the early period after transplantation is most commonly due to graft failure but also in part secondary to technical complications related to the transplant operation. In contrast, ACHD patients were found to have superior survival at >15 years post transplant when compared to controls. This favorable survival was related to lower rates of infection, younger age of recipients and lower rates of malignancy-related death. This study shows that patients who survive the early 1-year post-transplant period have superior long-term survival compared to those undergoing transplantation for acquired heart disease. The authors refer to these findings as a "survival paradox".

Additional important observations from this study are that graft failure was the leading cause of death across all time intervals, younger patients (25-30 years) have lower 1-year survival compared to older recipients, and that there is additional risk of death conferred by re-transplantation in ACHD patients. The authors suggest that the increased risk of graft failure, lower risk of death due to infection, and higher mortality rates in younger patients raise the possibility of a more robust immune response in these comparatively younger patients with ACHD. All of these findings confirm the importance of graft preservation through tailoring of immunosuppression protocols based on patient demographics and rejection risk. The retrospective nature and constraints due to registry data availability, such as granularity of pre-transplant allo-sensitization data, prior cardiac surgeries, and congenital lesion information, are the major limitations of this study.

**Sahulee, R; et al. "Center for Disease Control "high-risk" donor status does not significantly affect recipient outcome after heart transplantation in children" *J Heart Lung Transplant* 2014;33:1173-1177**

In this retrospective analysis of the United Network of Organ Sharing (UNOS) database, the authors examined the effects of the Center for Disease Control (CDC) "high-risk" donor (HRD) status on graft utilization and outcomes in pediatric heart transplantation.

Using the UNOS database, all patients in the US <18 years old who underwent primary heart transplantation between June 2004 and July 2012 were identified and divided into two groups based on HRD status, as determined by the 1994 CDC guidelines. Data on pediatric and adult graft utilization during this period was also obtained from UNOS. Approximately 9.5% and 9.9% of pediatric and adult grafts offered for transplantation, respectively, came from HRD. There was a significant difference in the utilization of these grafts in the adult and pediatric population. Only 18.5% of HRD grafts, compared to 38.5% of standard risk donor grafts, were utilized in the pediatric population. In contrast, 63.2% of HRD grafts were used in adult recipients, comparable to the utilization rate of graft from standard risk donors.

Among the 2,782 pediatric patients identified in the study, 4.1% received a heart from a high-risk donor (n=116). High-risk donors were found to be significantly older and heavier compared to standard-risk donors. This corresponded with similar findings of older age and larger body mass in the recipients of HRD grafts. The authors found no difference in gender, circulatory support utilization, or inotropes between groups prior to transplant, although patients receiving grafts from a HRD had significantly lower number of days listed as Status 1A.

The most clinically significant finding in this study was that cumulative long-term survival was not different between patients who received high-risk or standard-risk donor grafts. Short-term outcomes were also similar

between groups, including no differences in rates of rejection prior to discharge and index hospitalization length of stay. However, this study did not examine rates of rejection, infection, or other transplant related complications occurring beyond the initial hospitalization.

This study highlights several important findings in pediatric heart transplantation. There was a significantly lower utilization of HRD grafts in this population, which signals apprehension to their use in a young patient population. In part, this is likely due to concern for transmission of communicable diseases during transplantation. Unfortunately, this could not be evaluated directly in this study due to database limitations. The authors were unable to determine if HIV, hepatitis, or other donor-transmitted diseases were acquired by any study recipient beyond the transplant hospitalization. Despite this important limitation, the impact on outcomes of the HRD status does not appear to be significant as cumulative long-term survival and short-term outcomes were equivalent between groups.

Given these findings, there is a potential opportunity to expand donor utilization in a group of patients where the donor pool is already limited. In addition, further evaluation is needed to determine the overall effect on morbidity, if any, associated with HRD usage. Rates of disease transmission, episodes of rejection over longer time intervals, re-hospitalization, infection, and quality of life should be evaluated further in the patient population who receive hearts from high-risk donors.

## ARTICLES OF INTEREST:

Journal of the American College of Cardiology (JACC):

Ro, R; et al. “Vector Flow Mapping in Obstructive Hypertrophic Cardiomyopathy to Assess the Relationship of Early Systolic Left Ventricular Flow and the Mitral Valve” *J Am Coll Cardiol* 2014;64:1984–95

•Mentz, R; et al. “Noncardiac Comorbidities in Heart Failure with Reduced versus Preserved Ejection Fraction.” *J Am Coll Cardiol* 2014;64:2281–2293 (Review)

New England Journal of Medicine:

•Lacro, R; et al. “Atenolol versus Losartan in Children and Young Adults with Marfan’s Syndrome.” *New England Journal of Medicine* 2014; 377:2061-71

JACC-Heart Failure:

No Issue in November 2014, next issue December 2014.

Circulation-Heart Failure:

•Adamson, P; et al. “Wireless Pulmonary Artery Pressure Monitoring Guides Management to Reduce Decompensation in Heart Failure with Preserved Ejection Fraction.” *Circulation Heart Failure* 2014;7:935-944

Khazanie, P; et al. “Clinical Effectiveness of Cardiac Resynchronization Therapy vs. Medical Therapy Alone Among Patients with Heart Failure: Analysis of the ICD Registry and ADHERE.” *Circulation Heart Failure* 2014;7:926-934

••Rowin, E; et al. “Advanced Heart Failure with Preserved Systolic Function in Nonobstructive Hypertrophic Cardiomyopathy: Under-Recognized Subset of Candidates for Heart Transplant.” *Circulation Heart Failure* 2014;7:967-975

Smith, CI et al. "Multidisciplinary Group Clinic Appointments: The Self-Management and Care of Heart Failure (SMAC-HF) Trial" *Circulation Heart Failure* 2014;7:888-894

European Journal of Heart Failure:

Adabag, S; et al. "A prediction model for sudden cardiac death in patients with heart failure and preserved ejection fraction" *European Journal of Heart Failure* (2014) 16, 1175-1182

Luttik, M; et al. "Long-term follow-up in optimally treated and stable heart failure patients: primary care vs. heart failure clinic. Results of the COACH-2 study." *European Journal of Heart Failure* (2014) **16**, 1241-1248.

American Journal of Transplant:

Taylor, D.A.; Sampaio, L.C; Gobin, A. "Building New Hearts: A Review of Trends in Cardiac Tissue Engineering." *American Journal of Transplantation*. 14(11):2448-2459, November 2014.

•Hofmann, N; et al "Comprehensive Bio-Imaging Using Myocardial Perfusion Reserve Index During Cardiac Magnetic Resonance Imaging and High-Sensitive Troponin T for the Prediction of Outcomes in Heart Transplant Recipients." *American Journal of Transplantation*. 14(11): 2607-2616, November 2014.

Journal of Cardiac Failure:

Stolen, C; et al. "Plasma Galectin-3 and Heart Failure Outcomes in MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy)" *Journal of Cardiac Failure* 2014; 20: 793-799

Yamada, T; et al. "Prognostic Impact of Combined Late Gadolinium Enhancement on Cardiovascular Magnetic Resonance and Peak Oxygen Consumption in Ambulatory Patients with Non-ischemic Dilated Cardiomyopathy" *Journal of Cardiac Failure* 2014; 20: 825-832

Verbrugge, F; et al. "Prognostic Value of Glomerular Filtration Changes Versus Natriuretic Response in Decompensated Heart Failure With Reduced Ejection" *Journal of Cardiac Failure* 2014; 20: 817-824

Journal of Heart and Lung Transplantation:

••Burchill, L; et al. "Impact of adult congenital heart disease on survival and mortality after Heart Transplantation." *J Heart Lung Transplant* 2014;33:1157-1163

Kransdorf, E; et al. "Donor evaluation in heart transplantation: The end of the beginning." " *J Heart Lung Transplant* 2014;33:1105-1113

••Sahulee, R; et al. "Center for Disease Control "high-risk" donor status does not significantly affect recipient outcome after heart transplantation in children" *J Heart Lung Transplant* 2014;33:1173-1177