Title: Characteristics of Pediatric Cardiac Donors and Impact on Outcomes

BACKGROUND

As the results of pediatric cardiac transplantation continue to improve, the importance of this treatment strategy in managing patients with life threatening and disabling conditions continues to be realized. However, transplantation as a viable option is limited by the number of available and suitable donor hearts. There is limited information about pediatric cardiac donors and what specific donor factors effect short and long term outcomes. This information is essential as it has the potential to expand the current donor pool.

Analysis of the UNOS database between July 2000 and November 2008 identified 6000 potential pediatric cardiac donors, with only 66% of the hearts actually being utilized [1]. The particular reasons for refusal of these organs have not been specifically reported but donor quality may be a factor. Bailey et al. recently described their single center experience with the use of donor hearts that had previously been refused based on donor quality. They specifically examined outcomes of hearts turned down under UNOS policy code 830 compared to hearts accepted with no previous refusals. The refusal of a donor heart can be categorized under code 830 for any of the following reasons: donor age, prolonged hypotension, high dose vasopressors/inotropes, cardiac arrest, evidence of infection or positive culture, death after cardiac arrest, etiology of death, unstable donor, diabetes and other medical history [2]. This policy allows UNOS to track reasons for donor refusal but is not meant as a guideline for practice. In Bailey’s et al. retrospective review there was no difference in the two donor groups with respect to incidence of cardiac arrest or the use of high dose vasopressors [1]. However, the underlying cause of death did differ significantly between the two groups with the cause of death in the primary donor hearts being head trauma as compared to anoxia in the previously refused donors. Post transplant outcomes were similar between the two groups with no difference in the need for mechanical circulatory support or ventilation. As well, operative mortality and late survival did not differ despite the fact that the previously refused hearts had longer ischemic times and primary cause of death was most often anoxia [1].

There are a number of other studies that have identified potential donor factors that affect outcomes post heart transplant. The recent report from the ISHLT registry indicates that donor age, height and cause of death has been associated with 1 year mortality [3]. The risk factors for 1 year mortality did differ when analyzed by recipient age. In recipients < 1 year of age the donor cause of death and presence of a clinical infection were significant, whereas donor age is the only risk factor identified in adolescents [3]. Other donor factors identified in the pediatric population that affect survival in single center and multi-institutional studies include: donor –recipient race mismatch, donor age, and mechanism of donor death in recipients < 1 year [4,5,6,7]. However, these findings have not been consistently replicated [1,8]. The role of donor
ischemic time (DIT) is known to be a risk factor for death in the adult population [9]. This is not the case in pediatrics, where longer DITs have been associated with primary graft dysfunction but not identified as a risk factor for mortality [5,9,3].

The suitability of the donor heart for transplantation can be altered by both the brain death process and the subsequent management. Brain death has been shown to have a deleterious effect on ventricular function with the right ventricle being particularly susceptible [10]. Therefore, the goals of treatment following brain death are to preserve ventricular function and prevent further myocardial damage. Intensive care management usually focuses on optimizing intravascular volume status, maintaining cardiac output with the lowest amount of inotropes possible and preventing elevations in afterload [11,12,13]. An additional strategy that has been used in donor management is hormonal resuscitation. This has been shown to decrease the amount of inotropic support required and increase the suitability of the hearts for transplantation in the adult population [14,15,12]. There is limited information of these strategies in the pediatric population.

Although listed in the UNOS coding system as reasons for donor refusal, there is little evidence in the pediatric literature to suggest that high dose inotropes, cardiac arrest or etiology of the donor’s death effects outcomes post transplant. As Bailey et al.’s study did not compare donors with and without these characteristics further research is needed. These results may potentially expand the donor pool to hearts that have previously been thought of as marginal. A better understanding of the donor related risk factors for survival, long term morbidities and the effects of donor management strategies in the pediatric population will also have the potential to increase the number of suitable donors.

**OBJECTIVES**

To describe and analyze the donor characteristics of pediatric heart transplant recipients and determine donor factors that may affect the clinical course and outcomes of pediatric patients listed for heart transplantation.

**Specific Aim #1**
To describe the clinical characteristics of pediatric cardiac donors including: demographics, past medical history, cause and mechanism of death, need for and length of resuscitation, pretransplant echocardiographic information (function, wall motion), pretransplant hormone resuscitation, type of cardioplegia, infectious status, and ischemic time.

**Specific Aim #2**
To determine the effects of a ‘marginal’ donor quality on survival by comparing the outcome of recipients whose donors did or did not have one of the following characteristics: use of high dose inotropes (to be defined concurrent with review of Form 2), use of CPR, and mechanism of death not head trauma.
Specific Aim #3
To determine the effects of pretransplant donor management on survival by comparing the outcomes of recipients whose donors did or did not have hormonal resuscitation

Specific Aim #4
To attempt to identify the donor related factors that effects survival at 30 days, 1, 5 and 10 years and risk of long term morbidities (rejection, retransplantation, allograft vasculopathy, infection)

RESEARCH DESIGN AND DATA ANALYSIS

Study Population
All cardiac donors for a pediatric heart transplant between 1993 and 2009 and listed with the Pediatric Heart Transplant Study Registry. In order to determine the effects of donor characteristics on outcomes, information for transplant recipients between 1993 and 2009 will also be collected. Patients will be analyzed as a group as well as in three different age categories <1 year, 1-10 years and >11 to determine if there are age related factors.

A preliminary review of the PHTS database revealed that there was 2741 transplant between 1993 and 2008, therefore there are 2741 potential donors that can be analyzed. Each donor to recipient pairing will be analyzed as a separate event, ie: if a recipient has had multiple transplants these will each be analyzed separately.

Exclusion Criteria
Recipients and their information will be excluded from analysis if there is no donor related information.

Design
This is a retrospective review of the Pediatric Heart Study Registry of all donors in patients transplanted ≤18 years of age.

Methods
With the use of the PHTS database, all donors listed and the associated recipient will be queried. The following demographics, clinical course, perioperative data and transplant outcomes will be included for analysis [this list is not exhaustive].

Donor Information (Form 2, 5):
date of birth, Age, sex, race, height, weight, cause of death, mechanism of death, chest compressions, duration of arrest, blood type and Rh, HLA allotype, past medical history, pretransplant echo and angiogram information, serologies, cardioplegia use and type, inotrope use and amount, hormone use and dosing, donor ischemic time.

Recipient information (Forms 1,1T,4,5,6,7,8,10,11):
Date of birth, etiology, race, gender, blood type, PRA, Date of listing, Status at listing
Support at time of listing (inotropes, mechanical ventilation, prostaglandins, ECMO, VAD, pacemaker, etc.), surgical palliation, hemodynamics at listing, hemodynamics if repeated, use of VAD pretransplant, PRA at time of transplant, date of transplant, age at transplant, weight and height at transplant, status at transplant, support at time of transplant (inotropes, mechanical ventilation, VAD, ECMO pacemaker, etc.), CPB time, hospital stay, death when and cause, incidence of rejection/allograft vasculopathy/malignancy and infection

**Transplant Specific (Forms 1, 1T, 2)**
Donor-recipient age, race matching, sex matching, size matching, blood group matching

**Analysis (final SAP to be determined in discussion with the DCC)**
Data will be described using frequencies, means with standard deviations and medians with ranges.

Primary endpoint will be survival at 30 days, 1, 5 and 10 years using a Kaplan-Meier analysis between comparison groups. Comparison groups will be analyzed for differences in their demographic and clinical information. The comparison groups will include: those with marginal vs. nonmarginal donors, and those with and without hormone resuscitation.

Multivariate analysis in the hazard function domain will be used to identify specific donor risk factors for death, rejection, retransplantation, allograft vasculopathy, infection

**REFERENCES**


