Kate Avitabile, MD (PGY3)
ICCR Rotation
IRB Proposal
September 23, 2009

Relationship between pre-transplant psychosocial assessment and episodes of acute rejection in pediatric heart transplant recipients

A. Study Purpose and Rationale:

Despite improvements in surgical techniques and immunosuppressive regimens for pediatric heart transplant recipients, transplant coronary artery disease (TCAD) limits the long-term success of the graft and survival of the patient [1-3]. TCAD is a concentric myointimal proliferation that involves the length of the vessel and finally results in luminal occlusion [4]. TCAD can result in symptoms of congestive heart failure requiring medical management or re-transplantation, or may be asymptomatic and result in sudden cardiac death. In a 9-year multi-institutional study of pediatric heart transplant recipients, 25% had evidence of mild, moderate or severe CAD on angiography 7 years post-transplant. In this study, two or more episodes of acute rejection in the first year post-transplant were significantly associated with TCAD several years post-transplant [5].

Furthermore, it is recognized that rejection, both acute and chronic, results from a combination of immune and non-immune mediated factors. Research has shown a close relationship between psychosocial factors and post-transplant outcomes, especially those factors related to medication adherence [6,7]. Pediatric transplant recipients, especially adolescents, are vulnerable to non-adherence [8]. Non-adherence may have serious impact on higher rates of rejection, re-transplantation, and graft loss. In survey studies, pediatric transplant recipients have cited various reasons for medication and treatment non-compliance including forgetfulness [9], insufficient information regarding medications, and a lack of trust in the physicians [10]. Risk factors for non-compliance have included poor medication knowledge (unable to name >50% of medications), lack of parental involvement in medication habits, social class, symptoms of post-traumatic stress syndrome, and transfer of care from a pediatric to adult transplant unit [11-14].

Despite general agreement that psychosocial assessment of the patient and parents should be part of the pre-transplant evaluation, there was no standardized method for assessment in pediatric patients for many years. Assessment tools in adult patients include the Psychosocial Assessment of Candidates for Transplantation (PACT) and the Transplant Evaluation Rating Scale (TERS), but they are not entirely applicable to pediatric populations. The Pediatric Transplant Rating Instrument (P-TRI) is adapted from these two validated tools in order to identify potential psychosocial risk factors associated with post-transplant treatment adherence in pediatric populations. It incorporates a developmental framework as well as psychosocial and family factors (psychiatric history, drug abuse, parental supervision, financial concerns, etc.) that have been shown in the literature to correlate with treatment adherence [15].

B. Study Design and Statistical Analysis:

Hypothesis: Lower scores on pre-transplant P-TRI are associated with more episodes of acute rejection in the first year after heart transplant.

Study Design: The study will be a retrospective case control study performed via chart review of data from recipients of pediatric heart transplants at the Morgan Stanley Children's Hospital of New York-Presbyterian Hospital (MS-CHONY) from 2007 to the present. Existing data from the electronic surgical database, Eclipsys electronic medical record, and written records from the Division of Pediatric Cardiology patients' charts will be used.

Prior to transplant all patients and/or parents complete the P-TRI. Raw scores ranging from 17-68 are possible on the 17-item assessment tool. Mean and standard deviation P-TRI scores will be computed for all subjects.

The primary outcome is episodes of acute rejection in the first post-transplant year. An episode of acute rejection is a clinical event that results in acute augmentation of immunosuppressive therapy. The episode begins at the time of acute augmentation of immunosuppression and ends at the time of the last biopsy that does not trigger additional immunosuppressive therapy [16].

Statistical Analysis: A t-test will be used to compare mean P-TRI scores of those subjects experiencing <2 versus those experiencing >/= to 2 episodes of acute rejection in the first year after heart transplant.

Additional patient data including demographic data (age of donor and recipient, sex, race), pre-transplant clinical data (diagnosis, mechanical ventilation, pressor support, ECMO/VAD), and post-transplant clinical data (CMV infection, CRP) will be gathered. Multiple regression analyses will be used to determine interaction among the variables.

Since MS-CHONY performs approximately 25 pediatric heart transplants per year, a sample size of 75 patients is potentially available over the last 3 years (2007-2010). Estimated mortality and loss to follow-up in the first post-transplant year at MS-CHONY is <10%, therefore, a realistic sample size of 65 was chosen. There is approximately 10% risk of >/= 2 episodes of acute rejection in the first year post-transplant [16] so the Group2/Group1 ratio was set at 10. Assuming 80% power and an alpha of 0.05, an effect size of 1.1 standard deviation can be detected between the two groups.

C. Study Procedure: Not applicable.

D. Study Drugs: Not applicable.

E. Medical Device: Not applicable.

F. Study Questionnaires: As above, all patients and/or the parents of those listed for heart transplant at MS-CHONY routinely complete the Pediatric Transplant Rating Instrument (P-TRI) prior to transplant. This pediatric-specific questionnaire was adapted from validated questionnaires in the adult solid organ transplant communities.

G. Study Subjects: All recipients of pediatric heart transplants at MS-CHONY from 2007 to present are eligible. Subjects and/or their parents must have completed the P-TRI prior to transplant. Those patients who died within the first year post-transplant and those who transferred care to another institution are excluded from the study.

H. Recruitment of Subjects: As this is a retrospective review of existing data, subjects will not have to be contacted for recruitment.

I. Confidentiality of Study Data: All data will be coded with a unique patient identification number and will be stored on a password-protected computer.

J. Potential Conflict of Interest: None.

K. Location of the Study: All patients will have undergone a heart transplant at MS-CHONY.

L. Potential Risks: As this study is a retrospective chart review, there are no risks to the subjects.

M. Potential Benefits: This study could identify a potential relationship between pre-transplant psychosocial assessment of patients/parents and post-transplant clinical outcomes.

N. Alternative Therapies: Not applicable.

O. Compensation to Subjects: The subjects will not receive any compensation.

P. Costs to Subjects: The subjects will not incur any costs.

Q. Minors as Research Subjects: As this is a retrospective review of existing data, minors will not be asked to directly participate in the study design.

R. Radiation or Radioactive Substances: Not applicable.

S. References:

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