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IRB Proposal
12/15/2010

Effect of Left Ventricular Assist Device (LVAD) on the Prognostic Value of Pre-Transplant GFR in Patients Undergoing Heart Transplantation (HTX)

A. Study Purpose and Rationale

Chronic kidney disease (CKD) is a common, long-term complication of (HTX).[1-3] Prior to HTX, renal hypo-perfusion in the setting of uncompensated heart failure is thought to be responsible for the renal insufficiency (RF) seen in a majority of HTX patients.[4,5] In the post-HTX period, RF in these patients is further complicated by the use of nephrotoxic immunosuppressants.[3-6] Identifying patients more likely to have worsening renal disease may have implications in both patient selection for HTX and the need for heart/kidney transplantation.

Pre-HTX GFR is one of the variables used to risk-stratify these patients at the time of transplant.[7-8] The use of LVADs is shown to improve GFR in patients prior to HTX.[9-11] These devices are used as a bridge-to-transplant (BTT) for patients awaiting HTX who continue to deteriorate clinically despite inotropic or intra-aortic balloon pump (IABP) therapy.[12] Previous studies addressing patients BTT with LVADs as well as those BTT with medical therapy, report post-transplant outcomes, such as survival, infection, thromboembolic complications, and hemodynamic measurements, but do not specifically focus on renal function.[13-16] The value of the pre-HTX GFR has not been well-defined in either group. This study aims to compare the prognostic value of the GFR at the time of HTX for worsening renal disease in patients undergoing HTX with and without concurrent LVAD support.

B. Study Design and Study Procedure

Study Design

This study is a retrospective analysis comparing the difference in mean GFR at different time points post-HTX for patients BTT with medical therapy against those BTT with a LVAD. Baseline characteristics of these patients (age, etiology of ischemic cardiomyopathy, DM, pre-transplant GFR) will be compared to ensure the two populations are similar. GFR will be calculated according to the Modification of Diet in Renal Disease (MDRD) equation, as this has been shown to more accurately reflect GFR in patients with advanced heart failure than the Cockcroft-Gault equation.[5,17] Please see study subjects section for inclusion and exclusion criteria.

C. Statistical Analysis

Baseline characteristics will be compared using student's *T*-test and chi-square for continuous and categorical categories, respectively.

Results for GFR will be expressed as a continuous variable with mean +/- standard deviation (SD). The data will be analyzed using the unpaired student's *T*-test since there are two groups and a continuous variable is being measured. In the Med-HTX group, there are 291 patients; and in the LVAD group, there are 113 patients. In order to calculate power, the difference in the sample size between the two groups was factored into the calculation, and 1 was assigned as the value for standard deviation. This allows for the study to detect a minimum mean difference in GFRs between study groups of [0.31 X SD] with a power of 80% and a p=0.05. Based on preliminary data, the

difference in mean GFR between the two groups is expected to be ~ 7-10 at one year post-transplant. If 8.5 is used as the standard deviation, the study is powered at 80% to detect a minimum difference of (0.31X 8.5 =) 2.64 in mean GFR between the groups at 1 yr post-transplant.

In order to examine whether the difference in time of listing to time of transplant (i.e., time on the transplant list) affects the primary outcome, a linear regression analysis will be utilized for different time intervals prior to transplant, i.e., 3-6 months, 6-9months, 9-12months, >1yr. Linear regression analysis will also be used to detect whether the baseline pre-HTX GFR at the time of transplant will affect outcome, i.e., patients will be grouped by stages of CKD at time of transplant (i.e., GFR 0-30, GFR 30-60, GFR 60-90).

D. Study Drugs
No study drugs will be used in this study.

E. Medical Device
Not applicable as this is a retrospective analysis.

F. Study Questionnaires
No study questionnaires will be used in this study.

G. Study Subjects
Inclusion Criteria:
- Age >18
- Underwent HTX at CUMC from 2004-2010

Exclusion Criteria:
- Patients will be excluded if a salvage device was implanted at any point or if they were bridged from one device to another prior to HTX
- Only data from the first HTX will be used if a patient required re-transplantation

H. Recruitment of Subjects
Study subjects have been identified by querying CUMC's database for the above inclusion criteria.

I. Confidentiality of Study Data
This study will request permission for all data from the Columbia IRB board, and ensure confidentiality of all patient data information. All data will be coded using a unique code number for each study subject. Data will be stored in a secure location, accessible only to study investigators. Given the nature of the study, no formal consent will be obtained from the individual patients.

J. Potential Conflict of Interest
There are no potential conflicts of interest.

K. Location of the Study
Columbia University Medical Center.

L. Potential Risks
There are no potential risks to subjects in this study.

M. Potential Benefits

Examination of the prognostic value of the pre-HTX GFR may have implications in both patient selection for HTX and the need for heart/kidney transplantation.

N. Alternatives
This study does not involve an experimental therapy.

O. Compensation of Subjects
No compensation will be provided to study subjects.

P. Costs to Subjects
No additional costs will be incurred by subjects in this study.

Q. Minors as Research Subjects
This study will not involve the participation of subjects under the age of 18 years.

R. Radiation and Radioactive Substances
This study will not involve radiation or radioactive substances.

S. References

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