Short Application for Institutional or Ethics Review Approval
Human Subject Health Record/Database Research

Registry Methodology

Background

Studies of Pediatric Liver Transplant (SPLIT) is a research effort that was organized in 1995 by a group of physicians and surgeons committed to the success of liver transplants in children. The group represents a collaborative effort between transplant centers in the United States and Canada, and works to collect and analyze information required to advance the science of pediatric liver transplantation. Participation in this registry is voluntary. A Data Coordinating Center, located at The EMMES Corporation, is responsible for data collection and analyses. The registry is supported by a cooperative agreement through NIDDK, NIH. Additional educational grants are made available by several pharmaceutical companies and these contributions are obligation free.

Due to the voluntary nature of this registry, there are no contracts or grants between the funding agencies and the participating transplant centers, with the exception of the following co-investigators listed on the grant; Sue McDiarmid, John Bucuvalas, J. Michael Millis, and Estella M. Alonso. Letters of Agreement are required by the Data Coordinating Center to ensure that participating institutions comply with Good Clinical Practice with regards to data collection and submission. Participating Transplant Centers are required to follow their local Institutional Review or Ethics Board requirements for participating in this endeavor.

SPLIT has established oversight committees to ensure that policies pertaining to the Registry are conducted in an organized and consistent manner. A copy of the SPLIT organizational chart is attached (Appendix A). The SPLIT study chair and vice chair have oversight responsibilities in addition to being members of the Scientific Advisory Board. The Scientific Advisory Board (SAB) consists of a majority of physicians or surgeons from SPLIT transplant centers. The SAB is responsible for the scientific integrity of the registry, as well as approving all operational issues pertaining to SPLIT.

Other voting members of the SAB include the Clinic Coordinator Chairperson, and the Director of the Data Coordinating Center, and representatives of the sponsors as outlined in the MOP, including an NIDDK representative. Study data submitted become the property of SPLIT and belong collectively to all participating centers.

To date, over 2,700 patients have been registered in SPLIT. Forty-three centers participate, four from Canada, with the potential for more centers to join through the duration of the study. SPLIT contributes to publications and presentations that impact the medical community it is intended to affect (see attached bibliography - Appendix B). Each year an Annual Report is published and distributed to participating Transplant Centers, and presented at the Annual Meeting.

(Insert name of institution here) has been participating in the SPLIT registry since _____.

Hypotheses or Questions

The specific objectives of SPLIT are:

- to develop and test models which predict short and long-term patient and graft survival, and graft function of children after liver transplantation
- to develop and test models that predicts overall patient survival from the time of listing, including pre-, peri-, and post-transplant factors
- to determine the prevalence of morbidities associated with long term
- immunosuppressive treatment, and identify the predictors of these morbidities (e.g. renal function, PTLD, cardiovascular complications, growth and nutrition)
- to characterize and follow trends in immunosuppressive therapy
- to characterize the side effects of various immunosuppressive regimens

Methods

SPLIT is comprised of participating Transplant Centers who have responsibility for enrolling patients and collecting follow-up information on patient outcomes. In addition to the Transplant Centers, a Data Coordinating Center provides support for logistical, data capture, quality-control monitoring, and statistical design and analysis.

Data collection is the responsibility of each participating center. Patient entry criteria include:

- patients who are currently listed or who are being considered for liver transplantation and are evaluated on or after the Transplant Center's initiation date, and have not reached their 18th birthday
- patients who receive a liver transplant on or after the Transplant Center's initiation date and prior to their 18th birthday
- patients who have not previously received any organ transplant other than liver or kidney
- informed consent and data authorization (privacy statement) has been obtained and is on file at the participating Transplant Center

The endpoints for data collection for each of the enrolled subjects are:

- patient reaches their 18th birthday and has not received a transplant
- patient is removed from waiting list for liver transplant and has not received a transplant
- patient dies
- patient's care is transferred to a non-participating transplant center
- patient has complete recovery from fulminant hepatic failure prior to transplantation
- patient is listed for a non liver or kidney transplant

Statistical Analysis

The analysis plan for SPLIT includes data quality, study progress, and patient outcome analyses. A comprehensive annual report summarizing data received, is issued to each participating center in the fall each year. In addition, biannual reports summarizing key aspects of the registry's experience compared to individual center experience is issued. Database assessments are performed by the Data Coordinating Center to evaluate database quality on a monthly basis. In addition to these planned analyses, the Data Coordinating Center conducts various unplanned analyses precipitated by evolving registry needs. Requests for such analyses come from the Publication/Presentation Committee with approval by the SAB.

SUMMARY OF NEW DATA ELEMENTS AND FORMS is attached (Appendix C).

IF YOU ARE PLANNING ON EXTRACTING SOCIODEMOGRAPHIC INFORMATION, E.G., RACE OR ETHNICITY, PLEASE PROVIDE JUSTIFICATION.

Socio-demographic data is extracted for the purposes of characterizing diseases and immunologically driven complications such as graft rejection. Ethnicity is used for some subgroup analysis.