

SECTION II: Research Plans

- A. **Research Description:** In the space below, describe in detail your project's (1) **Research question;** (2) **Hypothesis;** (3) **Study Design** (including basic approaches for statistical analysis)

Introduction/Question

Nonalcoholic fatty liver disease (NAFLD) is hepatic steatosis without a secondary cause such as excessive alcohol consumption, infection, hereditary disorder, or medications. The histologic pattern of NAFLD is graded from simple steatosis to cirrhosis. Nonalcoholic steatosis (NASH) is an intermediate stage which is characterized by inflammation of hepatocytes. The prevalence of NAFLD is currently estimated to be at 25-30% in western countries, and in the last ten years we have seen a fivefold increase in frequency of liver transplantation for NASH. NAFLD has been intimately associated with components of the metabolic syndrome.

It has been established that NASH is associated with posttransplant morbidity and mortality from cardiovascular events, graft loss, and accelerated fibrosis. In our project, we wish to compare peri-operative outcomes in cryptogenic/NASH cirrhosis versus alcoholic cirrhosis recipients.

Hypothesis

We hypothesize that NASH/cryptogenic cirrhosis patients will have a higher incidence of peri-operative morbidity compared to alcoholic cirrhosis patients.

Study Design**- Subjects**

We have identified 80 recipients for NASH or cryptogenic cirrhosis from 2002 to 2013 at the University of California, San Francisco (UCSF). We will also identify 240 individuals who have undergone orthotopic liver transplant for alcoholic cirrhosis at our academic center. We will exclude patients transplanted for hepatitis B as this subgroup may not have progressed to cirrhosis before transplantation and thus represent a different pathophysiology before transplant. We will also exclude patients infected with hepatitis C or HIV.

-Methods

In addition to basic demographic variables such as recipient age, sex, and ethnicity of the recipient, we will also calculate donor risk index as predictors. Our outcomes peri-operative variables that can prolong the length of hospital stay, such as operative blood loss, infections, biliary complications, acute rejection, operating room takebacks, and ultimately length of hospital stay.

-Data analysis

We will analyze which variables are most predictive of peri-operative outcomes using chi-square and logistic regression.

B. Time-Line, Deliverables and Competencies:

- Organize your specific goals and "deliverables" into a time-line that corresponds to the intervals of time that you will receive research elective credit as indicated in the table on page 1. (eg, Interval 1 Research phase - research and compile the reference list, read background literature, complete interviews of study subjects)
- For example, if you propose 10 weeks of elective work broken into two four-week blocks and one two-week block, list specific goals and expected deliverables for each of these three time intervals.
- For any research block intervals that occur during the heavy residency interview season (November-January), be sure to indicate how you will accomplish full-time research while interviewing.
- The purpose of this time-line with specific goals and deliverables is to help you and your research supervisor clarify expectations; to help other reviewers with their approval process, and – most importantly – to help your research supervisor and the department representative provide performance-based assessment. Please refer to the "Standard Research Block Student Evaluation Form" at the end of this application form.

I have listed in order the steps in which I will take to complete my research project in a timely and organized manner.

1. Design project that examine peri-operative morbidity in NASH and alcoholic cirrhosis patients. I will have a clear definition for each predictor and outcome variable. I will define inclusion and exclusion criteria for my cohort. At this time, I will also perform a comprehensive literature search, collecting articles that will be useful when writing my manuscript: 2 weeks (11/15-11/30)
2. Establish retrospective cohort by applying strict exclusion criteria and create a database containing predictor and outcome variables by chart review through Apex and TITUS for each subject: 3 weeks (12/01-12/21)
3. Data analysis using STATA and interpretation of results with the help of my faculty supervisor: 1 weeks (12/22-12/31)
4. Comprehensive review of literature with concurrent compilation of reference list. Write manuscript: 8 weeks (1/01-2/28).

During this time I will meet regularly with my supervisor, every 2-4 weeks, and communicate by email.

My project officially begins 11/15/2013, therefore, I will schedule all my residency interviews in early 11/2013. If that is not possible I can work on the project while I am traveling and on weekends to make up for lost time.