**Blog Post: Predicting Outcomes of Liver Transplants**

Does body composition play a role in liver transplant outcomes?

By: Sarah Torrence

Did you know that 2 million people die every single year of liver disease? Further cirrhosis, a disease where healthy liver tissue is replaced with scar tissue, is the 11th most common cause of death. And cirrhosis isn’t even the only cause of liver disease. Liver damage actually cannot be undone either. The good news is a liver transplant from a healthy donor can save the lives of those with chronic liver disease. However, this is currently the only cure of liver disease, therefore understanding and improving outcomes of liver transplants is extremely important.

I was fortunate enough to work with data from 422 liver transplant patients at Vanderbilt University Medical Center that had surgery between 2009 and 2019. My goal was to predict short term outcomes for 90 days post-transplant and understand what factors are most important in predicting outcomes. More specifically, I was interested in whether body composition affect outcomes of liver transplants.

A picture containing text, electronics

Description automatically generated

Each of the 422 patients had 140 variables and after a good amount of cleaning, transforming and data reduction, which included using domain knowledge, a redundancy analysis, variable clustering and backward selection, I ended up with 37,501 observations of 16 predictors plus of course one outcome variable. This accounts for each of 90 days post-liver transplant for each of the 422 patients, removing days post death as death is an absorbing state. The outcome variable is ordinal with 4 levels, whether the patient was at home or an inpatient long term care facility, in the hospital, in the ICU and/or on a ventilator, and dead. As this is a state transition analysis, two of the most important predictors are day post-transplant and the state of the patient on the previous day. Other predictors include:

* Age
* Sex
* Etiology of liver disease
* Surgery duration
* Meld score
* Hepatic Encephalopathy
* Comorbidities (diabetes and chronic kidney disease)
* Body Composition

The body composition measures are derived from CT scans at the level of third lumbar vertebra and were captured using image analysis software. These include different measures of muscle and fat areas and densities shown in the figure below.

A picture containing graphical user interface

Description automatically generated

To understand if any of these body composition measurements significantly affect the outcomes of liver transplants, I fit a proportional odds model and then use the robust sandwich covariance estimator to account for intra-patient correlation as there are up to 90 observations for each patient in the data set. A proportional odds model outputs odds ratios just like logistic regression, however unlike logistic regression, it treats outcomes as ordinal. In the model, all of the continuous predictors were added using splines, and I also added interaction terms for skeletal muscle area and age as well as skeletal muscle area and sex.

The model performs very well, with an adjusted R2 of 0.913, and using bootstrap validation there does not seem to be concerns of overfitting. This sounds like great results, but the goal of my analysis was to understand what factors impact liver transplant outcomes and specifically if body composition plays a role. This of course means looking at feature importance.

Chart

Description automatically generated

The figure above shows the ranking of features by chi-squared accounting for degrees of freedom. In addition to model predictors, I also added a chunk test of significance of overall body composition which is simply testing the significance of all the body composition measures combined. You can see that the previous state dominates the model followed by MELD score, a score based on several lab tests showing overall body function. Body composition does seem to associate with outcomes, based on an α = 0.05, however the only individual body composition measure that is significant is skeletal muscle area. There are in total 8 significant predictors, however, the previous state is the only predictor with substantial effects on the outcome state. Patients tend to stabilize over time, meaning their previous state more likely becomes their current state which could explain some of the reasons why previous state dominates the model.

This model can be used to provide “live” daily updates about a patient’s status after liver transplant and it’s also very flexible to use. The output is 4 x 90 x 422, with an odds ratio for each state for each day for each patient making it easy to examine average probabilities across a state or across time or even hone in on a specific day, date range or patient. However, the main goal of determining body composition’s role in liver transplant outcomes, is inconclusive as it seems to be significant in the model but the effective size it has on outcomes is negligible. Many other analyses could be done with this data set to understand the relationship between body composition and liver transplant outcomes. For example, survival analysis or a longitudinal study utilizing body composition measures taken overtime at checkups as these are included in the data set for up to 10 years for some patients. There are also many other outcome variables in the data set that were not included in this analysis including infections, complications and readmission which could be studied as well in regards to understanding body composition’s role in liver transplant outcomes. Any insights that can help clinicians understand how to minimize liver disease in order to reduce the need for liver transplants but also improve liver transplant outcomes is crucial as there is currently no cure for this awful illness.