ISHAK STAGE PROGRESSION MODEL IN POST LIVER TRANSPLANT (POLT) PATIENTS WITH CHRONIC HEPATITIS C VIRUS (HCV) INFECTION

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BACKGROUND

The Ishak Stage (IS) Score is a commonly used 7-point staging system to describe architectural changes and fibrosis in patients with chronic HCV infection. It is commonly accepted that IS progression rates may be different in POLT HCV patients.

AIM

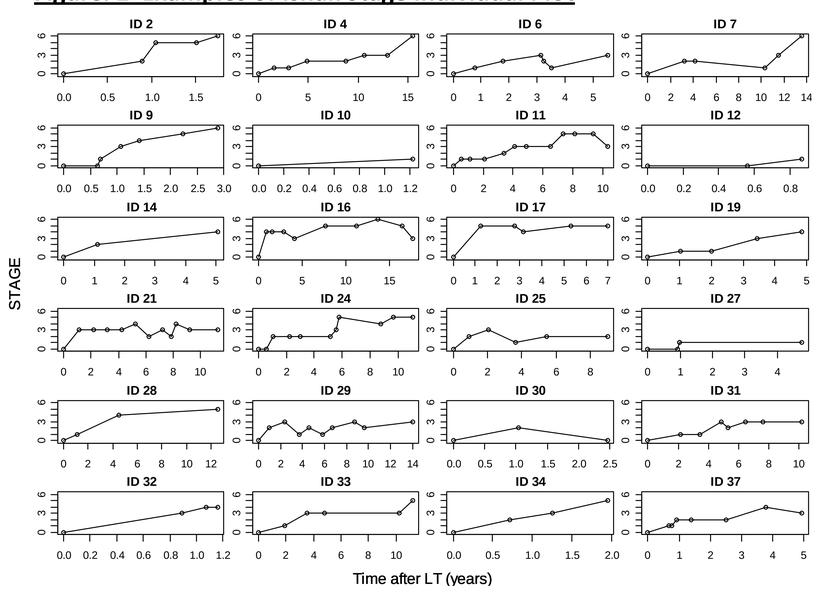
To build an IS progression model for POLT HCV patients and explore potential patient characteristics affecting disease progression rates.

METHODS

Longitudinal IS together with demography, HCV genotype, medical and immunosuppressive therapy from 219 POLT HCV patients were analyzed [Figure. 1 and Figure. 2]. IS was treated as ordered categorical data and modeled with proportional odds method.

Figure. 1 Ishak Stage Raw Data from 219 POLT HCV Patients

Figure. 2 Examples of Ishak Stage Individual Plot



Nonlinear mixed effects modeling technique was used to estimate model fixed effect parameters and inter-subject variability (ISV). Acute HCV, donor sex and age, steroid treatment, presence of diabetes, genotype and overall survival were investigated as potential covariates. A stepwise forward inclusion ($p<0.05$) and backward exclusion ($p<0.005$) method was used to assess covariate effect. Model fit was evaluated by graphical and numerical diagnostic tools [Figure.3 and Figure. 4].

RESULTS

Probabilities (IS>=m for m=0, 1, to 6) of POLT HCV patients' IS progression can be described as the following equations:

$$P=\exp(base+ISprog+ETA)/(1+\exp(base+ISprog+ETA))$$
$$ISprog = (Emax+AHC+DAGE)*Time/(T50+Time)$$

where base corresponds to a baseline probability, ISprog represents IS progression, and ETA accounts for the inter-patient variability. AHC and DAGE represent acute HCV and donor age, respectively.
Estimated Emax and T50 were 16.6 and 1.42 yrs, respectively.
AHC and DAGE were 5.1 and 2.29 respectively.

Figure. 3 Examples of Individual Predictions /Goodness of Fit Plot

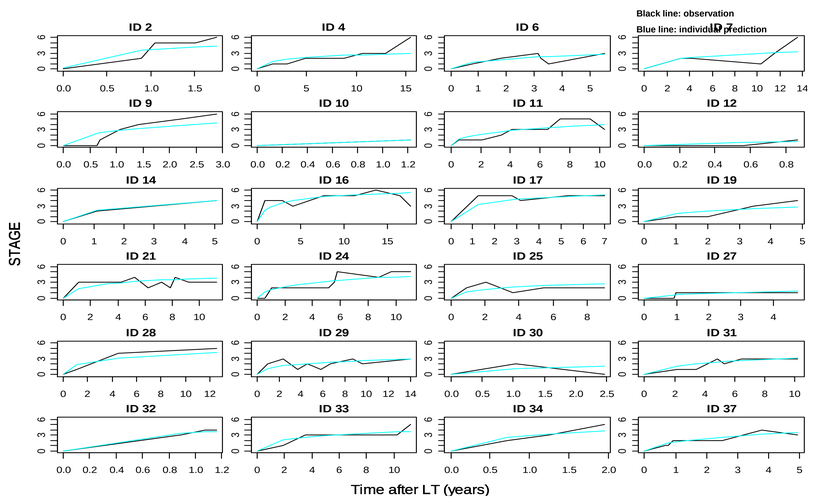
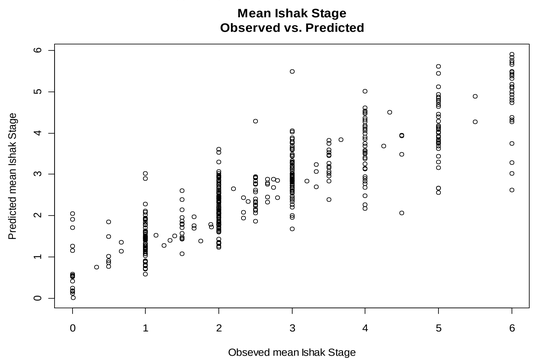


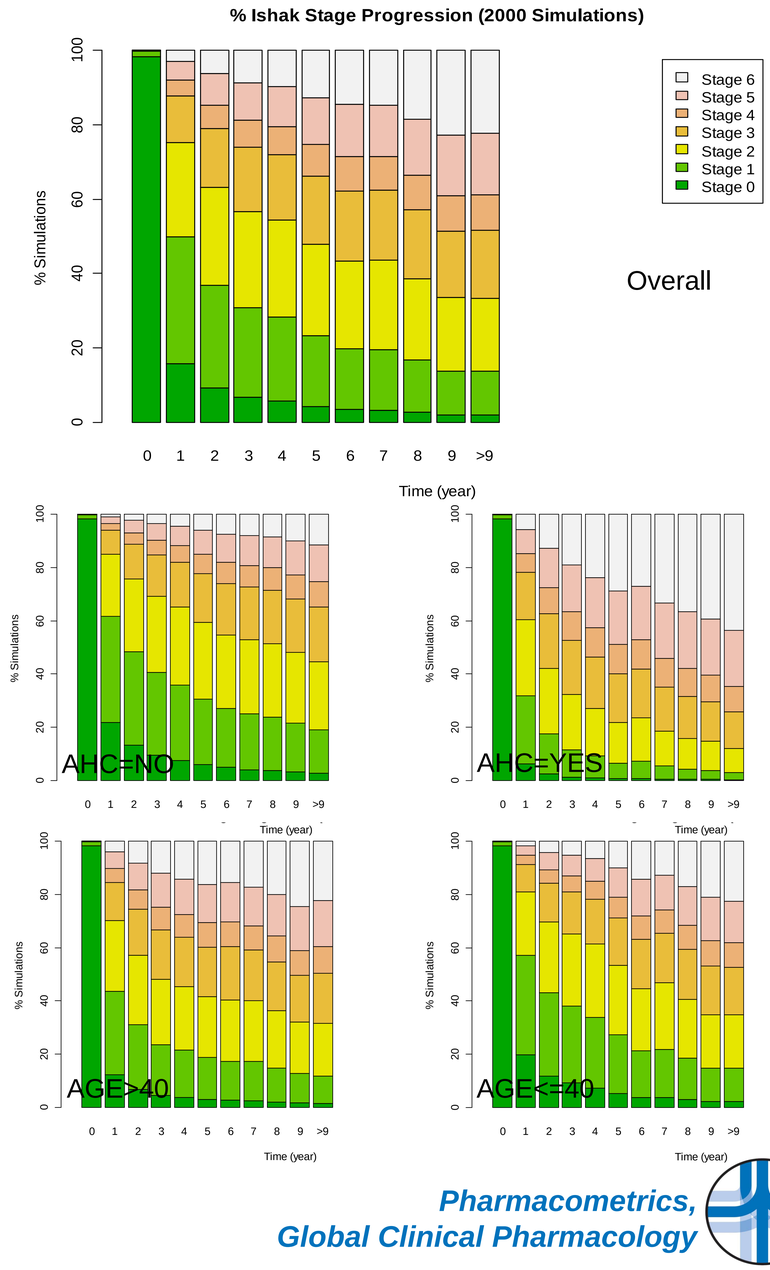
Figure. 4 Goodness of Fit Plot



CONCLUSIONS

An IS progression model developed for POLT HCV patients suggests that in the first 1-2 years POLT the disease stage progression rate to IS 2 is more than the subsequent progression rate to more advanced stages. Analysis of rate of collagen deposition with liver tissue collagen quantification may offer a more robust indication of actual liver fibrosis progression in these patients. Acute HCV and donor age appeared to be important covariates in determining Ishak stage progression [Figure. 5].

Figure. 5 Simulation Plots



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