Ishak stage and quantitative fibrosis measurement (Collagen Proportionate Area) progression in post liver transplant (post-LT) patients with chronic hepatitis C infection.

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Introduction

The progression of fibrosis has previously been modelled using both Ishak stage and a method of fibrosis quantification[(1)] , collagen proportionate area (CPA).[(2)]

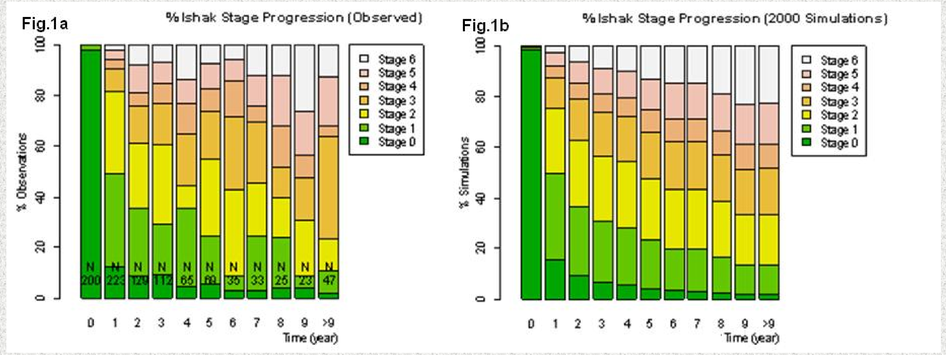
Our aims are to present i.) an overview of the data from which the progression models were built and ii.) a simulation of both the Ishak and CPA fibrosis progression models.

Methods

Demographic data together with HCV genotype, medical and immunosuppressive therapy was collected from consecutive patients (n=219) undergoing liver transplant. Liver biopsies in which changes were attributable to HCV infection were assessed for Ishak stage and CPA (biopsies where there were additional confounding conditions were excluded). The data was used to model post-LT progression of fibrosis[(2)] and variables that affect HCV disease progression were evaluated.

Results

The HCV biopsy observations show that: 48.9% (model simulated 49.9%) of biopsies are Ishak stage 0-1 at 1 year post transplant, 29.5% (30.6%) at 3 years and 24.6% (23.2%) at 5 years; 45.3% (42.2%) of biopsies are Ishak stage 2-4 at 1 year post transplant, 55.4% (50.5%) at 3 years and 58.0% (51.4%) at 5 years; 5.8% (8.0%) of biopsies are Ishak stage 5-6 at 1 year post transplant, 15.2% (18.9%) at 3 years and 17.4% (25.4%) at 5 years, Fig.1.



Observed fibrosis stages (Fig.1a) and those predicted by the model (Fig.1b). Observed CPA (Fig.2a) and those predicted by the CPA model (Fig.2b).

The HCV biopsy observations show that; 75.1% (model simulated 80.2%) of biopsies measured CPA < 6% at 1 year post transplant, 66.7% (60.2%) at 3 years and 58.7% (57.0%) at 5 years; 18.9% (15.3%) of biopsies measured a CPA >=6% and <12% at 1 year post transplant, 21.6 % (23.6%) at 3 years and 23.8% (23.4%) at 5 years; 6.1% (4.5%) of biopsies measured CPA >=12% at 1 year post transplant, 11.8% (16.3%) at 3 years and 17.5% (19.7%) at 5 years, Fig.2.

Discussion

These data offer a detailed year by year description of the proportion of post OLT HCV patients who can be expected to have each stage of HCV related liver disease and the corresponding quantitative degree of liver biopsy fibrosis. The simulation model of post-LT fibrosis progression in patients with HCV needs validation in independent cohorts.

Conclusion

The differences between the stage of disease and fibrosis quantification data emphasise the need to appreciate that liver disease stage and fibrosis collagen quantification are interrelated but essentially different entities.

References

1. *Calvaruso V, Burroughs AK, Standish R, et al. Computer-assisted image analysis of liver collagen: relationship to Ishak scoring and hepatic venous pressure gradient. Hepatology 2009 Apr;**49**(4):1236-1244.*
2. *G Ma, Dhillon A, Hall A, Burroughs AK, Tsochatzis E, Burgess G, Guo F. Ishak stage progression rate modelling for post transplant (POLT) patients with chronic hepatitis C virus (HCV) infection. World conference on pharmacometrics. PA11-12:154.*