The risk of cardiovascular disease and death over 10 years in HIV/HCV co-infected patients with and without steatosis

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Abstract

Background: Co-infection with HIV/HCV is associated with more severe liver disease including increased frequency of steatosis and significant fibrosis compared to patients mono-infected with HIV or HCV. Hepatic steatosis has been associated with greater fibrosis in cross sectional studies. We sought to explore the impact of steatosis on cardiovascular disease (CVD), liver fibrosis, and survival over time.

Methods: An IRB-approved, single-center retrospective cohort study was undertaken to analyze 10-year clinical outcomes in patients co-infected with HIV and HCV previously studied by Marks et al in 2020. Patients included underwent liver biopsy between 1996-2003 for the evaluation of HIV disease. Biopsy samples were assessed by a study pathologist (blinded) for fibrosis and steatosis. Clinical outcomes including cardiac events, liver function, and survival were collected over 10 years. Liver fibrosis progression was assessed using FIB4 and APRI scoring systems.

Results: 105 patients met criteria for this study. At cohort entry, mean age 45 ± 7 yrs, 70% male, 85% on ARVs, 8% had undetectable HIV VL, median CD4+ count was 410 and 12 patients had CD4+ < 200, mean BMI was 26.3, 45% had diabetes, and 27.5% had HTN. 10-year CVD risk estimated by the Framingham Risk Score was 8.6%. Analysis of clinical outcomes showed non-significant trends towards DM (22%), decompenesated liver disease (13%), MI (5%), CAD (5%), and PVD (5%) in the study group compared to those without steatosis (15%, 16%, 1%, 2%, 4%, respectively) over the 10-year period. On average FIB4 and APRI scores were higher in the steatosis group at the 10-year time point, however this trend was not statistically significant. Survival analysis was performed which showed a trend towards decreased survival in the steatosis group at the 5-year and 10-year timepoints with 5-year survival 85% and 10-year survival 65% in the steatosis group vs 93% and 73% at respective time points in the nonsteatosis group.

Conclusions: Given the prevalence of steatosis in approximately half of co-infected patients, the impact of hepatic cardiovascular, fibrosis progression and survival differences observed over 10 years warrant further study. Furthermore, mortality for this population was very high; variables responsible for decreased survival in this population should be further examined.

Primary Objective

Assess the clinical outcomes of patients with HIV/HCV co-infection over 10 years based on degree of steatosis and fibrosis.

Methods

- We compiled a retrospective cohort of HIV/HCV co-infected patients, liver biopsy at time of enrollment
- Baseline factors collected: demographic data, steatosis grade, fibrosis stage, HCV genotype and subtype, HIV and HCV treatment history
- Treatment-related data collected: HAART or no HAART therapy, HCV regimen and duration, on treatment styriptic response
- Cardiac Outcomes: CVD was defined as history of MI, CAD, PCI, PAD or stroke
- Hepatic Function Outcomes: Liver fibrosis progression was assessed using FIB4 and APRI scoring systems.

Summary of Results

Analysis of clinical outcomes showed non-significant trends towards diabetes (22%), decompenesated liver disease (19%), MI (5%), CAD (5%), and PVD (3%) in the steatosis group compared to those without steatosis (11%, 18%, 2%, 4%, 4%, respectively) over the 10-year period.

Survival analysis was performed which showed decreased survival in the steatosis group at the 5-year and 10-year timepoints with 5-year survival 85% and 10-year survival 65% in the steatosis group vs 93% and 73% at respective time points in the nonsteatosis group. However this trend was not significant (HR=1.95, p=0.56).

Mean FIB4 and APRI scores were higher in the steatosis group at time of biopsy and the 10-year timepoint. Change in FIB4 unadjusted HR=1.081 (p=0.0001), and change in APRI unadjusted HR=1.151 (p=0.0001). This relationship remained highly significant with any potential interacting factors such as alcohol use, age, diabetes, obesity or hyperlipidemia.

Multivariate analysis was performed to determine if alcohol use, diabetes, hyperlipidemia, obesity, HIV viral load or HCV viral load correlated with survival, no significant relationship was found between any of these variables.

Conclusions

This retrospective cohort study did not detect a significant association of steatosis with overall survival or cardiovascular or diabetic events. However, the data trends towards an increased rate of cardiovascular events, diabetes and decreased survival in patients with steatosis. Incomplete 10-year data for many patients may underestimate total number of events.

Nonivastatin measures of liver fibrosis, FIB4 and APRI scoring, prove clinically useful for monitoring progression of disease over time, and are related to mortality risk.

The treatment for CVD has evolved greatly in the 15 years since this study was undertaken, and with the availability of DAAAs, HCV is now a curable condition.

The overall survival in this HIV/HCV co-infected cohort study was strikingly low (25% mortality) given age and demographics at time of enrollment.