

Abstract #1005

Alteration of the Portal Circulation across the Entire Spectrum of Fibrosis in Patients with Chronic Hepatitis C as Measured by Dual Cholate Clearances

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Introduction. Chronic Hepatitis C (CHC) progresses through inflammation and fibrosis culminating in cirrhosis and liver failure. Biopsy can assess the degree of fibrosis but is invasive and subject to sampling error. Standard blood tests that assess liver function are maintained until late stage disease. Functional assessment using Cholate Testing has demonstrated that low clearance of orally administered cholate, herein defined as Portal Hepatic Filtration Rate (HFR), and high portal-systemic SHUNT correlate with clinical complications and improve the prediction of outcomes in compensated CHC patients (Hepatology 2012, 55: 1019-1029). The current study examined the relationships of Portal HFR and SHUNT to fibrosis stage over all Ishak stages and in comparison to healthy controls.

Methods. Biopsy determined fibrosis stage was evaluated on the Ishak scale. Cholate testing was performed on healthy controls (n=32), CHC patients from a study of patients with early stages of HCV (F1 n=6, F2 n=14), and CHC patients from the HALT-C trial (F2 n=19, F3 n=63, F4 n=44, F5 n=41, F6 n=40). Oral cholate-2,2,4,4-d₄ targets the portal circulation, and its clearance defines Portal HFR. IV cholate-24-¹³C clearance measures Systemic HFR. The ratio of Systemic to Portal HFR defines SHUNT. Cholate clearances were measured in serum by an LCMS method validated to FDA guidelines for accuracy, precision, and freedom from interferences.

Results. As shown in the figure, compared to healthy controls (C), patients with CHC demonstrate an exponential increase in SHUNT and exponential decrease in Portal HFR over all stages of fibrosis. Cholate testing could distinguish the early stages when patients often have no symptoms. Cholate testing could also distinguish advanced fibrosis stages F3-F4 and cirrhosis stages F5-F6 when patients experience increasing severe complications.

Conclusions. Functional assessment by Cholate Testing could assess the entire spectrum of fibrosis stages. Cholate Testing may represent an alternative to biopsy or other fibrosis tests for monitoring CHC.
(values are means +/- SEM)

