A Disease Severity Index (DSI) from the HepQuant®-SHUNT Test is Reproducible and Quantifies Hepatic Impairment in Patients with Non-Alcoholic SteatoHepatitis (NASH), Chronic Hepatitis C (CHC), and Primary Sclerosing Cholangitis (PSC)

James R. Burton, Steve Helmke, Shannon Lauriski, and Gregory T. Everson
University of Colorado, Denver, CO

Background/Aim
The dual cholate test (HepQuant®-SHUNT) yields a disease severity index, DSI, that quantifies global liver function and physiology. Herein, we define the performance and reproducibility of DSI across a spectrum of chronic liver diseases, including Non-Alcoholic SteatoHepatitis (NASH), Chronic Hepatitis C (CHC), and Primary Sclerosing Cholangitis (PSC).

Patients
Patients: 16 healthy controls, 16 patients with CHC (8 with METAVIR fibrosis stage F0 to F2, 8 with F3 or F4), 16 patients with NASH (6 with Brunt/Kleiner fibrosis stage F0 to F2, 8 with F3 or F4), and 46 patients with a wide clinical spectrum of PSC were studied. CHC and NASH patients with cirrhosis had compensated disease. There were only 3 NASH patients with compensated cirrhosis so 6 additional NASH patients with compensated cirrhosis were tested to establish the relationship to fibrosis stage.

Methods
HepQuant®-SHUNT Testing: The 16 Controls, 16 HCV, and 16 NASH cases were tested 3 times, and the 46 PSC cases were tested twice. The additional 6 NASH cirrhotics were tested once. Hepatic filtration rates (HFRs) were defined from clearances of cholic acid-24-13C, 20 mg administered intravenously (Systemic), and cholic acid-2,2,4,4-d4, 40 mg administered orally (Portal). Clearances were calculated from labeled cholate serum concentrations at baseline and 5, 20, 45, 60, and 90 minutes after simultaneous administration of IV cholic acid-24-13C and oral cholic acid-2,2,4,4-d4. DSI was calculated from HFRs:

\[
\text{DSI} = 10.86 \times \sqrt{[\log_{10}(51.69) - \log_{10}(\text{Portal HFR})]^2 + (\log_{10}(10.72) - \log_{10}(\text{Systemic HFR})]^2}
\]

Results
1. The means ± SDs of DSIs for NASH (16.8 ± 3.4), HCV (18.9 ± 6.0), and PSC (18.2 ± 7.4) were higher than for controls (9.8 ± 3.3) (p < 0.001).

2. DSI (mean ± SEM) correlated with fibrosis stage in NASH and HCV.

3. The healthy controls, NASH patients, and HCV patients were tested in triplicate (● ● ○) and PSC patients were tested in duplicate (○ ○). Average deviation from the mean of the replicates was 0.94 ± 0.86 DSI units (mean ± SD). Intra-class correlations (ICCs) for DSI were > 0.9 and the testing reproducibility was consistently maintained across the entire range of DSI.

Conclusions
- DSI quantifies hepatic impairment and is reproducible over a broad spectrum of etiologies of liver disease, stages of fibrosis, and clinical severity.
- The minimally invasive HepQuant®-SHUNT test could be useful for defining severity and monitoring progression of chronic liver diseases, including Non-Alcoholic SteatoHepatitis (NASH), Chronic Hepatitis C (CHC), and Primary Sclerosing Cholangitis (PSC).