Background: Disease progression of CLD and nonalcoholic steatohepatitis (NASH) is variable and may be influenced by comorbid conditions and concomitant drug therapy. We used the HepQuant SHUNT test, to evaluate the impact of NASH, diabetes (DM), and drug therapy on hepatic function and portal-systemic shunting in subjects with CLD enrolled in the SHUNT-V study.

Methods: The 270 subjects for this preliminary analysis had either compensated cirrhosis, fibrosis stage F3 with platelet count <175,000, or Child-Pugh B without refractory ascites, refractory encephalopathy, or history of variceal hemorrhage. HepQuant tests involved dosing [24-13C]-cholic acid, IV, and [2,2,4,4-2H]-cholic acid, PO, and blood sampling at t = 0, 5, 20, 45, 60, and 90 minutes. Serum was analyzed for cholate concentrations by LC-MS/MS and a disease severity index (DSI), assessing hepatic function, and portal systemic shunt fraction (SHUNT) were calculated. Lower DSI indicates better hepatic function; lower SHUNT denotes less portal-systemic shunting.

Results: Subject characteristics (means or percentages): age 61.6 years, body weight 95.3 kg, BMI 33.4, male 49%, white race 92%, Hispanic ethnicity 14%; 64% were obese, 50% had NASH, and 48% were taking diabetic drug therapy. Compared to other etiologies for CLD, NASH subjects were older, heavier, had higher BMI and more were obese. In contrast, NASH and non-NASH subjects had similar blood tests, clinical scores, elastography and endoscopic findings.

Conclusions: In the SHUNT-V study of clinically stable but advanced CLD, concomitant use of statins was independently associated with preserved hepatic function and reduced portal-systemic shunting. The HepQuant SHUNT test may be useful for quantifying treatment effects in CLD.

In uni-variable regression, diabetic drug therapy and statins were associated with lower DSI and SHUNT.

In multi-variable regression of prescribed medications, statins and metformin exhibited the strongest associations with lower DSI (p=0.003, p=0.06) and SHUNT (p<0.015, p<0.05, not shown).

The estimated effect of combined treatment with statins and diabetic drugs was a 20% lowering of both DSI and lower SHUNT.

Conclusion: The HepQuant SHUNT test may be useful for quantifying treatment effects in CLD.

Financial disclosures: Gregory T. Everson and Steve M. Helmke are employees of HepQuant, LLC