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TITLE: Diagnosing of NASH and Assessing NASH Disease Severity by a Global Measure of Liver Function, the HepQuant® (HQ)-SHUNT Test

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ABSTRACT BODY:

Abstract Body: Background and Aims: NASH is very difficult to diagnose and stage and the only accepted method is liver biopsy. The patchy nature of NASH fibrosis causes biopsy sampling error and 40% variability in staging (Ratziu, et al, 2005). The HepQuant® (HQ)-SHUNT test generates a disease severity index (DSI) which is a global measure of liver function. The goal of this pilot study was to determine if DSI could diagnose NASH and assess NASH disease severity.

Methods: Healthy controls (N=50) included 30 of normal weight (BMI 18.5-25), 16 overweight (BMI 25-30), and 4 obese (BMI>30). Patients were from 2 centers, University of Colorado Denver (N=16) and Baylor University Medical Center Dallas (N=15), and 27 had biopsy-diagnosed NASH and 4 had cryptogenic cirrhosis, concurrent obesity, and presumed late stage NASH. There were 4 patients with Brunt-Kleiner fibrosis stage F1, 4 with F2, 5 with F3, and 18 with F4 (cirrhosis). Clinical manifestations of NASH disease severity were captured from patient histories and included medium/large varices and any decompensation events (ascites, encephalopathy, variceal bleed, or jaundice). The HQ-SHUNT test involves serum sampling prior to, and at 5, 20, 45, 60, and 90 minutes after simultaneous administration of IV ^{13}C-cholic acid (CA) and oral 4D-CA. Clearances of ^{13}C-CA and 4D-CA were measured and DSI calculated from the clearances. The ability of DSI to diagnose NASH and to assess NASH disease severity was evaluated by AUROC analyses (c-statistic) and by the diagnostic performance (sensitivity, specificity, PPV, NPV) at the optimum cutoffs which were defined by the maximum Youden Index (J).

Results: The HQ-SHUNT DSI could differentiate NASH patients from healthy control subjects, even overweight and obese controls, with high c-statistic, specificity, PPV, and Youden Index (J) (Table section A). A biopsy diagnosis of cirrhosis could identify NASH patients at risk of medium/large varices or those at risk of decompensation, but HQ-SHUNT DSI could identify both groups with a higher c-statistic, and much better specificity, PPV, and Youden Index (J) (Table sections B & C).

Conclusions: The HQ-SHUNT test could be a minimally-invasive alternative to biopsy for the diagnosis of NASH. The HQ-SHUNT test DSI could outperform fibrosis stage in assessing NASH disease severity.