Abstract Category: Diagnostic procedures NASH / liver fibrosis

Abstract Title: "Diagnosing NASH Patients and Their Risk of Varices and Decompensation by a Global Measure of Liver Function, the HepQuant®-SHUNT Test"

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Background/Aim: Currently NASH is diagnosed by liver histology. Because NASH biopsies are subject to sampling error and 40% variability in staging (Ratziu, et al, 2005), assessing risk for portal hypertension, varices, and liver decompensation is problematic. FibroScan may be inaccurate and subject to interference by steatosis (Durango, et al, 2013), and HVPG is invasive and not used routinely. HepQuant®-SHUNT is a minimally-invasive test that provides a global measure of liver function, the disease severity index (DSI). The goal of this pilot study was to determine if DSI could diagnose NASH and assess the risk for varices and decompensation.

Methods: The study comprised 81 subjects, of whom 50 were healthy controls, (30 normal weight (BMI 18.5-25), 16 overweight (BMI 25-30), and 4 obese (BMI>30)). In addition there were 16 NASH patients from the University of Colorado Denver and 15 NASH patients from Baylor University Medical Center Dallas. Of these, 27 had biopsy-diagnosed NASH, and 4 had cryptogenic cirrhosis, concurrent obesity, and presumed late stage NASH. Patients had a range of Brunt-Kleiner fibrosis stages, F1 (N=4), F2 (N=4), F3 (N=5), and F4 (cirrhosis, N=18). Clinical manifestations of NASH disease severity were captured from patient histories and included endoscopy findings (small, medium, or large varices) and any clinical 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 cholic acid-24-^{13}C and oral cholic acid-2,2,4,4-d4. Clearances of labeled cholates, measured by LCMS of serum samples, were used to calculate a disease severity index (DSI). The ability of DSI to diagnose NASH and to assess the risk for varices and decompensation was evaluated by ROC analyses (c-statistic and the sensitivity, specificity, PPV, NPV at the optimum cutoff defined by the maximum Youden Index) and logistic regression.

Results: The HQ-SHUNT DSI could differentiate NASH patients from healthy control subjects, even overweight and obese controls (ROC c-statistic 0.94, optimum cutoff DSI >16.5, sensitivity 84%, specificity 98%, PPV 96%, NPV 91%, Youden Index 0.82). Within the NASH cohort, DSI could identify patients at risk of any varices (ROC c-statistic 0.87, optimum cutoff DSI >21.2, sensitivity 86%, specificity 82%, PPV 80%, NPV 88%, Youden Index 0.68), those at risk of medium/large varices (ROC c-statistic 0.93, optimum cutoff DSI >28.0, sensitivity 89%, specificity 91%, PPV 80%, NPV 95%, Youden Index 0.80), and those at risk of decompensation (ROC c-statistic 0.99, optimum cutoff DSI >28.0, sensitivity 100%, specificity 95%, PPV 90%, NPV 100%, Youden Index 0.95). By logistic regression, DSI was a highly significant predictor for diagnosing NASH, and also DSI could significantly predict the risk of any varices, medium/large varices, and decompensation. The DSI cutoffs for 50% probability for any varices (DSI 24.7) and for medium/large varices (DSI 30.4) were similar to the DSI cutoffs found in a previous study of varices risk in 217 HCV patients (DSI 24.8 and 33.2, respectively).

Conclusions: This pilot data suggests that the HepQuant®-SHUNT test could be a minimally-invasive alternative to biopsy for the diagnosis of NASH. DSI could be a measurement for assessing risk for any varices, for medium/large varices, and for liver decompensation in NASH.