The HepQuant SHUNT Test of Global Liver Function and Physiology Identifies the Patients with Advanced Fibrosis or Compensated Cirrhosis Who are At-Risk for Hepatocellular Carcinoma

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Introduction: The key to cost-effective screening of patients with chronic liver disease for hepatocellular carcinoma is identification of high-risk groups. In this study we examined the relationship of hepatic functional impairment to HCC risk by analysis of prospectively collected data from the QLFT Ancillary Study of the HALT-C trial. HepQuant's Disease Severity Index (DSI) greater than 18.3 may identify cases with increased likelihood for varices and risk for future clinical outcomes, including HCC.

Methods: In the QLFT Ancillary study of the HALT-C Trial, the HepQuant SHUNT test evaluated the link of hepatic impairment to risk for future clinical outcome, including development of HCC. In this study, 220 subjects with advanced fibrosis or compensated cirrhosis and ongoing active HCV infection underwent baseline HepQuant SHUNT testing, and were followed for a mean of 6.1 years. Clinic visits with standard blood and AFP testing was conducted every 3 to 6 months, US of liver every 6 to 12 months, and CT or MRI for elevated or rising AFP or new lesions of US. The HepQuant SHUNT test measures global hepatic function and physiology from the simultaneous clearances of intravenously administered 13C-cholate and orally administered d4-cholate. In the test, blood samples are collected at 5, 20, 45, 60, and 90 minutes post-dosing for measurement of hepatic filtration rates (HFRs) from systemic (Systemic HFR) and portal (Portal HFR) circulations. Portal-systemic spillover (SHUNT), and a disease severity index (DSI) are calculated from the HFRs.

Results: 13 of 220 subjects (6%) developed HCC 1.6 to 7.0 years after initial assessment – 9 were confirmed histologically and 4 based upon imaging. The baseline DSI of HALT-C patients who developed HCC ranged from 16.3 to 33.0. Twelve of these 13 had baseline DSI >18.3, and the one with DSI <18.3, had DSI 23.3 two years later and prior to his HCC diagnosis at year 4.6. DSI dropped from 19.0 at baseline to 17.2 at year 2 prior to his HCC diagnosis at year 2.8. The relative risk for incident HCC was 12/113 vs 1/107, or 11.4 fold-increase, for patients with baseline HCC >18.3.

Conclusion: Hepquant DSI may be a useful tool in identifying HCC risk in otherwise stable patients with advanced fibrosis or compensated cirrhosis. Further studies of HepQuant SHUNT in the clinical management of HCC are warranted.