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

Steve M. Helmke[1,2] and Gregory T. Everson[1,2]

1. University of Colorado; 2. HepQuant, LLC, Greenwood Village, CO

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. The HepQuant SHUNT Test'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 and serial 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 – 6 months, and US of the liver every 6 – 12 months. CT or MRI was performed for elevated or rising AFP, or new lesions found by 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 the disease severity index (DSI) are calculated from the HFRs.

Results:

Baseline Characteristics of Subjects who Developed HCC

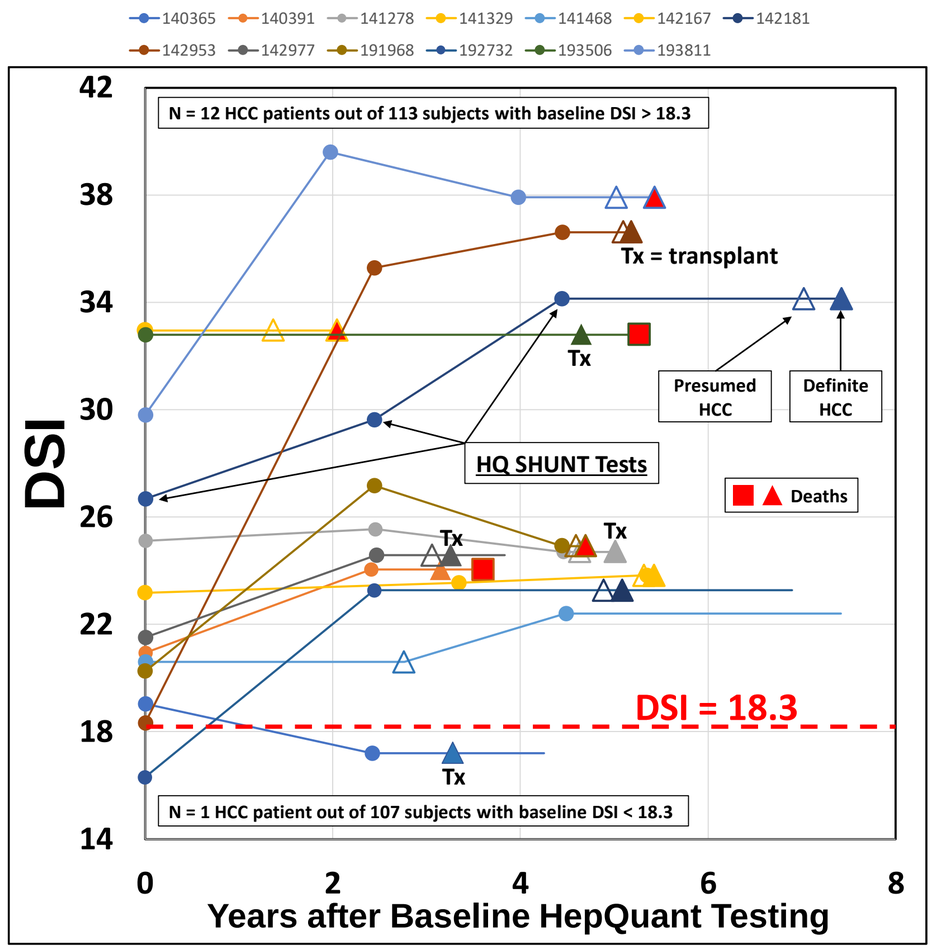
• N = 13	
• Average age	50.6 ± 7.8 yrs
• Gender ratio (M:F)	9:4
• HCV Genotype (GT 1:GT 3)	11:2
• CTP Score	5.7 ± 1.6
• MELD Score	7.4 ± 1.6
• ISHAK Fibrosis (F3:F4:F5:F6)	(3:3:3:4)
• Bilirubin, Total	0.85 ± 0.59
• Albumin, g/dL	3.52 ± 0.34
• INR	1.07 ± 0.09
• Creatinine, g/dL	0.78 ± 0.15
• Platelet count, 10^9 L^{-1}	111 ± 53

Progression in DSI and Risk for Definite HCC

	DSI at Baseline	DSI Proximal to HCC	ΔDSI	Time between DSIs	Annual DSI Progression	Yr from Baseline DSI to Definite HCC	Yr from Proximal DSI to Definite HCC	Yr from Serial DSI Proximal to Definite HCC
140365	19.03	17.20	-1.83	2.42	-0.76	3.28	0.86	0.86
140391	20.94	24.04	3.10	2.41	1.29	3.15	0.74	0.74
141278	25.12	24.70	-0.42	4.46	-0.09	5.02	0.56	0.56
141329	23.18	23.82	0.64	5.34	0.12	5.42	0.08	0.08
141468	This Case Excluded from this analysis since no definite HCC diagnosis was established.							
142167	32.95	Only had Baseline DSI				2.05	2.05	
142181	26.68	34.13	7.45	4.44	1.68	7.43	2.98	2.98
142953	18.32	36.62	18.30	4.44	4.12	5.19	0.74	0.74
142977	21.51	24.57	3.06	2.46	1.24	3.26	0.80	0.80
191968	20.25	24.92	4.67	4.44	1.05	4.70	0.25	0.25
192732	16.30	23.27	6.97	2.44	2.86	5.08	2.64	2.64
193506	32.80	Only had Baseline DSI				4.65	4.65	
193811	29.80	37.91	8.11	3.97	2.04	5.43	1.46	1.46
N:	12	10	10	10	10	12	12	10
Mean:	23.91	27.12	5.01	3.68	1.35	4.55	1.48	1.11
SD:	5.61	6.72	5.76	1.13	1.44	1.42	1.36	0.97

p = 0.0226 for change in DSI from Baseline DSI to the DSI most proximal to the HCC; two-tailed paired t-test

Baseline and Serial DSI Prior to HCC



Relative Risk of HCC for Baseline DSI >18.3 is 11.4

Conclusions

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

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