Hepatic functional deterioration after locoregional therapy (LRT) for hepatocellular carcinoma (HCC) measured by hepatic cholate clearance: a pilot study

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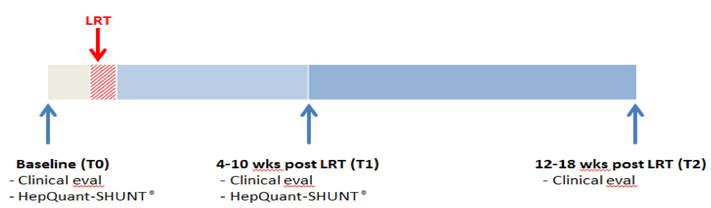
Background

- Locoregional Therapy (LRT) is the treatment of choice for Hepatocellular Carcinoma (HCC) when limited to the liver, but is associated with a risk of liver toxicity
- Using clinically available measures of liver function, an upper limit of liver dysfunction that allows the safe administration of LRT is not well defined
- The dual cholate clearance assay (HepQuant-SHUNT®) measures the hepatic clearance rate of ^{13}C labelled cholate administered orally, and ^{2}H labelled cholate administered intravenously. A liver disease severity index (DSI) is derived from a combination of oral and IV clearance parameters [1]
- The primary objective of our pilot study is to evaluate the effect of LRT for HCC on hepatic cholate clearance parameters
- The secondary objective is to determine whether baseline cholate clearance parameters correlate with subsequent development of liver toxicity

Methods

- Patients with HCC limited to the liver, without vascular invasion, who are scheduled for LRT at the University of Pennsylvania were recruited
- The dual cholate clearance assay (HepQuant-SHUNT®) was administered as previously described [1], at baseline (T0) before LRT, and 4-10 weeks after LRT (T1)
- Clinical and laboratory assessment of liver function was obtained at baseline (T0), at 4-10 weeks after LRT (T1), and at 12-18 weeks after LRT (T2)
- Clinically significant liver toxicity was defined as the development of a new complication of liver disease, or an increase in Child-Turcotte-Pugh (CTP) score by 2 or more points
- The Wilcoxon signed rank test was used to compare parameters before and after LRT

Figure 1. Study Design



Results

- Eleven patients were recruited and completed the baseline evaluation
- Two patients did not have complete data from the post LRT HepQuant-SHUNT® for technical reasons (inability to obtain IV access in one case, no detectable ^{13}C cholate in another)
- Complete per protocol assessment was available in 9 patients

Results (continued)

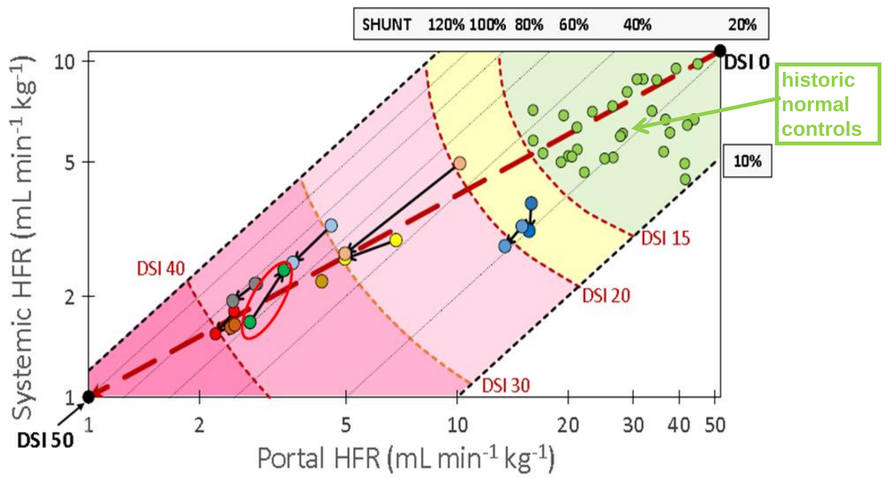
Table 1. Baseline Characteristics

N	11
Men	8/11 (73%)
Age (yrs, median [IQR])	61 [59-73]
Etiology	HCV (6/11, 55%) NASH (3/11, 27%) Alcohol (2/11, 18%)
CTP class	A (4/11, 36%) B (7/11, 64%)
BCLC stage	A (7/11, 64%) B (4/11, 36%)
Modality of LRT	TACE (5/11, 45%) XRT (6/11, 55%)

Table 2. Change in median [IQR] values of clinical and Cholate clearance parameters

	Pre LRT (T0)	Post LRT (T1)	P-value
PO Cholate Clearance (mL/min)	422 [235-768]	339 [208-362]	0.03
IV Cholate Clearance (mL/min)	210 [150-300]	191 [144-203]	0.04
Portal Hepatic Filtration Rate (HFR) (mL/Kg/min)	4.3 [2.4-15.9]	3.6 [2.2-15.7]	0.05
Systemic HFR (mL/Kg/min)	2.2 [1.8-3.2]	2.4 [1.8-2.7]	0.06
Disease Severity Index (DSI)	32.0 [19.6-37.8]	33.0 [29.6-38.0]	0.10
CTP score	7 [5-8]	7 [6-8]	0.15
MELD score	12 [9-13]	11[10-12]	0.72
MELD-Na score	12 [9-14]	11[10-13]	0.64

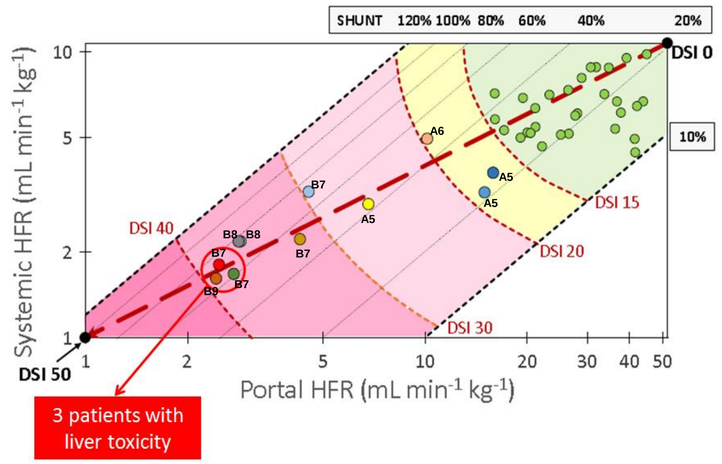
Figure 2. Change cholate clearance parameters between T0 and T1, individual patient data



- All but one of the 9 patients (89%) who had a complete evaluation had worse DSI after LDT
- Only 4/9 (44%) had an increase in CP score, and 5/9 (56%) had an increase in MELD or MELD-Na scores

Results (continued)

Figure 3. Baseline cholate clearance parameters and liver toxicity



- Three patients had clinically significant liver toxicity (2 at T1, 1 at T2)
- Liver toxicity was observed in 3/7(43%) CTP B patients and 0/4 CTP A patients; and in 3/5 (60%) patients with a DSI>35, and 0/6 of the patients with DSI<35.
- Two patients had evidence of tumor progression, both at T2 (none at the time of cholate clearance assessment)

Discussion

- The HepQuant-SHUNT® assay appears to detect a deterioration in hepatic function of patients treated with LDT at 4-10 weeks after treatment. One patient was an outlier in that trend.
- DSI>35 might be a cutoff for risk of clinical decompensation after LRT for HCC, as it appears to perform better than clinical parameters in this pilot study.
- Additional research is needed to evaluate the role of the HepQuant SHUNT® test in improving the selection of Child B patients for LRT.

Reference

[1] Everson GT, et al. Portal-systemic shunting in patients with fibrosis or cirrhosis due to chronic hepatitis C: the minimal model for measuring cholate clearances and shunt. *Aliment Pharmacol Ther* 2007: 26, 401–410.