NASH cirrhosis: The intra-hepatic hemodynamic abnormality (IHHA) of cirrhosis as measured by PHM baseline and change per year predicts clinical outcomes and survival in patients followed for up to 13 years

John Hoefs, MD., *University of California Irvine*

BACKGROUND

The intra-hepatic hemodynamic abnormality (IHHA) of cirrhosis characterized primarily by forms of intra-hepatic shunting(1-9) determines quantitative hepatic function and correlates with clinical outcomes. In hepatitis C (investigated in the HALT-C trial), the IHHA was measured on the quantitative liver-spleen scan (QLSS) as PHM (perfused hepatic mass) and out-performed any combination of histology and routine liver function tests (LFT) in correlation with clinical outcomes over 8 years (Hepatology, 55,1019-1029, 2012) (10). Early studies showed that patients with chronic liver disease (CLD) have the IHHA regardless of cause and correlates with the functional hepatic mass (Am J Gastro, 92, 2054-2058, 1997) (11). We hypothesize the outcomes of NASH cirrhosis are likely to be related to IHHA as measured by PHM.

METHODS

Methods: 13 patients with NASH cirrhosis were identified based on liver biopsy or nodularity of liver surface with collaterals by CT/MRI/US and followed for up to 13 years. Sulfur colloid liver-spleen scan as processed by HEPATIQ for measurement of PHM (n=100-110), functional spleen volume (fSV) (n=<2.5 cc/lb IBW), and functional liver volume (fLV) (n=7-12 cc/lb IBW). Data was obtained from a clinical database for clinical complications (death, ascites, encephalopathy, variceal bleeding VB), ultrasound and routine blood tests.

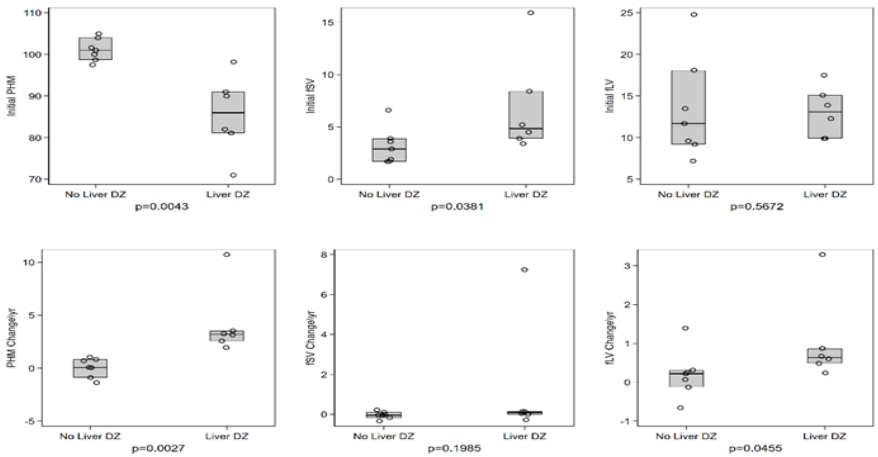
Statistics: Change over time was measured as delta (=initial – last scan), delta/time observed and by the linear regression slope of change over time. A linear regression r2 of >.4 was considered significant for description of slope. Results are presented as box plots (chart 1) w/observed data overlays and tested using a Kruskal-Wallis rank test (ie, nonparametric t test).

RESULTS

The mean number of scans per patient was (7.5+/-2.5) over the mean number of years (8.1+/-3.2) of follow-up. 6 patients had complications and 1 had VB and Ascites prior to the first scan with no problems thereafter. 1 patient had a gastric bypass and lost 30 lb prior to the first scan. The main therapy was by control of predisposing factors of DM (11), hyperlipidemia (10), and obesity (3 patients had lean body NASH). Vitamin E was given for all patients and was taken by most.

We divided patients into 2 groups based on progression to clinical complications including death: 1) 7 patients with no clinical problems and 2) 6 who progressed to clinical problems 5 of which died, had a liver transplant (LT) or were accepted on the LT list. One death was from HCC. All 5 patients in group B who died had a PHM < 95 at baseline and had progression in PHM by linear regression slope and delta initial to final PHM (table).

			FU Years	# Scan	initial Wt (lb)	IBW Wt (lb)	Wt loss Lb/yr	initial PHM	delta PHM	Delta/ year	PHM slope
A	8	mean	9.0	7.6	178.5	124.6	10.0	98.7	4.7	0.30	-0.0013
		SD	2.9	2.7	27.9	26.7	31.7	7.2	9.6	1.07	0.0032
B	5	Mean	5.7	7.3	208.6	116.0	6.6	86.3	23.1	4.65	-0.0139
		SD	3.0	2.9	66.5	11.4	16.4	10.5	9.6	3.42	0.0110
p			<.05	NS	<.05	NS	NS	<.05	<.05	<.05	<.05



DISCUSSION

The IHHA is common to all forms of cirrhosis, correlating with quantitative liver function and clinical outcomes. We measured IHHA with PHM as processed by HEPATIQ in patients with NASH cirrhosis to follow and predict outcomes in this group. We had a group of patients that progressed and this correlated with baseline low IHHA as measured by PHM and more rapid deterioration of IHHA. Surprisingly, some patients with NASH cirrhosis did not progress to clinical outcomes.

The patients who did not progress to clinical outcomes had PHM deterioration of 0.30/year, while those that progressed had PHM deterioration of 4.65/year ($p<0.05$). Knowledge of these groups will help with 1. clinical estimates of prognosis and 2. selection of patients in future studies with low or high incidence of clinical complications. It will also help with early detection of patients who deteriorate.

CONCLUSIONS

- Many patients with NASH cirrhosis do not progress over time to clinical problems or death.
- IHHA as measured by PHM could identify patients at baseline or by deterioration during f/u who would progress to clinical problems and die.
- The presence of NASH cirrhosis is not sufficient to predict a bad outcome.
- IHHA should be measured to predict clinical outcomes.