



HEPATIQ: AUTOMATED MEASURE OF LIVER DISEASE SEVERITY THAT CORRELATES WITH ADVERSE CLINICAL OUTCOMES (ACO)

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ABSTRACT

OBJECTIVE: Functional quantitative tests have been largely ignored in the search for non-invasive methods for staging CLD. The perfused hepatic mass (PHM) is a precise measure of liver function correlating with the functional mass of the liver ($r = .905$) (AmJGastro;92:2054). PHM <95 has 15X higher risk of ACO than patients with PHM ≥ 95 (HALT-C 2012;Hepat;55:1019). PHM measured by manually drawn regions of interest (ROI) on SPECT images is tedious. HEPATIQ is an automated computer program developed to make quantitative image analysis of SPECT images easier. Validation requires that automated PHM (PHM-A) correlate closely with manual PHM (PHM-M) and with ACO. **METHODS:** Sequential SPECT scans in 204 patients: normal 9, HBV 31, HCV 67, NASH 24, PBC 7, ACAH 10, ALD 8, abnormal AST/ALT 22, post liver transplant (LT) 5, misc. 13, and unknown 8. Any ACO in the present or past was recorded in 196 patients with available clinical information including 159 never having ACO and 37 patients with current or prior ACO: current ascites 23 (8 refractory), VB 8, HE 11, HCC 7 and death 2. **SCAN:** Patients were fed prior to IV injection of 5-6 mCi 99mTc sulfur colloid with subsequent SPECT/planar images. PHM was calculated manually and by HEPATIQ on summarized transaxial images. **RESULTS:** PHM-A (97.3+/11.5) was strongly correlated with PHM-M (97.5+/11.8) ($r = .96$, $p < .0001$) (figure). Since PHM-A and PHM-M were not significantly different in any clinical parameter, only PHM-A clinical correlation is reported. PHM-A in 9 normals (103.7+/3.3) and 150 patients never having ACO was 101.6 ± 4.1 with 5% < 95 compared to those with active and prior ACO (81.5+/15.2) with 75% < 95 ($p < .001$). PHM-A in patients with prior, but not active ACO included 6 patients with LT 98.5+/5.5 and 7 patients with prior ACO that had resolved more than 2 years prior to scan after effective treatment (94.8+/3.0) ($p < .5$). In 25 patients with active ACO PHM was 74.4 ± 14.1 ; 23 of these with ascites 72.7 ± 13.3 (100% < 95); and 2 death (36.1, 63). 15 patients with treatable ascites had higher PHM 73.9 ± 10.2 compared to 6 refractory ascites (65.5+/14.0) ($p < .05$). PHM was 71.5 ± 10 in 9 patients with HE and 76.3 ± 16.7 in 7 with HCC. **CONCLUSIONS:** 1. PHM-A using HEPATIQ correlates closely with PHM-M. 2. PHM-A using HEPATIQ is a precise measure of CLD severity correlating with clinical outcomes regardless of CLD cause. 3. PHM-A with HEPATIQ is a hepatic function test, valuable for non-invasive staging of CLD.

BACKGROUND

1. Gradual accumulation of fibrosis is the hallmark of progressive CLD eventually causing abnormal hepatic function, portal hypertension and carcinogenesis.

2. In the quantitative liver function test (QLFT) ancillary study of the prospective (HALT-C) (Hepatitis C Antiviral Long-term Treatment Against Cirrhosis) trial, baseline hepatic function measured via perfused hepatic mass (PHM) and portal hypertension measured via spleen volume per IBW (SV/IBW) on the sulfur colloid quantitative liver-spleen scan (QLSS) are precise in predicting clinical outcomes (2010 Hep 51:585)

3. HEPATIQ is a program that automates calculation of the PHM-A as a measure of Hepatic function and volumes (liver/spleen).

4. We identified in this population the range of PHM in patients with/without ACO (adverse clinical outcome) and report the threshold of hepatic function for clinical problems.

HYPOTHESIS:

HEPATIQ measure of PHM correlates with clinical outcomes.

AIMS:

- Determine whether the automated PHM (PHM-A) by HEPATIQ correlates with the standard PHM manual (PHM-M) method
- Determine the distribution of PHM in ACO and thresholds for clinical disease

PATIENTS:

- 204 sequential patients with Quantitative liver spleen scan (QLSS) enrolled
- Liver Disease:** normal 9, HBV 31, HCV 67, NASH 24, PBC 7, ACAH 10, ALD 8, abnormal AST/ALT 22, post liver transplant (LT) 5, misc. 13, and unknown 8.
- ACO (196 patients with available information):** Prior ACO 7 (recovered by at least 2 years), VB 8 (6 with prior ACO), ascites 23 (8 refractory), hepatic encephalopathy 11, HCC 7, liver transplant (LT) in past 5 and death 2

METHODS

QLSS Protocol: Standard meal, IV Tc 99m Sulfur Colloid followed by SPECT LSS and planar parameters.

PHM calculations processed manually (PHM-M) and by HEPATIQ automatically (PHM-A)

SL = spleen length on posterior planar scan

Total count L/L+S ratio = $(L/L+S) \times 100 / (1-(SL-6) \cdot 0.125)$, $LBl = 50 \cdot \log (L/(L+S))$

Perfused hepatic mass (PHM) = $(LBl + LSI) / 2$

Adverse Clinical Outcomes definition

Ascites

- new onset ascites and controlled with treatment
- refractory or difficult – requires repeat paracentesis for control (last paracentesis within 2 months of scan) or TIPPS

liver related death or transplant for liver failure

Other: hepatic encephalopathy (reversible confusion), variceal bleeding, HCC

Groups (196 with clinical information)

- never had a clinical outcome in past or present (# 159) including 9 normals
- adverse clinical outcomes (# 25)
- clinical abdominal fluid (scan only and untreated were excluded) – new onset ascites or controlled on treatment
- prior ACO – history of ACO > 2 yr prior to scan, but not requiring on-going treatment (# 7)
- liver transplant prior to recent QLSS (# 5)

STATISTICS

- Mean +/- standard deviation
- Students t-test of the means
- Linear regression analysis of the relationship between 2 variables

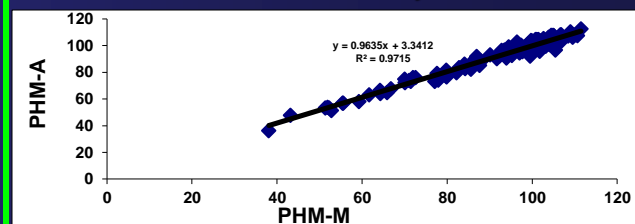
RESULTS:

	#	PHM	Ct/b IBW	Gm/cc	Platelet	INR	Albumin	Bilirubin	creatinine
Normal	9	104(3)	1.0(18)	14(1)	258(67)	1(0)	4.5(1)	.6(2)	.8(2)
No ACO	150	102(4)	1.5(1)	14(1.4)	212(77)	1(1)	4.4(4)	.7(7)	.9(2)
Prior ACO	7	95(3)	2.9(1.5)	13.3(1.9)	123(47)	1(1.0)	4.3(3)	.5(4)	1.8(2)*
LT	5	99(6)	2.2(1.4)	12.8(2.2)	154(70)	1(1)	4.0(3)	.5(2)	1.2(1)
Act ACO	25	74(14)							
Rx Asc	15	79(8)	4.7(1.1)	11.6(1.1)	89(63)	1.2(2)	3.5(5)	1.8(1.7)	.8(3)
Refr Asc	8	66(14)	8.1(5.2)	10.4(1.8)	109(57)	1.3(2)	3.4(5)	1.8(5)	2.4(1.9)*
Death	2	50(19)	5.3(5)	12.3(3)	102(61)	1.7(7)	2.7(0)	19(22)	2.9(1.4)

* DIALYSIS

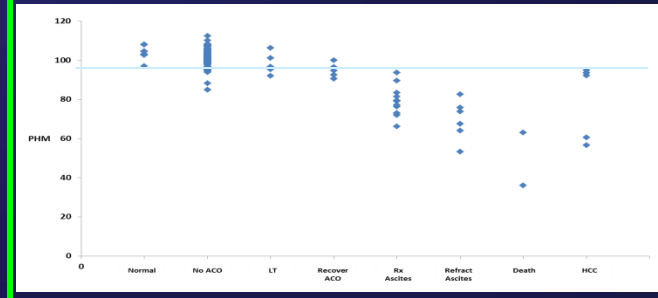
RESULTS:

The PHM-A correlates closely with PHM-M.



RESULTS:

PHM-A in Normals and CLD with/without ACO



CONCLUSIONS

- The HEPATIQ automated QLSS PHM-A measure of hepatic function Closely correlates with the older manual PHM method
- Adverse clinical outcomes (ACO) are closely related to hepatic function as measured by PHM
- All patients with ACO had a PHM < 95
- The threshold for clinical events is PHM < 95, for ascites PHM < 90, for refractory ascites PHM < 80, and death PHM < 65