Stratifying Disease Severity and Predicting Risk for Clinical Decompensation in Primary Sclerosing Cholangitis: Results with Next Generation HepQuant Tests

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Background

- We quantified liver function and portal-systemic shunting in primary sclerosing cholangitis (PSC) using:
  - The HepQuant SHUNT test (V1.1) [1] and
  - Next Generation tests (DuO and SHUNT V2.0) based on a compartmental model [2].
- We compared test results to standard laboratory tests and clinical models in the prediction of clinical outcome.

Aims

- To determine whether Next Generation could predict clinical outcome in PSC
- To measure reproducibility of Next Generation tests

Methods

Subjects

- 47 patients spanning the clinical spectrum of PSC
- 46 patients retested at baseline for reproducibility
- 40 patients followed prospectively for clinical outcomes were retested after 1 year

SHUNT Test Administration

- 13C-cholate injected by IV, d4-cholate administered orally
- Blood sampled at 0, 5, 20, 45, 60, 90 min. for serum cholate

HepQuant Test Versions

- SHUNT V1.1: 13C- and d4-CA concentrations at 20, 45, 60, and 90 min.
- SHUNT V2.0: 13C- and d4-CA concentrations at 20 and 60 min.
- DuO: only d4-CA concentrations at 20 and 60 min.

Test Parameters

- Disease severity index (DSI), portal-systemic shunt (SHUNT%)

Statistical Analysis

- Three risk subgroups were characterized from age-related degree of hepatic impairment: low (n=28), moderate (n=16), and high (n=3)
- Reproducibility by intraclass correlation coefficient (ICC), minimum detectable difference (MDD), coefficient of variation (%CV); ICC >0.7 considered acceptable
- AUROCs compared across test versions for prediction of clinical outcome (new clinical decompensation, liver-related death, liver transplantation), DeLong method
- Logistic regression of baseline SHUNT% for portal hypertension and varices

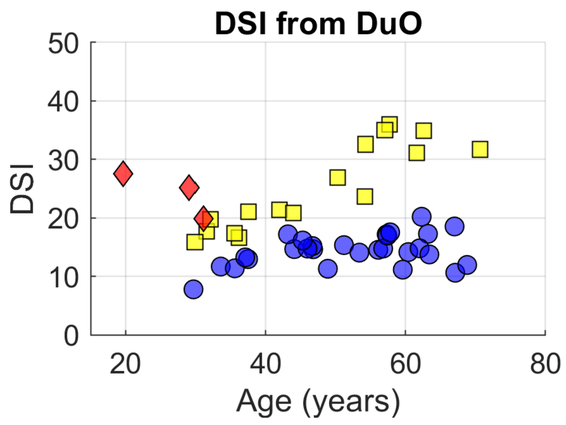
Results

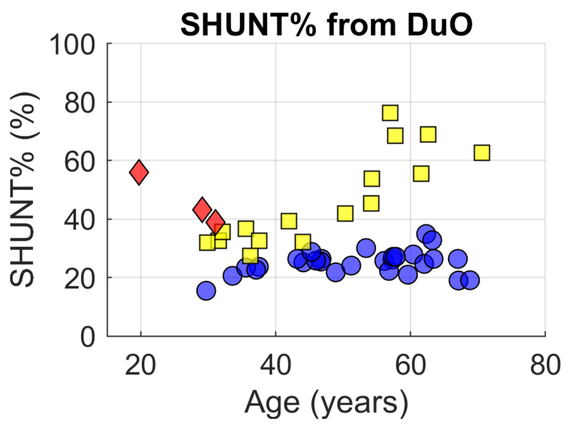
High risk patients were characterized by high SHUNT% at relatively young age. Moderate/high risk had worse HepQuant DuO parameters, worse laboratory tests, and were more likely to experience clinical outcome compared to low-risk patients.

	Low Risk (N=28)	Mod./High Risk (N=19)	Group t-test (p value)
HepQuant DuO			
SHUNT% (%)	25.0 ± 4.1	46.3 ± 14.7	**<0.001**
DSI	14.4 ± 2.7	25.0 ± 6.8	**<0.001**
Labs and Clinical Scores			
Alk. Phos. (IU/L)	128 ± 83	387 ± 353	**0.0006**
GGT (IU/L)	153 ± 141	341 ± 343	**0.0152**
AST (IU/L)	40 ± 15	88 ± 51	**0.0000**
ALT (IU/L)	46 ± 25	80 ± 59	**0.0086**
Bilirubin (mg/dL)	1.16 ± 0.46	2.99 ± 2.91	**0.0023**
INR	1.05 ± 0.28	1.29 ± 0.80	0.1500
Albumin (g/dL)	3.87 ± 0.31	3.31 ± 0.42	**<0.0001**
Platelets (nL^{-1})	201 ± 78	160 ± 103	0.1300
APRI	0.58 ± 0.31	1.92 ± 1.52	**0.0001**
FIB4	1.91 ± 1.16	4.05 ± 3.17	**0.0029**
MELD score	8.11 ± 2.23	11.58 ± 5.44	**0.0039**
Child-Pugh Score	5.25 ± 0.59	7.1 ± 1.8	**<0.0001**
CP A	26 (93%)	9 (47%)	-
CP B	2 (7%)	8 (42%)	-
CP C	0	2 (11%)	-
Mayo PSC Risk Score	0.31 ± 0.52	1.31 ± 0.94	**<0.0001**
Splenomegaly	4 (14%)	13 (68%)	**0.0002**
Varices	3 (11%)	12 (63%)	**0.0002**
Decompensation	1 (3.5%)	7 (37%)	**0.0030**

Risk Groups:

Low Risk
Moderate Risk
High Risk

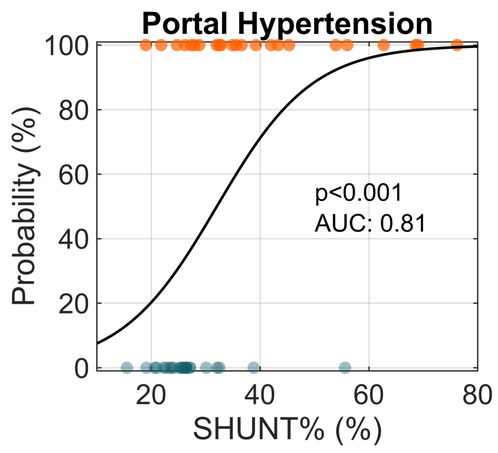


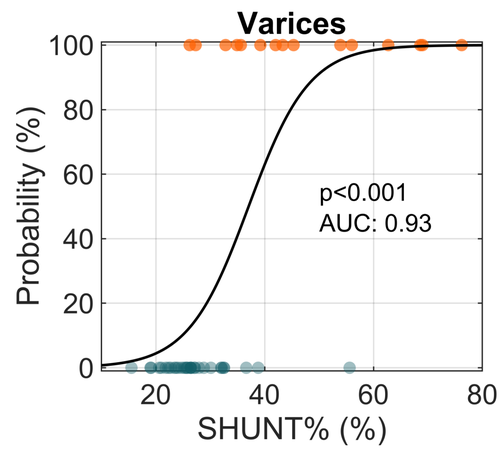


DSI and SHUNT% had excellent within-individual reproducibility and were the strongest predictors of new clinical decompensation, liver-related death, or liver transplantation (n=13) with no significant differences between Test versions.

Parameter	Version	Prediction of clinical outcome AUROC (95% CI)	Reproducibility %CV	MDD	ICC (95% CI)	p-value
DSI	SHUNT V1.1	0.81 (0.55-0.92)	9.21%	2.68	0.91 (0.84-0.95)	**<0.001**
	SHUNT V2.0	0.80 (0.59-0.93)	10.77%	3.19	0.89 (0.81-0.94)	**<0.001**
	DuO	0.81 (0.62-0.92)	10.33%	3.02	0.89 (0.82-0.94)	**<0.001**
SHUNT%	SHUNT V1.1	0.89 (0.73-0.96)	10.51%	5.88%	0.91 (0.85-0.95)	**<0.001**
	SHUNT V2.0	0.85 (0.71-0.94)	11.41%	6.86%	0.90 (0.82-0.94)	**<0.001**
	DuO	0.83 (0.62-0.94)	9.79%	5.57%	0.91 (0.84-0.95)	**<0.001**

SHUNT% is linked to baseline features of portal hypertension (varices, splenomegaly, platelets <140,000) and varices.





Conclusions

- **HepQuant's Test parameters of liver function and physiology correlate with laboratory and clinical evidence of PSC disease severity, identify risk subgroups, and predict risk for clinical outcome.**
- **There were no significant differences between test versions in terms of predicting clinical outcome and reproducibility.**
- **DuO and SHUNT V2.0 are easier to administer and less invasive, thus, having the potential to be more widely accepted by care providers administering the test and by patients receiving the test.**

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References

[1] Everson GT et al. Aliment. Pharmacol. Ther. 2007; 26:401-410.
[2] McRae MP et al. Transl. Res. 2023; 252:53-63.

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Disclosures

MPM is a paid consultant for HepQuant LLC. SMH and GTE are employees and equity members of HepQuant LLC. All authors have provisional patents pending. HepQuant tests are not FDA approved and are for investigational use only under FDA guidelines for investigational device exemption (IDE).