THE HEPQUANT SHUNT DISEASE SEVERITY INDEX (HEPQUANT DSI™) CAN AID THE DECISION TO AVOID ENDOSCOPIC SCREENING OR SURVEILLANCE FOR VARICES NEEDING TREATMENT

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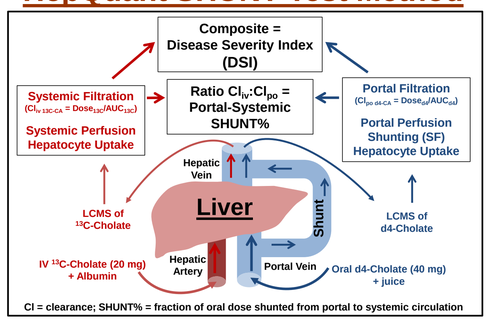
Background

Varices needing treatment encompasses large esophageal varices (LEVs) and varices with high-risk features, such as red wale signs. LEVs have a variceal diameter of >5 mm. Endoscopists treat varices based on subjective assessment of variceal appearance including size and red wale signs. Portal hypertension is a prerequisite for varices and is predicted by the HepQuant SHUNT test (Clin Gastroenterol Hepatol 2021). In the US multicenter HALT-C study, HepQuant DSI™ 18.3 was a cutoff for large varices. The purpose of the pivotal US multicenter SHUNT-V study was validation of DSI 18.3 for ruling out large esophageal varices.

Methods

Subjects, encompassing advanced liver fibrosis (both studies), compensated cirrhosis (both studies), and clinically stable Child-Pugh B cirrhosis (SHUNT-V only), were recruited from 3 clinical sites in HALT-C (N=217), and from 27 centers in SHUNT-V (N=270). Variceal hemorrhage, or prior variceal treatment were exclusions in both studies. Prior diagnosis of large varices was an exclusion in SHUNT-V. The HepQuant SHUNT test involved administration of 13C-Cholate (13C-CA) IV, and d4-Cholate (d4-CA) PO, and blood sampling at time 0, 5, 20, 45, 60, and 90 minutes. 13C-CA and d4-CA were quantified by LC-MS and clearances, portal-systemic shunting (SHUNT%), and a disease severity index (DSI) was calculated.

HepQuant SHUNT Test Method



Results

Subject Characteristics in SHUNT-V compared to HALT-C:

SHUNT-V subjects had a mean age 61.5 and BMI 33.4 kg/m2; 93% were white, 50% male, and 64% obese and 50% had NASH. In SHUNT-V, 127 subjects had varices (46.2%); 36 were large (13.1%). In HALT-C, 74 had varices (34.1%); 22 were large (10.1%). SHUNT-V subjects had significantly higher DSI (24.4 ± 8.1 vs 19.5 ± 5.7, $p < 0.0001$) and SHUNT% (42 ± 19% vs 38 ± 15%, $p = 0.02$) compared to HALT-C.

Diagnostic Performance of DSI compared to Elastography:

he diagnostic performance of DSI 18.3 as a cutoff to "RULE OUT" large esophageal varices and esophageal varices needing treatment in the SHUNT-V cohort is shown in the table below. The diagnostic performance of LSM 20 kPa is shown for the subset of SHUNT-V subjects that had elastography. Bayesian statistics confirmed an improvement in "RULE OUT" large esophageal varices with DSI cutoff 18.3. Two of the 3 false negative (FNR) cases with LEVs were not treated. The third FNR was the only subject in the entire SHUNT-V cohort taking wheat dextrin, an oral fiber supplement known to bind bile acids and, therefore, a potential cause for falsely low DSI and SHUNT% in this case with treated LEVs. 10 subjects had red wale signs, all in setting of LEVs, and the DSI ranged from 21.9 to 39.3 in this subset.

Diagnostic Performance of DSI and LSM Cutoffs

DSI cutoff 18.3 (N=270)	N	Se	FNR	NPV
LEVs	36	92%	8%	96%
Treated LEVs	29	97%	3%	99%
Treated Any EVs	34	97%	3%	99%
LSM cutoff 20 kPa (N=84)	**N**	**Se**	**FNR**	**NPV**
LEVs	7	71%	29%	95%
Treated LEVs	6	83%	17%	98%
Treated Any Evs	8	88%	13%	98%

DSI: disease severity index from HepQuant SHUNT test; LEVs: large esophageal varices; Treated LEVs: banded at EGD or varices medication prescribed post-EGD; Treated Any EVs included 5 small varices that were treated; LSM: liver stiffness measurement by elastography; Se: sensitivity; FNR: false negative (miss) rate; NPV: negative predictive value.

Conclusions and Key Takeaways

- HepQuant DSI 18.3 is a valid cutoff for "RULE OUT" of large esophageal varices that need treatment and can aid in the decision to avoid or proceed with endoscopic screening or surveillance.
- Fiber supplements and other compounds that intra-luminally bind bile acids should be avoided prior to the HepQuant SHUNT test.

References

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Disclosures

Mitchell L Shiffman, MD, member of HepQuant SAB; Steve M. Helmke, PhD, HepQuant employee (CSO) and equity member; Gregory T. Everson, MD, HepQuant employee (CEO) and equity member,