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PREDICTING DECOMPENSATION, DEATH, OR LIVER TRANSPLANTATION IN CIRRHOSIS BY USING A NON-INVASIVE LIVER FUNCTION TEST (HEPQUANT SHUNT®)

Biliary Tract Diseases
Non-Invasive Assessment of Liver Disease
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Background: Predicting decompensation in patients with cirrhosis is difficult given the lack of a test that captures functional decline. The dual cholate test is a novel noninvasive test that examines hepatic clearance of oral and IV cholate to assess hepatocyte function, hepatic blood flow, portal blood flow, and portal-systemic shunting. Cirrhotic patients are given a fixed dose of cholate substrate, and blood levels are measured regularly to document hepatic clearance. We hypothesized that the dual cholate test and its output, disease severity index (DSI), capture functional decline and predict decompensation.
Methods: In a prospective study, we examined cirrhotics that underwent dual cholate study from 2011 to 2018. The primary composite outcome was decompensation, death or liver transplantation. The primary variable of interest was DSI (a measure of global hepatic function and physiology calculated through a model including portal hepatic flitration rate (HFR), systemic HFR and Portal-systemic shunt). We examined the independent association of increased DSI with decompensation after adjustment for age, sex and Model for End-Stage Liver Disease (MELD) score using Cox proportional hazards analysis. The Kaplan-Meier method and log-rank test were used to compare the cumulative incidence of composite outcome in cirrhotics with low and high DSI. We further stratified by categories of MELD and DSI as MELD-DSI: High-risk (High DSI/High MELD), intermediate-risk (High DSI/Low MELD or Low DSI/High MELD) and low-risk (Low DSI/Low MELD).
Results: Overall, 85 patients (age 57.0 years (10.5), 73% male, 32% HCV) underwent testing. The median MELD score was 8.1 (6.2) and DSI 26.0 (15.5). The median follow-up was 3.9 years and 27.1% had the composite outcome. At baseline, DSI was significantly lower in patients with compensated cirrhosis as compared to decompensated cirrhosis (22.4 vs. 31.1, $P<0.001$). The cumulative incidence of composite outcome was significantly higher in patients with DSI>26 compared with the patients with DSI≤26 ($P=0.002$) (Figure 1a). Stratified by MELD-DSI categories, the cumulative incidence of composite outcome was significantly higher in high-risk group compared with intermediate- and low-risk ones ($P<0.001$) (Figure 1b). On adjusted analyses, DSI>26 was independently associated with increased risk of composite outcome (HR: 3.48, 95% CI: 1.42-8.53 (Table 1).
Conclusion: DSI is independently associated with increased risk of decompensation, death or liver transplantation in patients with cirrhosis. The dual cholate test may serve as a novel marker of functional decline and identify cirrhotics at highest risk of decompensation and need for liver transplantation, especially among patients with low MELD score.

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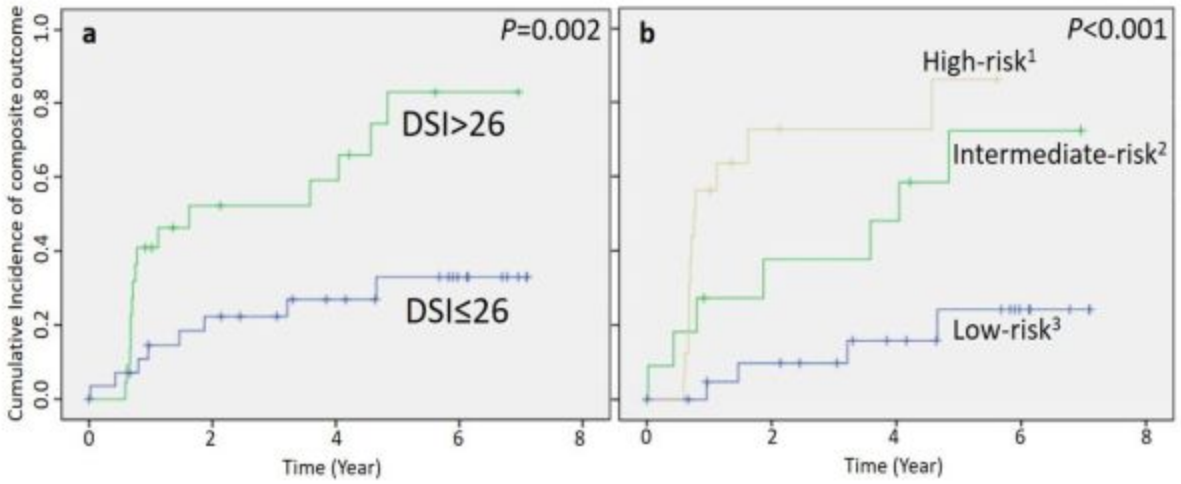
Figure 1. Cumulative incidence of composite outcome of decompensation, death or liver transplantation in DSI (a) and MELD-DSI (b) categories.



[1]High-risk group: DSI>26 and MELD score>8.
[2]Intermediate-risk group: DSI>26 and MELD score≤8 or DSI≤26 and MELD score>8.
[3]Low-risk group: DSI≤26 and MELD score≤8.

Abbreviations: DSI, disease severity index; MELD, Model for End-Stage Liver Disease

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Table 1. Multivariate analyses for composite outcome of decompensation, death or liver transplantation

	Composite outcome
	HR (95% CI)
Age	1.00 (0.96-1.05)
Sex (Male/Female)	1.17 (0.37-3.75)
MELD score	1.11 (1.03-1.19)
DSI (>26/≤26)	3.48 (1.42-8.53)

Abbreviations: CI, confidence interval; DSI, disease severity index; MELD, Model for End-Stage Liver Disease; HR, hazard ratio

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