

High duodenal permeability (“leaky gut”) predicts hospitalization in cirrhosis, but only in sicker patients

INTRODUCTION: Several complications of cirrhosis result from the translocation of bacteria or their products across the intestinal epithelium. We aimed to assess if duodenal permeability and mucosal bacteria associate with hospitalization in patients with cirrhosis.

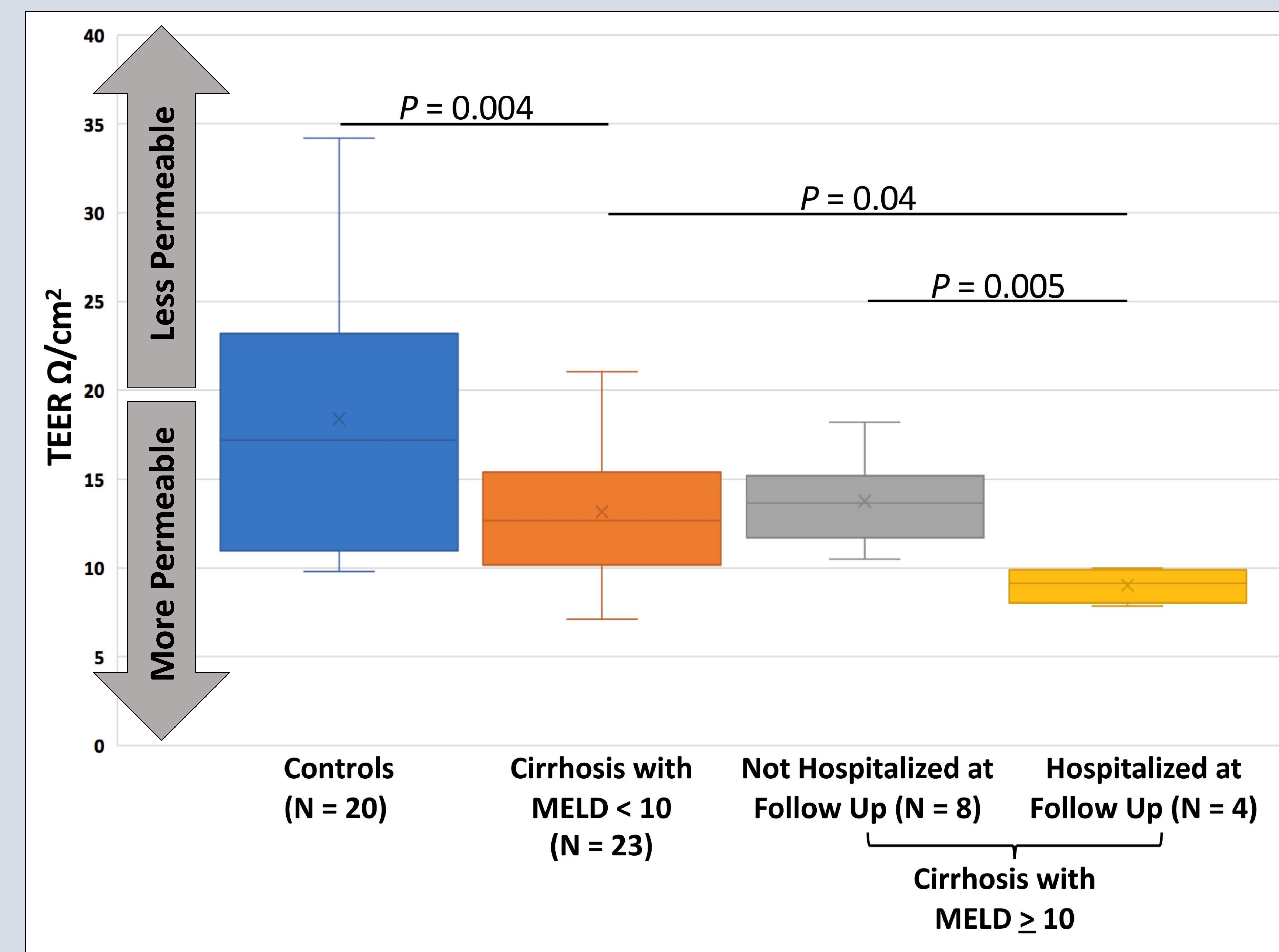
METHODS: We obtained duodenum, ileum, and colon tissue biopsies from patients with cirrhosis and controls without liver disease during routine outpatient screening endoscopy.

Composition of the mucosal microbiota was determined via 16S rRNA gene sequencing and epithelial permeability assessed by measuring transepithelial electrical resistance (TEER; test of intestinal permeability).¹

Outcomes of patients with cirrhosis at 6 months were assessed, with and without stratification by MELD.

RESULTS: We studied 46 patients with cirrhosis (10 alcohol-related) and 33 controls and obtained 62 duodenum, 31 ileum, and 34 colon biopsies. Patients with cirrhosis were similarly aged to controls (60 vs. 58 years) and had a similar number of extra-hepatic comorbidities (2 vs. 2). Patients with cirrhosis had median MELD 8 (IQR 7, 10); 66% were male. Compared to controls, patients with cirrhosis had lower TEER (i.e., increased epithelial permeability) in the duodenum ($12.9 \pm 3.4 \Omega/\text{cm}^2$ vs. $18.5 \pm 7.1 \Omega/\text{cm}^2$; $P = 0.002$) but not in the ileum or colon.

Duodenal Permeability by Patient Type



RESULTS: Among the 45 patients with cirrhosis followed for 6 months post-endoscopy, 13 patients were hospitalized, 4 for liver-related diagnoses, and none died.

Duodenal alpha diversity was lower in all patients with cirrhosis who were hospitalized compared to those not hospitalized (inverse Simpson: 5.8 vs. 9.8, $P < 0.05$).

TEER in each gut segment did not predict future hospitalization in the overall cohort of patients with cirrhosis. However, among patients with the highest quartile of MELD (≥ 10 ; $n = 12$), duodenal TEER was lower in those who were hospitalized than those not hospitalized ($9.0 \pm 1.0 \Omega/\text{cm}^2$ vs. $13.8 \pm 2.5 \Omega/\text{cm}^2$, $P = 0.005$; Figure) and lower in those hospitalized for a liver-related diagnosis than those not hospitalized for a liver-related diagnosis ($9.8 \pm 0.3 \Omega/\text{cm}^2$ vs. $12.7 \pm 3.2 \Omega/\text{cm}^2$, $P = 0.03$).

Compared to other etiologies, patients with alcohol-related cirrhosis trended towards lower duodenal TEER ($11.3 \Omega/\text{cm}^2$ vs. $13.4 \Omega/\text{cm}^2$, $P = 0.08$), even after controlling for MELD.

CONCLUSION: High duodenal epithelial permeability and low mucosa alpha diversity was associated with hospitalization and liver-related hospitalization in patients with moderately severe cirrhosis. Reversal of duodenal permeability may prevent hospitalizations among patients with cirrhosis.