Evaluation of Secondary Bile Acids in Stool as Predictors of Chronic Bile Acid (BA) Diarrhea

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INTRODUCTION

Bile acid diarrhea (BAD) accounts for ~25% of chronic "functional diarrhea" (FD) and causes increased colonic motility, secretion, and permeability, and worse quality of life.[1-5] Diagnosis of BAD is currently based on serum 7αC4, total fecal BA (TBA), or fecal primary BAs [cholic acid (CA) and chenodeoxycholic acid (CDCA)]. Secondary BAs [deoxycholic acid (DCA) and lithocholic acid (LCA)] are produced by 7α-dehydroxylation of CA and CDCA, respectively. Prior studies have shown that DCA promotes colonic secretion, serotonin release, and peristalsis. LCA is stimulates the Takeda G-protein coupled BA receptor (TGR5, or GPBAR1) which accelerates colonic transit.[6] However, the utility of fecal secondary BAs as markers of diarrhea [increased fecal weight (FW)] and BAD is unclear.

AIM

Characterize fecal 48-hour secondary BA composition among patients presenting with FD to assess for potential contributors to diarrhea.

METHODS

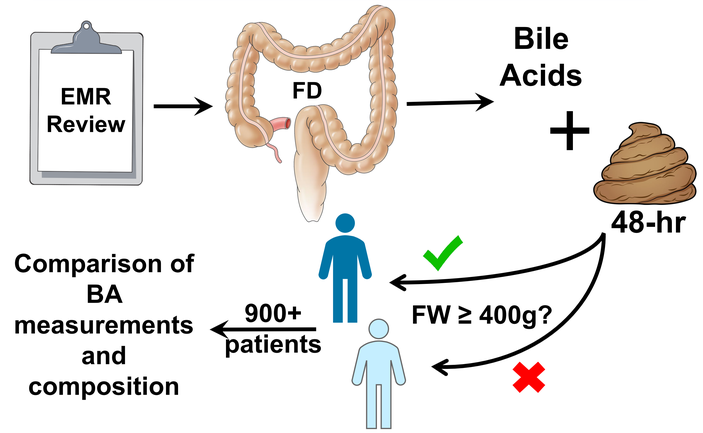
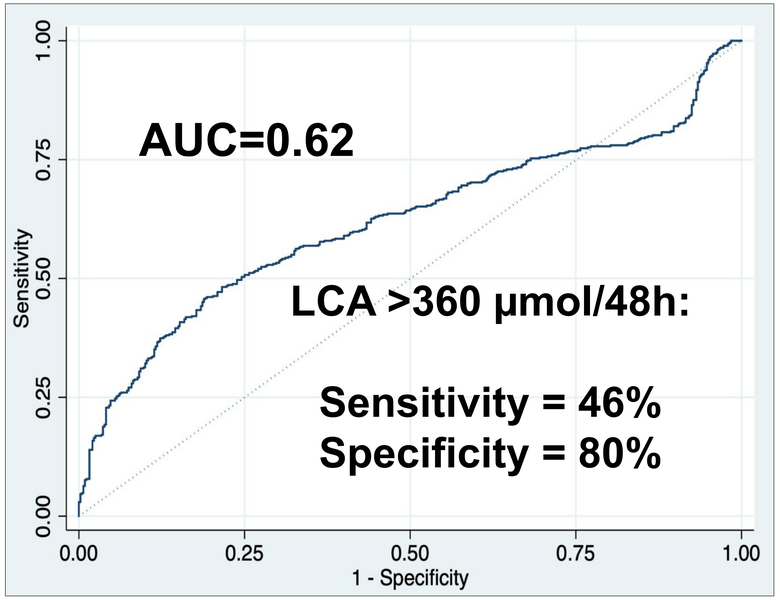


TABLE. ODDS RATIO OF FW ≥ 400G/48H.

Bile Acid	All patients (N=913)	TBA <2,337µmol/48h (N=676)	TBA >2,337µmol/48h (N=237)
CA	1.34 (1.16-1.55)***	1.22 (1.03-1.46)*	1.66 (1.11-2.49)*
CDCA^	0.98 (0.84-1.14)	0.95 (0.79-1.15)	0.73 (0.49-1.10)
DCA^	0.80 (0.67-0.95)*	0.82 (0.67-1.01)	0.51 (0.34-0.76)**
LCA	1.47 (1.20-1.80)***	1.34 (1.06-1.69)*	2.12 (1.41-3.19)***
UDCA	1.07 (0.99-1.15)	1.11 (1.02-1.22)*	0.91 (0.75-1.11)

Table (above). Data presents the estimated risk of diarrhea (defined as fecal weight [FW] ≥ 400 g/48 hours) for a 2-fold increase for each BA component after adjustment for age, sex, and the other BAs. This demonstrates that in all patients, a 2-fold increase in total CA and LCA result in a 34% (95% CI: 16-55%) and 47% (95% CI: 20-80%) increased odds of diarrhea. BAD, bile acid diarrhea; CA, cholic acid; CCY, cholecystectomy; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; FW, fecal weight; LCA, lithocholic acid; UDCA, ursodeoxycholic acid. ^secretory bile acid; *p<0.05; **p<0.01; ***p<0.0005

FIGURE. ROC OF LCA FOR FW ≥ 400G/48H.



DISCUSSION

Among patients presenting with FD, the mean age was 51.5y (range: 11-90y), and 67.6% were female. Mean 48h FW was 546.1g (10-90%ile: 158-1056g). Mean TBA was 1921 µmol/48h (10-90%ile: 256-4328 µmol/48h). 48h fecal total LCA was associated with stool weight. This association was comparable to that of CA. This is consistent with prior literature demonstrating that LCA promoted colonic motility via stimulation of TGR5. This suggests that LCA could provide some utility in the diagnosis of BAD. In all patients, the optimal cutoff for total fecal LCA had 46% sensitivity and 80% specificity for FW ≥400g/48h (AUC = 0.62). Furthermore, adding total fecal LCA to the total primary BA increased the AUC for FW ≥400g/48h from 0.75 to 0.78.

CONCLUSION

Among those with FD, 48h fecal total LCA is associated with FW ≥400g with comparable risk estimates to total primary BAs and with CA alone. Fecal LCA also has potential utility in the diagnosis of BAD.

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