Cirrhotic Patients Have Worse Bowel Preparation at Screening Colonoscopy than Chronic Liver Disease Patients without Cirrhosis

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Background: Cirrhosis has been shown in small studies to be a predictor of suboptimal bowel preparation at screening colonoscopy. It has yet to be established whether patients with chronic liver disease in the absence of cirrhosis experience equally poor colon cleansing. Intestinal dysmotility related to cirrhosis might impair bowel preparation in this population more than those with chronic liver disease without cirrhosis. **Objective:** This study compared the quality of bowel preparation in cirrhotic and non-cirrhotic patients with chronic liver disease and determined whether this influenced polyp detection rate. **Methods:** A retrospective study of patients with chronic liver disease, both cirrhotic and non-cirrhotic, who underwent screening colonoscopy was performed. Patient characteristics, concomitant medication use, adequacy of bowel preparation, and the total number and types of polyps found were compared between cirrhotic and non-cirrhotic groups. **Results:** 330 patients fulfilled inclusion criteria; 36% ($n = 120$) were cirrhotic. Cirrhotic patients had significantly worse bowel preparation scores compared with non-cirrhotics (mean 3.4 ± 1.1 vs. 3.7 ± 0.9 , $P = 0.003$). Worse bowel preparation scores in cirrhotics vs. non-cirrhotics persisted despite controlling for age, sex, and concomitant diabetes mellitus (DM) ($P = 0.0027$). Among the cirrhotics, 48% had the lowest preparation scores compared with 30% of non-cirrhotics. No difference in polyp detection rate was found between cirrhotics and non-cirrhotics. Severity of cirrhosis as assessed by the MELD score did not predict worse bowel preparation. **Conclusions:** Cirrhotics have significantly worse bowel preparation scores compared to non-cirrhotics with chronic liver disease. No correlation between MELD score and bowel preparation score was observed in the cirrhotic cohort. (J CLIN EXP HEPATOL 2016;6:297–302)

Colorectal cancer (CRC) is the fifth leading cause of cancer deaths in the world and the third leading cause in the United States.^{1–3} Colonoscopy is the preferred screening method for CRC given its ability to detect and remove precancerous adenomatous polyps.⁴ Adequacy of bowel preparation at the time of colonoscopy has emerged as an important quality indicator, as several studies have shown that adenoma detection rate (ADR) is reduced when preparation is suboptimal.^{5–7}

Established risk factors for inadequate bowel preparation include older age, male sex, higher body mass index (BMI), narcotic use, and diabetes mellitus (DM). In addition, small studies have identified liver cirrhosis as an

independent predictor of ineffective bowel cleansing.^{8–10} This finding is suspected to result from impaired intestinal motility in cirrhotic patients, related to autonomic dysfunction, metabolic derangements, and/or small intestinal bacterial overgrowth.^{11–13} It remains uncertain whether the extent of suboptimal bowel preparation at colonoscopy in cirrhotics is also present in patients with chronic liver disease without cirrhosis.

The aims of this study were to compare the quality of bowel preparation in cirrhotic and non-cirrhotic patients with chronic liver disease and also to determine whether this influenced polyp detection rate.

METHODS

Study Design/Setting/Participants

This is a retrospective cohort study of patients at NewYork-Presbyterian Hospital—Weill Cornell Medical College referred for screening colonoscopy between December 2004 and September 2011. The study was approved by the Institutional Review Board. Electronic charts were reviewed to identify all patients with chronic liver disease of any etiology, including those with and without cirrhosis, who underwent a screening colonoscopy during the study time period. Presence of cirrhosis was determined by

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Abbreviations: ADR: adenoma detection rate; BMI: body mass index; CRC: colorectal cancer; DM: diabetes mellitus; HE: hepatic encephalopathy; MELD: Model for End-Stage Liver Disease; SBP: spontaneous bacterial peritonitis; SIBO: small intestinal bacterial overgrowth
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corresponding pathology, radiographic and/or laboratory results, or complications of cirrhosis documented in the medical record. We excluded those patients who underwent colonoscopy for any indication other than CRC screening, those where quality of bowel preparation was not documented in the colonoscopy report, and those with a history of prior intestinal surgery, intestinal obstruction, or a known motility disorder including chronic constipation.

All pathological specimens from tissue removed during colonoscopy were reviewed by a group of dedicated gastrointestinal pathologists at our institution.

Study Procedures

Patient characteristics including age at the time of colonoscopy, gender, presence of DM, etiology of liver disease, type of bowel preparation, and concomitant use of lactulose, rifaximin, polyethylene glycol, narcotics, or beta-adrenergic blockers were recorded. The types of bowel preparation used included GoLYTELY[®], GoLYTELY[®] split, HalfLyte[®], Magnesium citrate, MiraLAX[®], MiraLAX[®] split, and Movi-Prep[®]. Data regarding whether patients experienced vomiting or other issues with tolerance of the bowel preparation were not available given the retrospective nature of the study. Adequacy of bowel preparation was determined by the performing endoscopist and documented at the time of the colonoscopy. All colonoscopy reports were reviewed to determine the quality of bowel preparation documented, and none of these reports indicated premature termination of the procedure. All pathology reports were reviewed to determine the total number and types of polyps removed and the incidence of invasive cancer.

Polyps were categorized as tubular adenomas (including sessile serrated polyps), advanced adenomas (including tubulovillous adenomas), adenocarcinoma, or non-adenomatous (hyperplastic, mucosal prolapse, inflammatory polyps). Quality of bowel preparation was rated as unsatisfactory (1), poor (2), fair (3), good (4), and excellent (5), as described by the endoscopist.

Data Analysis

In our cohort of patients identified as having chronic liver disease, we compared patients with cirrhosis to those without cirrhosis based on demographics (age, sex), etiology of chronic liver disease, presence of DM, bowel preparation score, and the number and pathology of polyps removed at colonoscopy. We also examined the concomitant use of lactulose, rifaximin, polyethylene glycol, narcotics, or beta-adrenergic blockers, which may affect intestinal motility. The comparisons between cirrhotic and non-cirrhotic patients were conducted using chi-square and *t*-test analysis. Chi-square tests were implemented in comparing cirrhotics and non-cirrhotics and the quality of bowel preparation, polyp detection rate, DM, and the use of lactulose, polyethylene glycol, rifaximin,

narcotics, and beta-adrenergic blockers. For the cirrhotic and non-cirrhotic groups, *t*-test was employed to examine the relationship between age and the presence of polyps, as well as bowel preparation score and presence of polyps. For cirrhotic patients only, the Model for End-Stage Liver Disease (MELD) score was correlated with bowel preparation score and polyp detection rate using linear correlation and *t*-test, respectively.

Multivariate analysis was conducted using ordered logistic regression analysis. Age, male sex, concomitant DM, and the presence of cirrhosis were included in the model given reported associations with inadequate bowel preparation.^{13,14} Chronic constipation was not included in the multivariate analysis because patients with a known history of any motility disorder were excluded from the study. We did not have reliable information from the medical record regarding smoking status, so it was not included. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

Patient Characteristics

A total of 330 patients with chronic liver disease (mean age 59 ± 10.1 years), of which 36% ($n = 120$) were cirrhotic, were included in the study. Demographic and clinical characteristics of the control (non-cirrhotic) and study (cirrhotic) groups are shown in Table 1. There were no significant differences regarding gender (48% vs. 45%, $P = 0.5875$) or concomitant DM (24% vs. 22%, $P = 0.6373$) between patients with cirrhosis and the control group. Cirrhotic patients were significantly more likely to be taking lactulose (30% vs. 0.5%, $P < .0001$), rifaximin (11% vs. 0.5%, $P < .0001$), and beta-adrenergic blockers (41% vs. 18%, $P < .0001$). The types of bowel preparation administered to cirrhotic and non-cirrhotic groups are shown in Table 2.

Bowel Preparation

Overall, 37% of all patients in both groups were categorized as having unsatisfactory, poor, or fair preparations (Figure 1). Cirrhotic patients were found to have significantly worse bowel preparation scores compared with non-cirrhotics (mean 3.4 ± 1.1 vs. 3.7 ± 0.9 , respectively, $P = 0.003$), as shown in Figure 2. Within the cirrhotic group, 48% had the lowest preparation scores of 1, 2, and 3 (unsatisfactory, poor, and fair, respectively) compared with 30% of non-cirrhotic patients. The presence of cirrhosis ($P = 0.003$) and DM ($P = 0.003$) independently predicted a lower bowel preparation score. After controlling for age, sex, and presence of DM, patients with cirrhosis were still found to have significantly worse bowel preparation scores compared with non-cirrhotics (OR = 0.520, 95% CI 0.339–0.797, $P = 0.0027$) in multi-variate analysis, as shown in Table 3.

Table 1 Baseline Characteristics and Demographics.

	Cirrhotics (n = 120)	Non-cirrhotics (n = 210)	P-value
Age (mean)	61	57	0.0003
Sex			
Male % (n)	48 (58)	45 (95)	0.5875
Female % (n)	52 (62)	55 (115)	
Etiology of liver disease (n)			
Hepatitis B	2	34	
Hepatitis C	71	149	
Alcohol	17	1	
NAFLD	5	17	
PBC and PSC	10	1	
Autoimmune hepatitis	3	3	
Cryptogenic cirrhosis	9	0	
Other	3	5	
Diabetes % (n)	24 (29)	22 (46)	0.6373
Lactulose % (n)	30 (36)	0.5 (1)	<.0001
PEG 3350% (n)	5 (6)	3 (6)	0.3171
Rifaximin % (n)	11 (13)	0.5 (1)	<.0001
Opiates % (n)	6 (7)	10 (21)	0.1913
Beta-blocker % (n)	41 (49)	18 (38)	<.0001

NAFLD: non-alcoholic fatty liver disease, PBC: primary biliary cirrhosis, PSC: primary sclerosing cholangitis, PEG 3350: polyethylene glycol 3350.

Polyp Detection Rates

No difference was found in polyp detection rate between non-cirrhotic (35%, $N = 74$) and cirrhotic (33%, $N = 40$) patients ($P = 0.7263$). Within the group of non-cirrhotics

with polyps detected ($N = 74$), 91% ($N = 67$) had 1–3 polyps and 64% were found to have 1 polyp. Of the 40 cirrhotics who were found to have polyps, 37 patients had 1–3 polyps and 45% of this group ($N = 18$) had 1 polyp reported. Overall, 2 colorectal adenocarcinomas were identified, both in the non-cirrhotic group. Of the cirrhotics found to have polyps ($N = 40$), the mean preparation score was 3.6 ± 0.9 and in the non-cirrhotics with polyps ($N = 74$), the mean preparation score was 3.6 ± 0.8 ($P = 0.945$).

Table 2 Types of Bowel Preparation Administered Prior to Initial Screening Colonoscopy.

Type of bowel preparation	Cirrhotics (n = 120)	Non-cirrhotics (n = 210)
Unknown % (n)	65.8 (79)	79 (166)
GoLYTELY® ^a % (n)	22.5 (27)	12.9 (27)
GoLYTELY® ^a split % (n)	0 (0)	0.5 (1)
HalfLyte® ^b % (n)	1.7 (2)	0.95 (2)
Magnesium citrate® ^c % (n)	0.8 (1)	0 (0)
MiraLAX® ^d % (n)	6.7 (8)	3.3 (7)
MiraLAX® ^d split % (n)	0 (0)	1.4 (3)
MoviPrep® ^e % (n)	2.5 (3)	1.9 (4)

^aGoLYTELY®: Polyethylene glycol (PEG) 3350 236 g, sodium sulfate 22.74 g, sodium bicarbonate 6.74 g, sodium chloride 5.86 g, and potassium chloride 2.97 g (4000 mL).

^bHalfLyte®: PEG 3350 210 g, sodium chloride 5.6 g, sodium bicarbonate 2.86 g, and potassium chloride 0.74 g (2000 mL).

^cMagnesium citrate®: magnesium citrate 1.745 g/30 mL (296 mL).

^dMiraLAX®: PEG 3350, 17 g in 240 mL (8 ounces) of clear liquid every 10 min until 2000 mL of volume are consumed, combined with bisacodyl tablets or magnesium citrate.

^eMoviPrep®: Pouch A: PEG 3350 100 g, sodium sulfate 7.5 g, sodium chloride 2.69 g, potassium chloride 1.02 g; Pouch B: Ascorbic acid 4.7 g, sodium ascorbate 5.9 g (1000 mL).

Follow-Up Colonoscopies

Of the 120 cirrhotic patients who had screening colonoscopies between December 2004 and September 2011, 27 patients underwent repeat colonoscopies between September 2011 and August 2015 as documented in the electronic medical record. Those with repeat colonoscopy ($N = 25$) performed at our institution were included in further analysis. The follow-up colonoscopy reports for

Table 3 Multivariate Analysis of Variables Affecting Quality of Bowel Preparation.

Variable	Odds ratio	95% confidence intervals	p-Value
Age	1.007	0.987–1.027	0.523
Sex (male)	0.882	0.581–1.318	0.541
Diabetes	0.479	0.297–0.772	0.003
Cirrhosis	0.520	0.339–0.797	0.003

Figure 1 Quality of bowel preparation.

2 of these patients were excluded because a bowel preparation score was not documented. For the remaining 23 patients, the mean bowel preparation scores were 3.08 ± 1.08 in the initial screening colonoscopies and 3.48 ± 0.95 in the follow-up colonoscopies. Overall, while the initial screening colonoscopies in this group detected polyps in 8/23 (34.7%) patients, the follow-up colonoscopies found polyps in 7/23 (30.4%) patients. Of these 7 follow-up colonoscopies that detected polyps, 3 patients did not have polyps detected on the initial colonoscopy, and their initial bowel preparation scores ranged from poor (2 patients) to excellent (1 patient). The bowel preparation scores for these 3 patients on follow-up colonoscopy ranged from fair (1 patient) to good (2 patients). The pathology from the follow-up colonoscopies revealed tubular adenomas including sessile serrated polyps and non-adenomatous polyps (hyperplastic), but no invasive cancer. Of the 7 cirrhotic patients with unsatisfactory (1) and poor (2) bowel preparation scores documented during the initial screening colonoscopy, all except

3 patients had improved bowel preparation scores of fair (3), good (4), and excellent (5) on subsequent colonoscopy. This improvement in bowel preparation score correlated with the detection of polyps on repeat colonoscopy in 3 patients who were not found to have polyps during the initial colonoscopy.

Correlation with MELD Score

The mean MELD score of all cirrhotic patients in the study was 11.1 ± 4.5 . The mean MELD score in cirrhotic patients with polyps found on colonoscopy was 10.8 ± 5.4 , while in cirrhotics without any polyps detected, the mean MELD score was 11.2 ± 4.1 ($P = 0.592$). No correlation was found between MELD score in cirrhotics and bowel preparation score ($R^2 = 0.017$).

DISCUSSION

The efficacy of colonoscopy in the diagnosis and prevention of CRC is highly dependent upon the ability of the endoscopist to detect malignant lesions and premalignant adenomas. Adequacy of bowel preparation at the time of screening colonoscopy has therefore been established as an important quality measure and certain high-risk populations for inadequate bowel preparation are recommended to undergo an enhanced bowel purge.^{9,14-16}

Our study demonstrates that the presence of liver cirrhosis impairs bowel preparation at screening colonoscopy more than non-cirrhotic chronic liver disease. Almost half (48%) of cirrhotic patients were found to have fair, poor, or unsatisfactory preparation. Cirrhotic patients had significantly worse bowel preparation scores than non-cirrhotics, even when controlling for age, sex, and the presence of DM. Similar to previous studies, the presence of DM was independently associated with worse bowel preparation scores

Figure 2 Bowel preparation scores.

in our cohort, presumably resulting from autonomic neuropathy and resulting delayed intestinal transit in diabetic patients.^{17,18}

A growing body of literature has begun to characterize the presence, severity, and consequences of intestinal dysmotility in patients with cirrhosis. These consequences include the development of small intestinal bowel overgrowth (SIBO), exacerbation of hepatic encephalopathy (HE), and an increased risk of spontaneous bacterial peritonitis (SBP).^{12,19,20} This study bolsters the findings of prior small studies which seek to include suboptimal bowel preparation at colonoscopy among these consequences. For example, a smaller study by Salso et al. of 53 cirrhotics and 52 non-cirrhotics demonstrated that a significant portion of cirrhotic patients had suboptimal bowel preparation and a lower adenoma detection as compared to non-cirrhotics (though not statistically significant).⁸ However, that study did not examine the concomitant use of medications like narcotics and beta-adrenergic blockers which are known to affect gastrointestinal motility. In our study, we also observed worse bowel preparations in cirrhotic patients despite many of these patients concomitantly taking medications such as lactulose and beta-adrenergic blockers, which have been shown to decrease intestinal transit time, as well as rifaximin, which is used in treatment of SIBO.^{21–23} These findings suggest that cirrhotics have considerably delayed intestinal transit time compared with non-cirrhotics. However, it is important to note that a significant subset (30%) of non-cirrhotic patients with chronic liver disease also had suboptimal bowel preparation at colonoscopy. It is possible that delayed intestinal transit in some patients develops earlier in the course of liver disease, not only as a consequence of cirrhosis. Our results confirm the findings of Hassan et al. and Ness et al. that cirrhosis is an independent predictor of worse bowel preparation.^{9,10} In the Hassan et al. study, diabetes, older age, and male sex were also independent predictors of a worse bowel preparation. Our data did not corroborate those contributors to poor bowel prep.

Although previous studies have shown higher rates of adenomatous polyps in cirrhotics, our study did not find a difference in polyp detection rate between non-cirrhotic and cirrhotic patients.^{24,25} This is likely explained by the worse bowel preparation in cirrhotic patients obscuring the detection of some colorectal polyps. Indeed, we found that 3 of the cirrhotic patients who initially had negative colonoscopies were found to have polyps on follow-up colonoscopy. In addition, we observed no correlation between the severity of cirrhosis as determined by the MELD score and quality of bowel preparation. It remains to be elucidated whether intestinal dysmotility in cirrhosis is related to the severity of cirrhosis as measured by the MELD score, the severity of portal hypertension which is not accurately captured by the MELD score, or other yet to be determined factors in cirrhotic patients.

Given the worse bowel preparation scores in cirrhotic patients compared with non-cirrhotics, further prospective trials are needed to determine the optimal bowel cleansing regimens for this population, which will enhance the yield of screening colonoscopy. In addition, future studies can help identify specific characteristics of cirrhotic patients that place them at increased risk for delayed intestinal transit and suboptimal bowel preparation, and whether these characteristics are also present to a lesser degree in chronic liver disease patients without cirrhosis.

This study has some limitations. Given the retrospective study design, patients underwent heterogeneous bowel preparation regimens, and we were only able to determine the type of bowel preparation used in 30% of the study population, as this information was not routinely documented in endoscopy reports at our institution during the study time period. Certain preparations might have been more effective in bowel cleansing than others. Of note, a prior study by Ness et al., which found that the presence of cirrhosis is associated with worse bowel preparation, included patients who received either sodium phosphate or polyethylene glycol, but did not find that the preparation itself was an indicator of bowel preparation adequacy.¹⁰ Numerous studies have demonstrated the superiority of split dose preparation in comparison to traditional one day bowel preparation, and guidelines regarding bowel preparation have varied during the study period.^{26,27} In our study, however, none of the cirrhotic and only 4 of the non-cirrhotic patients were administered split dose preparation prior to their initial colonoscopy (Table 2). Another limitation of this study is that the endoscopist subjectively determined the bowel preparation score as opposed to use of an objective standardized scoring system. The inclusion of varying endoscopists in this study may have also affected results due to inter-observer variability given differences in ADRs between endoscopists.²⁸ Also, the colonoscopies were performed by several attending gastroenterologists as well as gastroenterology fellows supervised by attendings, which may have affected the results. The seemingly low volume of procedures including during the study time period ($n = 330$) is to the result of strict exclusion criteria such as patients who underwent colonoscopy for any indication other than CRC screening, those where quality of bowel preparation was not documented in the colonoscopy report, and those with a history of prior intestinal surgery, intestinal obstruction, or a known motility disorder. In addition, we did not have information regarding intra-procedural attempts to improve the level of bowel preparation and its impact on polyp detection. These limitations should be addressed in future prospective studies to confirm our findings.

In this study, we demonstrate that cirrhotic patients have significantly worse bowel preparation scores in comparison to non-cirrhotic patients with chronic liver disease. Our findings identify cirrhosis as an independent risk

factor for suboptimal bowel preparation even after controlling for age, sex, and presence of DM. Our results did not suggest a correlation between severity of cirrhosis as assessed by the MELD score and bowel preparation. While we did not find a difference in polyp detection rates between cirrhotics and non-cirrhotics, this finding may have been impacted by the impaired bowel preparation in the cirrhotic patients. In addition to decreased diagnostic yield of colonoscopy, suboptimal bowel preparation has also been associated with increased procedural time, cost, and need for repeat procedures.²⁹ Given the importance of CRC detection in cirrhotic patients and the potential for complications resulting from unnecessary procedures, our finding of impaired bowel preparation in cirrhotics suggests that this population may derive significant benefit from utilization of enhanced bowel cleansing at screening colonoscopy.

CONFLICTS OF INTEREST

The authors have none to declare.

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