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MELD is the only predictor of short-term mortality in cirrhotic patients with *C. difficile* infection

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ABSTRACT

Background: Clostridium difficile infection (CDI) is the most common nosocomial infection in the US and cirrhotic patients with CDI have increased risk for poor outcome.
Aim: The aim of this study is to evaluate the impact of CDI on short-term mortality in patients with cirrhosis and identify predictors of mortality in these patients.
Methods: We retrospectively identified patients at Montefiore Medical Center from 2010 to 2014 with cirrhosis, diarrhea and a *C. difficile* toxin assay. Demographics, co-morbidities, medications, laboratory data and outcomes were recorded.
Results: Of 701 patients with cirrhosis who had a CDI assay, 183 were CDI+ and 518 CDI−. Patients with CDI were older, had more frequent CKD on hemodialysis and heart failure, were less frequently on rifaximin and lactulose and had increased glucocorticoid exposure. 30-day mortality was higher in patients with CDI (23.0% vs 16.6%, $p < 0.05$) compared to those without. Univariate predictors of 30-day mortality included WBC, corticosteroid use, AST, ALT, MELD, albumin, HBV and HCV infection; however, via multivariate analysis, only MELD (HR: 1.04 ± 0.02, $p < 0.05$) remained significant.
Conclusion: Patients with cirrhosis and CDI are at greater risk of 30-day mortality than those without CDI and the only multivariate predictor of mortality is MELD. These patients should have their disease severity triaged based upon MELD score.

1. Introduction

Clostridium difficile infection (CDI) is a major cause of diarrhea in the United States with increasing incidence and severity over the last few decades [1,2]. In 2011, there were 452,000 cases of CDI and 29,000 deaths from complications of this infection [3]. The emergence of hypervirulent strains, such as the NAP1/B1/027 strain, has further contributed to this epidemic [4,5] and with time, the incidence and severity of CDI seems to have worsened [6]. The prevalence of cirrhosis has also increased in recent decades with one Veterans Administration study showing an increase in prevalence from 664 per 100,000 enrollees in 2001 to 1058 per 100,000 enrollees in 2013 [7]. Mortality from complications of cirrhosis in the US has risen from 30,000 to over 36,000 deaths between 1998 and 2013 [8,9].

The incidence of *C. difficile* is increased in those with chronic liver disease [10] and cirrhotics with CDI are at increased risk of in-hospital mortality [11]. This disease association is believed to result from cirrhotics' increased use of prophylactic antibiotics and proton pump inhibitors (PPIs) [12,13]. In the general population, white blood cell count (WBC), creatinine and albumin are the strongest predictors of 30-day mortality, justifying their usage to triage disease severity [14,15]. In patients with CDI and cirrhosis, albumin and ICU admission have been reported to be predictors of short-term mortality [16]. We hypothesize that patients with CDI and cirrhosis will have worsened outcomes compared with those with cirrhosis and diarrhea but without *C. difficile* infection. We also hypothesize that the predictors of mortality in CDI for the general population will not be the same as in those with cirrhosis.

2. Methods

After institutional review board approval, we conducted a retrospective case-control study to assess the clinical outcomes and predictors of mortality in patients with cirrhosis and CDI hospi-

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talized at Montefiore Medical Center from 2010 to 2014. Clinical Looking Glass (CLG) software (Emerging Health, New York, NY) was initially used to identify consecutive patients with cirrhosis (via ICD-9 codes) who had a *C. difficile* toxin assay performed for diarrhea during any admission between 1 January 2010 and 31 December 2014.

Following the initial CLG search, a comprehensive chart review was performed on each identified patient to confirm the presence of cirrhosis and diarrhea. Diagnosis of cirrhosis was confirmed by review of liver biopsy. If biopsy was unavailable, cirrhosis was confirmed if patients had ultrasound (US), computed tomography (CT) or magnetic resonance (MR) evidence of cirrhosis *and* an AST/ALT ratio of greater than one. We chose these criteria given that the radiologic finding of nodular and shrunken liver on US, CT or MRI has a sensitivity of over 85% for diagnosis of cirrhosis [17] and the AST/ALT ratio of >1 has been reported to have a sensitivity ranging from 95 to 100% [18–20]. Other non-invasive testing modalities such as transient elastography (FibroScan®) or acoustic radiation force impulse (ARFI) were not readily accessible to patients at our institution prior to 2015, so they were not available to assess for cirrhosis in our study patients. Diarrhea was defined by a documented history of at least three watery bowel movements within a 24-h period with a stool *C. difficile* study sent. At Montefiore Medical Center, *C. difficile* is analyzed with a 2-step technique, initially with glutamate dehydrogenase assay (GDH) for *C. difficile* and enzyme-linked immunoassay (EIA) for *C. difficile* toxin; if the results are discordant, a polymerase chain reaction assay is used to confirm or refute the diagnosis. Any patient who did not fulfill criteria for cirrhosis and diarrhea was excluded.

Patients were subsequently subdivided into those with cirrhosis and CDI (*Cirr* + CDI+) and cirrhotics who had diarrhea but did not have CDI (*Cirr* + CDI−). For all patients, we recorded demographic data, including age, gender, date of birth and discharge (or death). We recorded presence of co-morbidities including diabetes, chronic kidney disease (CKD), end-stage renal disease, heart failure (HF), HIV, AIDS, malignancy and history of organ transplant. For each patient, the Charlson comorbidity score was calculated with assignment of 1, 2, 3, or 6 points for specific comorbidities based on the Charlson index [21]. WBC, platelet count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, creatinine, total bilirubin and international normalized ratio (INR) and MELD (Model for End-Stage Liver Disease) score on admission and at time of CDI assay were recorded for each patient. In January 2016, UNOS (United Network for Organ Sharing) officially incorporated sodium into the MELD score [22]. This new MELD-Na score was not evaluated in our study as data collection and analysis were completed prior to that date. The MELD was used since it was the standard of care at that time. We recorded outcomes including 30-day mortality, 30-day colectomy, any ICU requirement during hospitalization and recurrence of CDI within 90-days. Mortality data were obtained from hospital records and the social security death index.

We recorded characteristics of liver disease such as the stage and grade of cirrhosis and the etiology of liver disease, which included chronic hepatitis C (HCV), chronic hepatitis B (HBV), alcohol-induced liver disease (ALD), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and autoimmune hepatitis (AIH). The presence and history of hepatocellular carcinoma (HCC) was noted.

For all patients, we recorded antibiotic exposures within 90-days prior to CDI assay. We also recorded other medication exposures including glucocorticoids, PPIs, beta-blockers, rifaximin, lactulose, HIV anti-viral medications, HBV treatment and HCV treatment within 30 days of diagnosis. A patient's most recent episode of diarrhea prompting CDI assay was used as the index date for inclusion in the study and any history of CDI prior to the index episode was recorded. Characteristics and patterns of CDI treatment were noted, including the use of any oral (PO) metronidazole, intravenous (IV) metronidazole, PO vancomycin or vancomycin per rectum.

Table 1
Patient characteristics.

	Cirr + CDI− (n = 518)	*Cirr* + CDI+ (n = 183)	p-Value
Age (years; mean ± s.d.)	60.8 ± 11.2	64.0 ± 11.4	0.001
Sex (% female)	43.6%	48.1%	0.3
Charlson score	4.1 ± 2.0	4.2 ± 2.2	0.41
Past medical history			
AIDS	6.4%	5.5%	0.66
HF	8.3%	20.2%	<0.001
CKD	21.4%	31.7%	<0.01
CKD on HD	7.5%	13.7%	0.01
Diabetes	43.8%	39.9%	0.36
HIV	9.7%	8.7%	0.72
Malignancy present	16.2%	18.0%	0.57
Solid organ transplant	1.4%	0.5%	0.38

AIDS, acquired immunodeficiency syndrome; HF, heart failure; CKD, chronic kidney disease; HD, hemodialysis.

The *Cirr* + CDI+ and *Cirr* + CDI− cohorts were compared for demographics, characteristics of liver disease, risk factors for CDI and serologic values. The primary end-point of our study was 30-day mortality from the date of the index CDI assay and this, as well as other outcomes, were compared. We subsequently assessed various predictors of 30-day mortality in a univariate and multivariate analysis to consider which factors are most clinically useful to predict worsened outcome.

2.1. Statistical analysis

Data were initially collated in a Microsoft Excel database (Microsoft, Seattle, WA). After completion of data collection, the database was imported into SPSS for Windows (23.0, SPSS, Chicago, IL). Continuous baseline descriptive variables were expressed as means with standard deviations and were compared using the Student *t*-test. Categorical variables were expressed as absolute numbers and proportions. The χ^2-statistic was used to compare most categorical variables, whereas the Fisher's exact test was used for small numbers. Survival analyses were performed using the Kaplan–Meier method and compared by log-rank test. Survival data are presented as 30-day survival from the date of diagnosis. A Cox univariate analysis initially was performed to assess independent predictors of 30-day all-cause mortality in our patient population, and the results are presented as hazard ratios with 95% confidence intervals. The significant independent predictors of mortality were then added to the multivariate analysis using the Cox-proportional hazards model. A two-sided *p* value of <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics (Table 1)

Our initial search identified 1407 patients, of which 706 were excluded for not meeting inclusion criteria. 701 patients with confirmed cirrhosis and symptomatic diarrhea were included, of which 183 (26.1%) were *Cirr* + CDI+ and 518 (73.9%) *Cirr* + CDI−. Patients in the *Cirr* + CDI+ cohort were significantly older than those in *Cirr* + CDI− (64.0 ± 11.4 and 60.8 ± 11.2 years; p = 0.001) and had a higher incidence of CKD (p < 0.01), CKD requiring dialysis (p = 0.01) and HF (p < 0.001) (Table 1). When considering liver-related factors *Cirr* + CDI+ had less ALD and NAFLD as an etiology of cirrhosis and less frequently was complicated by HCC compared with *Cirr* + CDI−.

Table 2
Risk factors for CDI.

	Cirr + CDI− (n = 518)	*Cirr* + CDI+ (n = 183)	p-Value
Recent hospital admission	46.9%	53.6%	0.12
Prior episodes of CDI (no. ± s.d.)	1.2 ± 1.9	1.5 ± 2.5	0.09
Prior antibiotic use	72.2%	75.4%	0.4
PPI exposure	39.8%	43.2%	0.42
Corticosteroid exposure	1.2%	4.4%	<0.01
Rifaximin use	25.1%	10.4%	<0.001

CDI, *Clostridium difficile* infection; PPI, proton pump inhibitor.

Table 3
Serologic comparison of *Cirr* + CDI− and *Cirr* + CDI+.

	Cirr + CDI−	*Cirr* + CDI+	p-Value
MELD	16.7 ± 8.8	15.9 ± 8.6	0.36
Albumin (g/dL)	2.8 ± 0.7	2.7 ± 0.6	0.2
ALT (units/L)	54.3 ± 84.4	77.7 ± 334.3	0.21
AST (units/L)	120.9 ± 405.7	116.4 ± 380.9	0.91
Creatinine (mg/dL)	1.7 ± 1.6	1.9 ± 2.0	0.08
INR	1.7 ± 0.7	1.8 ± 1.6	0.36
Platelet (10^3cells/μL)	111.7 ± 75.9	127.6 ± 81.2	<0.05
Total bilirubin (mg/dL)	6.9 ± 9.5	3.8 ± 6.3	0.001
White blood cell (10^3cells/μL)	8.3 ± 6.1	9.5 ± 8.1	<0.05

MELD, Model for End-Stage Liver Disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio.

3.2. C.difficile *risk factors (Table 2)*

There were no significant differences in the frequency of recent hospital admissions, prior antibiotic or PPI exposures. There was a non-significant trend towards increased number of prior episodes of CDI in the *Cirr* + CDI+ cohort compared with *Cirr* + CDI− (1.5 ± 2.5 vs. 1.2 ± 1.9; p = 0.09). *Cirr* + CDI+ had higher rates of glucocorticoid exposure (4.4% vs. 1.2%, p < 0.01) and lower rates of rifaximin exposure (10.4% vs. 25.1%, p < 0.001).

3.3. *Serological assessment (Table 3)*

Cirr + CDI+ patients had a higher WBC count and platelet count. *Cirr* + CDI− patients had a significantly higher total bilirubin but had slightly lower mean values of creatinine and INR, which are weighted much more heavily in the MELD composite score and may have nullified the effect of the increased bilirubin levels. Overall, there were no differences in MELD score between the *Cirr* + CDI+ and *Cirr* + CDI− cohorts.

In regards to the MELD score according to specific etiology of cirrhosis, patients with alcoholic cirrhosis had the highest mean MELD score of 16.9 ± 9.1. This was followed by patients with chronic HCV, NASH and chronic HBV with MELD scores of 16.6 ± 8.3, 15.8 ± 7.9 and 13.4 ± 6.1 respectively.

3.4. *Clinical outcomes*

The 30-day mortality rate was significantly higher in the *Cirr* + CDI+ cohort than in the *Cirr* + CDI− patients (23.7% vs. 17.5%, p < 0.05) (Fig. 1). Kaplan–Meier survival curve analysis showed that patients with cirrhosis who had *C. difficile*-associated diarrhea were at significantly greater risk of short-term (30-day) mortality (Fig. 2). There were no differences in ICU requirements, 30-day colectomy (0.5% vs 0.0%, p = 0.09) rates or 30-day readmissions.

In the *Cirr* + CDI− group, the most common cause of mortality was sepsis (36.9%) followed by hepatic failure (13.1%), cardiac arrest (9.5%), hepatic encephalopathy (8.3%), hepatorenal syndrome (8.1%), variceal bleeding (6.0%) and heart failure (6.0%). In the *Cirr* + CDI+ group, the most common cause of mortality was sepsis (50.0%), followed by cardiac arrest (14.3%), hepatic failure (9.5%), hepatic encephalopathy (7.1%) and hepatorenal syndrome (7.0%). All other causes of death represented less than 5% of cases.

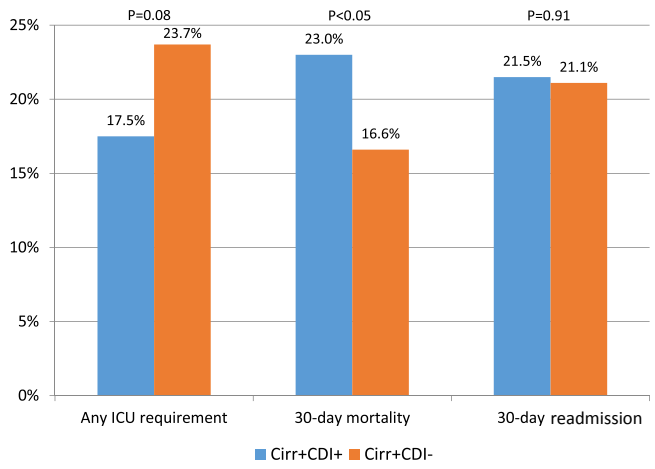

Fig. 1. Outcomes of patients with *C. difficile* infection compared to those without.

Table 4
Multivariate analysis of predictors of 30-day mortality.

	B	SE	Wald	df	Sig.	Exp (B)
HCV	−0.376	0.336	1.256	1	0.263	0.687
HBV	0.986	0.626	2.485	1	0.115	2.682
Corticosteroid exposure	0.951	0.617	2.378	1	0.123	2.588
CDI WBC	0.021	0.016	1.886	1	0.170	1.022
CDI AST	0.003	0.002	2.681	1	0.102	1.003
CDI ALT	−0.002	0.002	1.659	1	0.198	0.998
CDI Alb	−0.407	0.253	2.581	1	0.108	0.665
CDI MELD	0.039	0.017	5.265	1	0.022	1.039

HCV, hepatitis C virus; HBV, hepatitis B virus; WBC, white blood cell count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Alb, albumin; MELD, Model for End-Stage Liver Disease.

3.5. *Predictors of mortality*

3.5.1. *Cirr* + CDI−

In the cohort of patients without CDI, univariate predictors of 30-day mortality included recent hospitalization (p = 0.01), CKD (p = 0.01), piperacillin exposure (p < 0.001), IV vancomycin exposure (p < 0.001), chronic lactulose use (p < 0.001) and serologic studies at presentation including WBC (p < 0.001), AST (p < 0.001), ALT (p < 0.001), Alb (p < 0.001), creatinine (p < 0.001), total bilirubin (p < 0.001), INR (p < 0.001) and MELD (p < 0.001). When each univariate predictor was considered in multivariate analysis, only IV vancomycin exposure (1.9 ± 0.30, p < 0.05), WBC at presentation (1.04 ± 0.01, p < 0.01), creatinine (1.19 ± 0.08, p < 0.05) and MELD (1.03 ± 0.02, p < 0.05) were significant predictors of 30-day mortality.

3.5.2. *Cirr* + CDI+

When considering independent variables as predictors of 30-day mortality in *Cirr* + CDI+ patients, significant univariate predictors included HBV status (p < 0.05), glucocorticoid exposure (p < 0.05), WBC (p < 0.001), AST (p < 0.01), ALT (p < 0.01), albumin (p < 0.01) and MELD (p < 0.01). Antibiotic exposure, PPI exposure, creatinine and INR were not significant factors. Using multivariate analysis and considering only the significant univariate factors, the only significant predictor of mortality was MELD (1.06 ± 0.02, p < 0.022) (Table 4). Based on a beta of 0.039, for every 5-unit increase in MELD score, there was an associated 21.5% increase in mortality.

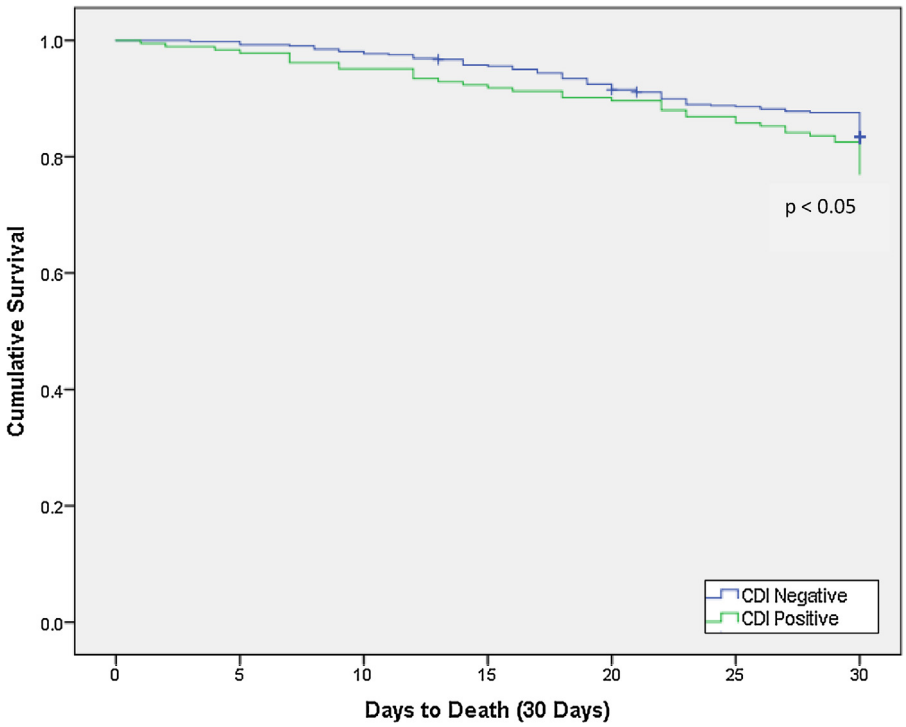

Fig. 2. Kaplan–Meier survival curve of mortality at 30 days after *C. difficile* infection.

4. Discussion

In patients with cirrhosis who have diarrhea, those with CDI had worse outcomes compared with those without CDI. In addition, MELD was the only significant multivariate predictor of 30-day mortality in *Cirr* + CDI+. In the general population, WBC, creatinine and hypoalbuminemia are commonly associated with mortality and used to predict disease severity, but these factors were not significant in the cirrhotic population.

Our study cohort of cirrhotic patients with CDI showed similar trends to the general population. *Cirr* + CDI+ patients were older with higher rates of CKD and without a difference in Charlson co-morbidity score compared with cirrhotics with diarrhea but without CDI. This is consistent with previous reports in which increasing age [4,23] and CKD [24,25] were significant factors associated with acquisition of CDI, while Charlson score was not [26,27].

Antimicrobials are a very strong risk factor for CDI because of their perturbation of the intestinal microbiome [14,15,28]. When we compared antibiotic exposures prior to presentation with diarrhea in those with cirrhosis, we found no differences in those with and without CDI. There are several explanations for this observation. The microbiome of patients with cirrhosis has fewer Bacteroidetes and larger proportions of Proteobacteria and Fusobacteria than that of the general population [29,30]. The effects of antimicrobials on the microbiome in cirrhotics may differ from such effects in the general population given the differing baseline microbial diversity. Patients with cirrhosis also frequently are administered chronic antimicrobial therapies, such as rifaximin for encephalopathy. Rifaximin has known activity against *C. difficile*, [31,32] and in one study of 211 cirrhotic patients on rifaximin for encephalopathy, none developed CDI within a mean follow up of 250 days [33]. In our study, some patients did develop CDI while on chronic rifaximin, but overall the cohort of Cirr + *CDI*− patients had a higher rate of rifaximin use than did the Cirr + *CDI+* patients (Table 2). Further work is needed to clarify whether and how risk factors for the acquisition of CDI differ in cirrhotics compared with the general population and whether different alterations of the microbiome might leave those with cirrhosis susceptible to CDI.

In their study on cirrhotic patients with CDI, Bajaj *et al.* reported a significant association between antibiotic exposure and CDI and showed an antibiotic exposure rate of 63% in patients with CDI and 26% without CDI ($p = 0.0001$). Antibiotic exposures in our study were very high (73.0%) in *both* the CDI and non-CDI cohorts and the mean MELD score of patients in our study was higher than that of those in Bajaj et al. (15.9 vs. 9.0). Patients in our study may have had a higher prevalence of antibiotic exposure due to more severe liver disease and this may have impacted the association of antibiotics with CDI in our study cohort

Glucocorticoids are another known risk factor for CDI due to their anti-inflammatory and immunosuppressive effects [34]. In our study 8 of 183 (4.4%) *Cirr* + CDI+ patients had steroid exposure compared with 6 of 518 (1.2%) *Cirr* + CDI− patients. This is consistent with prior studies, although the overall small number of exposures in either group may have magnified the actual difference.

In the general population with CDI, elevation of WBC and creatinine or decrease in albumin is associated with 30-day mortality. As a result, these factors are used to triage disease severity and guide therapy [14,15]. In cirrhotic patients, these serologic values are significantly influenced by the pathophysiologic disturbances of chronic liver disease, which may impact their ability to predict outcome in those with CDI. Leukopenia (WBC $\leq 4 \times 10^3$ cells/μL) is found in 42% of chronically decompensated cirrhotic patients, resulting from hypersplenism and increased consumption of WBCs [35]. Hypoalbuminemia is frequently seen from protein wasting and decreased rates of synthesis [36]. Elevation of creatinine has been reported in 54% of cirrhotics resulting from infection, intravascular volume disturbance and excessive diuretic use [37].

In the general population with CDI, the mean WBC was estimated to range from 14.4 to 15.8×10^3 cells/μL [38–40]. For inpatients with CDI, the mean creatinine was 1.2 mg/dL and mean albumin 3.3 g/dL [41]. In our cohort, *Cirr* + CDI+ had a lower mean WBC ($9.5 \pm 8.1 \times 10^3$ cells/μL), higher mean creatinine (1.9 ± 2.0 mg/dL) and lower mean albumin (2.7 ± 0.6 g/dL) than the

estimates from these other studies in the general population. Given these alterations in the serologic values used to triage disease severity, clinicians should contextualize thresholds for disease severity and consider the cirrhotic sub-group differently than the general population.

Bajaj et al. reported that CDI was associated with increased in-hospital mortality in cirrhotic patients compared with cirrhotics without diarrhea or CDI (13.8% vs 8.2%, $p < 0.001$) [11]. Our study compared cirrhotic patients with symptomatic CDI with cirrhotic patients with diarrhea but without CDI. We found that having CDI was associated with increased mortality (23.7% vs. 17.5%, $p < 0.05$). The higher mortality in our study compared with Bajaj et al.'s study may be attributed to our cohort's having more severe baseline liver disease (MELD: 15.9 vs. 9.0) and older age (64.0 vs. 54.0 years). In patients with cirrhosis infected with *C. difficile,* consideration should be made for more aggressive therapy to potentially reduce the risk for poor-outcomes.

In our *Cirr* + CDI+ cohort, under univariate analysis, significant predictors of mortality included glucocorticoid exposure as well as WBC and albumin, despite their known variations with significant liver disease; this is consistent with known predictors in the general population [34,42,43]. Creatinine was not a significant predictor and, as mentioned above, this could result from the variations in renal function seen in the cirrhotic population. Considering liver disease-specific variables, significant univariate predictors included chronic Hepatitis B infection, AST, ALT and MELD; INR was not a significant predictor.

A recent study by Smith et al. also reported an increased 30-day mortality in patients with CDI and cirrhosis and found that mortality was associated with albumin <3 g/dL and ICU admission in their multivariate analysis, which did not include MELD score [16]. In our study, in which ICU admission was studied as a primary outcome rather than a prognostic variable, MELD was the *only* significant predictor of mortality. This finding may be explained by the fact that inclusion of MELD score in a multivariate analysis nullifies the prognostic value of hypoalbuminemia by accounting for the true severity of the patient's liver disease.

In our study, MELD score had a hazard ratio of 1.06 ± 0.02 which, based on a beta of 0.039 and applying an exponential distribution, indicates that for every 5-unit increase in MELD score, there is an associated 21.5% increase in mortality in those with CDI. In *Cirr* + CDI+, none of the other known predictors of mortality in the general population (WBC, creatinine, albumin) were statistically significant. This differed from the *Cirr* + CDI− cohort which had many more univariate predictors of mortality, although exposure to IV vancomycin ($p < 0.05$) and WBC ($p < 0.01$), creatinine ($p < 0.05$) and MELD ($p < 0.05$) were significant multivariate predictors of short-term mortality. Since 2002, the MELD score has been adopted as the standard disease severity scale for allocating liver transplants based on its high degree of accuracy for predicting mortality. In cirrhotic patients with CDI, the MELD score remains the strongest and only overall predictor of short-term mortality and WBC; creatinine and albumin are less helpful to triage disease severity in this cohort.

There are several potential weaknesses of our study. First, it is retrospective with all of the known weakness inherent in such studies. Second, although liver biopsy is the gold standard for diagnosis of cirrhosis, a large number of patients in our cohort did not undergo a liver biopsy. In clinical practice, patients are often diagnosed with cirrhosis based on a combination of known risk factors, liver imaging, serology, and corresponding clinical findings. For patients without liver biopsies, we used the standard parameter of AST/ALT ratio >1 as an indicator of fibrosis, which has since been replaced by other serologic scores such as the APRI or FIB-4 or imaging with transient elastography. At the time of our data collection, these tests had not yet been validated or used widely to assess liver fibrosis. Third, the sample size of our *Cirr* + CDI+ cohort was much smaller than the comparison *Cirr* + CDI− cohort. However, given the large population that was screened, this likely reflects the overall low incidence of *C. difficile* in cirrhotic patients with diarrhea. Lastly, our institution is a tertiary care center for patients including those referred for liver transplantation; as such, liver disease in our population is likely more severe than in some other institutions.

In conclusion, our study shows that patients with cirrhosis and CDI have worsened outcomes compared with those with cirrhosis and diarrhea but without CDI. Patients with *Cirr* + CDI+ might benefit from more aggressive treatment given their risk for poor outcome. In addition, in our study MELD was the only reliable predictor of short-term mortality in patients with *Cirr* + CDI+. Given the known alterations in baseline serologic testing of patients with cirrhosis, and our findings, clinicians should consider using the MELD score to triage for disease severity and risk of poor outcome. Future research should focus on validation of the MELD score to stratify severity of illness in *Cirr* + CDI+ patients, and consideration of more aggressive therapeutic strategy for those with CDI and a high MELD score.

Conflict of interest

Lawrence Brandt: Merck and Co.: Scientific Advisory Board, Crestovo Inc.: Scientific Advisory Board, Seres Therapeutics Inc.: Scientific Advisory Board.

Paul Feuerstadt: Merck and Co.: Consulting and Speakers Bureau, Allergan: Speakers Bureau, Enterahealth: Speakers Bureau.

Guarantor

L.J. Brandt serves as the guarantor and assumes full responsibility for this study.

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