Bristol Stool Scale as a Determinant of Hepatic Encephalopathy Management in Patients With Cirrhosis

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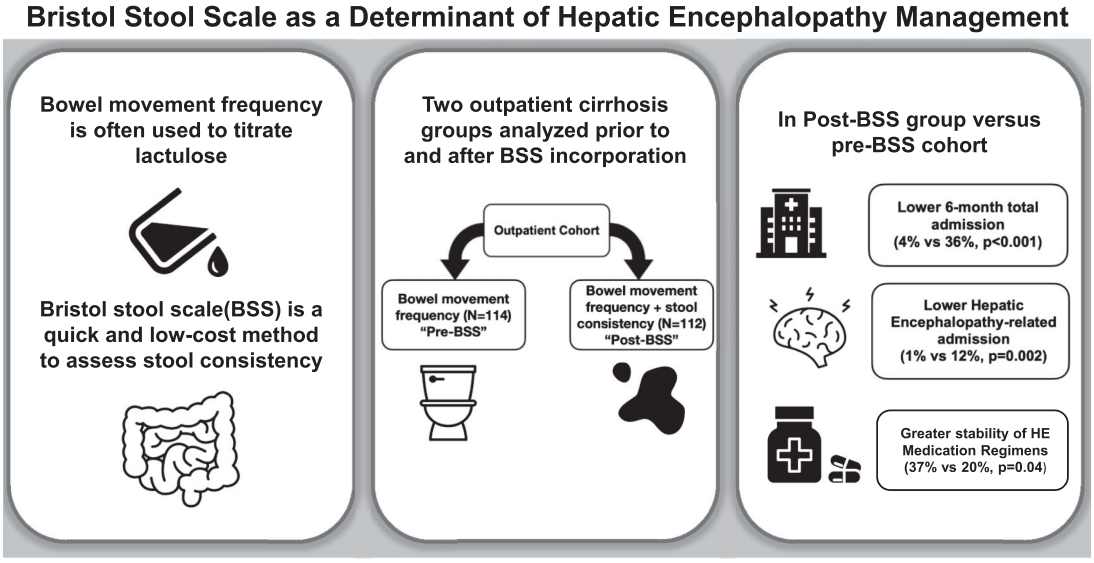
INTRODUCTION: **Bowel movement (BM) frequency is used to titrate lactulose for hepatic encephalopathy (HE). However, stool consistency using the Bristol stool scale (BSS, 0–7) is often ignored.**

METHODS: **The study included pre-BSS and post-BSS cohorts. BSS was incorporated into decision-making after training in outpatients with cirrhosis. Two to 3 BMs/d and BSS 3–4 were considered normal, whereas the rest were considered high or low; concordance between the metrics was evaluated. Medication changes and 6-month admissions were compared between this group (post-BSS) and a comparable previous group (pre-BSS). Concordance and regression analyses for all-cause admissions and HE-related admissions were performed, and comparisons were made for HE-related medication stability. In the longitudinal analysis, an outpatient group seen twice was analyzed for BSS and BMs.**

RESULTS: **In the post-BSS cohort, 112 patients were included with only 46% BSS and BMs concordance and modest BSS/BMs correlation ($r = 0.27$, $P = 0.005$). Compared with a pre-BSS cohort (N = 114), there was a lower 6-month total (4% vs 0.36%, $P < 0.001$) or HE-related admission (1% vs 0.12%, $P = 0.002$). Regression showed model for end-stage liver disease (odds ratio [OR]: 1.10, $P = 0.003$) and pre-BSS/post-BSS (OR: 0.04, $P < 0.001$) for all-cause admissions and HE (OR: 3.59, $P = 0.04$) and preera/postera (OR: 0.16, $P = 0.02$) for HE-related admissions as significant. HE medication regimens were more stable post-BSS vs pre-BSS (32% vs 20%, $P = 0.04$), which was due to patients with BSS > BMs ($P = 0.02$). In the longitudinal analysis, 33 patients without medication changes or underlying clinical status changes were tested 36 ± 24 days apart. No changes in BSS ($P = 0.73$) or BMs ($P = 0.19$) were found.**



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DISCUSSION: **BSS is complementary and additive to BM frequency, can modulate the risk of readmissions and stabilize HE-related therapy changes in outpatients with cirrhosis, and could help personalize HE management.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/C304, http://links.lww.com/AJG/C305

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LIVER

INTRODUCTION

Hepatic encephalopathy (HE) is a major burden on the patients, families, and health-care systems through frequent hospitalizations, falls, and poor psychosocial outcomes (1). The first-line therapy for HE recurrence prevention and treatment is lactulose (1,2). Although the mechanism of action is unclear, the dogma for lactulose prescription remains achieving at least 2–3 soft bowel movements (BMs) daily (1). Lactulose can result in multiple GI adverse events, has a high rate of nonadherence within Western patients, and not only often leads to multiple medication changes but also can precipitate acute kidney injury, hyponatremia, and worsening of HE. Thus, caution should be applied when using bowel frequency alone as an end point for lactulose therapy (3). Moreover, this one-size-fits-all policy does not consider baseline BM frequency or consistency and is not associated with objective cognitive performance data (4). Therefore, we need to amalgamate other criteria to potentially reduce admissions and reduce changes in medications. The Bristol stool scale (BSS) is a patient-reported characterization of the BM consistency that has been validated in several conditions but has not been used in patients with cirrhosis (5–7). Our hypothesis is that BSS would complement the BM frequency in modifying the risk for admissions and HE occurrence and stabilize the treatment course in outpatients with cirrhosis.

METHODS

We performed 2 separate analyses across outpatients with cirrhosis (Figure 1). For all analyses, data were collected regarding daily BSS and BMs after showing patients and caregivers a visual BSS chart. BSS ranges from 1 through 7 (see Supplemental Table 1, Supplementary Digital Content 1, http://links.lww.com/AJG/C304), and ranges of 3–4 were considered normal; 5–7 were considered high and 1–2 considered low. BMs between 2 and 3/d were considered normal, whereas 0–1/d were considered low and ≥4 BMs/d considered high. Concordance and discordance between BMs and BSS were analyzed, and correlations between BMs and BSS were performed. For example, if BSS is high and BM is normal, that indicates BSS > BM; on the other hand, if BSS is low and BM is normal, that indicates BSS < BM.

Two outpatient groups were studied. The first group comprised patients with cirrhosis who were seen in the GI and Hepatology clinics at the Richmond Veterans Hospital before implementation of BSS when only BM frequencies were used to develop plans for HE therapies and monitoring as needed as per standard of care. Demographics and disease details, including presence of HE; use and dose of lactulose, rifaximin, and opioids; and use of fiber and other laxatives were evaluated, and patients were followed up for 6 months for medication changes or admissions, especially related to HE. We excluded patients with concomitant inflammatory bowel disease, colon resection, those with recent (<3 months) change in opioids, and those with current or recent (within 6 months) *Clostridium difficile* or other diarrheal infections.

After this, the outpatient hepatology team at the Richmond veterans affairs medical center (fellows, nurse practitioners, and attendings) was trained to assess for BSS for every outpatient, regardless of HE status and lactulose use. This included showing the patients and caregivers a visual of the BSS on the computer and asking them to pick their usual stool form after they had given us their daily BM frequency. The team was asked to incorporate the BSS with the BMs in HE therapy initiation and monitoring, including slowing the rate of lactulose increase in those with BSS that was higher than BMs and considering rifaximin initiation earlier in patients with higher baseline BSS scores. This guidance was only advisory for the clinicians, and no specific standard operating procedure was adopted. This was also to ensure that the clinician(s) could individualize care. Clinicians involved in both periods were the same from an attending (J.S.B. and B.C.D.) and NP perspective (Z.M., M.L.G., and A.M.), but the fellows who were supervised by the attendings differed because of the rotations. Similar data as collected for the pre-BSS cohort were recorded. In addition, we performed correlations between BSS and BMs. Again, outcomes and HE-related medication changes (started lactulose, stopped lactulose, and reduced/increased lactulose or added rifaximin) over the next 6 months were recorded and compared with the pre-BSS period.

We compared outcomes (stability of HE-related medications, all and HE-related admissions over 6 months) between pre-BSS

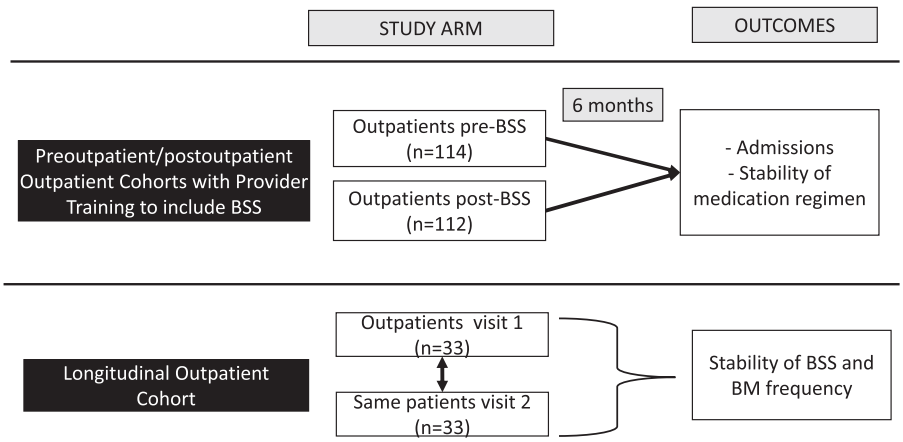

Figure 1. Overview of the study design and outcomes showing the 2 arms. BSS, Bristol stool scale.

and post-BSS groups using unpaired parametric or non-parametric tests as appropriate. Adherence on medications was defined by direct questioning of the patient during return clinical encounters or hospitalizations, filling of the medications using the VA pharmacy, and patient contact through phone calls as needed during clinical follow-up. In addition, binary logistic regression using backward elimination was performed for future admissions using all demographic information, cirrhosis severity and medications, and pre-BSS vs post-BSS time points. Only variables with $P < 0.10$ were included in the multivariable analysis.

Longitudinal analysis

Analysis was performed in a separate group of outpatients with cirrhosis who were stable clinically without medication changes and were evaluated twice over 3 months with BSS and BMs. These were assessed for changes over time using paired *t* tests. This was a quality improvement analysis performed across both hospitals.

RESULTS

Preoutpatient/postoutpatient cohorts

We included 114 patients in the pre-BSS cohort and 112 patients in the post-BSS outpatient cohort (Table 1). Both cohorts were statistically similar regarding demographics, HE, and medication details.

Analysis within BSS-incorporated cohort

In the cohort of patients where BSS and BMs were both incorporated after training hepatology staff, only 46% had concordant BSS and BM, whereas 44% had higher BSS than daily BMs (Table 2). There was a modest correlation between the 2 metrics (Figure 2a). Of the 51 patients who had concordant BSS and BM, 46 had both BMs and BSS that were low, whereas only 5 had both high BSS and BM metrics.

There were no major differences in disease severity and other medications apart from other laxatives in those who had differences between BSS and daily BMs in outpatients. Patients using rifaximin and lactulose had a higher daily BM rate compared with those who were not. However, BSS was similar regardless of lactulose and rifaximin use. Daily BMs and BSS were not significantly different between those on opioids, laxatives, fiber, and antibiotics compared with those who were not (Table 3).

Medication changes within 90 days

A significantly higher rate of patients in BSS group had stable medications related to HE compared with those without BSS incorporated into HE therapy (Table 1). Of the 37 patients in the BSS group that had stable medications, 15 had BSS > BMs, 10 had concordant BSS and BM, and 3 had BSS < BMs. When compared with those where HE-related medications were changed, a higher proportion of patients who had BSS > BMs had stable HE-related medications ($P = 0.02$), but the comparisons were statistically similar between patients who had BSS < BMs and those who had concordant BSS and BM (Figure 2B–D).

Admission rates

In addition, the previous cohort had a significantly higher 3-month total and HE-related admission rates compared with those where BSS was incorporated. HE-related admissions were seen in 14 patients; the remainder were due to ascites (n = 13), GI bleeding (n = 9), infection (n = 5), and liver unrelated (n = 6). None of the 5 admissions occurred in patients with concordant BSS and BM: 2 with low BSS and high BMs and 3 with high BSS and low BMs. One admission was due to HE, whereas the remaining was due to ascites (n = 2), infection (n = 1), and GU bleeding (n = 1) in this period.

Table 1. Comparison of pre-BSS and post-BSS outpatient cohorts

	Previous cohort without BSS (N = 114)	Cohort with BSS included (N = 112)	*P* value
Age	61.0 ± 6.01	62.3 ± 12.2	0.57
Male sex	103 (90%)	98 (88%)	0.49
MELD score	12.6 ± 5.6	12.3 ± 5.4	0.30
Ascites	52 (46%)	49 (44%)	0.77
Previous HE	50 (44%)	56 (50%)	0.36
Lactulose	50 (44%)	56 (50%)	0.36
Lactulose dose (mL)	24.5 ± 28.6	27.8 ± 38.2	0.49
Rifaximin	20 (18%)	28 (25%)	0.18
Opioids	24 (21%)	18 (16%)	0.36
Other laxatives	22 (19%)	14 (13%)	0.16
Fiber	10 (9%)	14 (13%)	0.37
Daily bowel movements	2.1 ± 1.2	2.3 ± 1.0	0.67
Outcomes			
Stable course of HE medications over 6 mo	22 (20%)	37 (32%)	0.04
Future admissions over 6 mo	41 (36%)	5 (4%)	<0.0001
Future HE-related admission over 6 mo	14 (12%)	1 (1%)	0.002

BSS, Bristol stool scale; HE, hepatic encephalopathy; MELD, model for end-stage liver disease.

Regression analyses

On logistic regression preera vs postera, model for end-stage liver disease (MELD) score, antibiotic use, and opioids had $P < 0.1$ on univariable analysis, of which only MELD score (odds ratio [OR] 1.10, confidence interval [CI]: 1.03–1.18, $P = 0.003$) and preera vs postera (OR: 0.04, CI: 0.02–0.12) remained significantly associated with admissions. When only HE-related admissions were considered, MELD score, previous HE, and preperiods/postperiods were significant on univariable analysis, but only previous HE (OR: 3.59, CI: 1.02–12.7, $P = 0.04$) and preperiods/postperiods (OR: 0.16, CI: 0.03–0.75, $P = 0.02$) were significant.

Longitudinal outpatient cohort

Thirty-three patients (age 60.2 ± 12.9 years, 31 men) were seen 36 ± 24 days apart. Of them, 22 had previous HE with all being on lactulose and 17 on rifaximin. Twenty patients had ascites, 4 had HCC, and 2 had previous SBP. Eight patients were on opioids. MELD score did not change significantly over time (11.8 ± 3.5 vs 12.1 ± 4.8, $P = 0.24$), and none of the medications were changed

Table 2. Details of the cohort who had BSS data collected

Cross-sectional outpatients (n = 112)	Concordance between BSS and daily BMs			*P* value (ANOVA, χ^2 test)
	BSS < BMs (n = 12)	Concordant BSS and BM (n = 51)	BSS > BMs (n = 49)	
Age (yr)	63.3 ± 9.7	62.2 ± 9.3	62.2 ± 9.3	0.96
Male sex	9 (75%)	48 (94%)	41 (84%)	0.11
MELD score	11.6 ± 4.1	12.3 ± 5.0	12.3 ± 6.1	0.90
BSS	2.6 ± 1.3	3.8 ± 0.6	5.0 ± 1.0	<0.0001
Daily BMs	2.0 ± 1.2	2.5 ± 0.8	2.2 ± 1.1	0.09
Previous HE	7 (58%)	32 (63%)	39 (80%)	0.92
On rifaximin?	4 (33%)	25 (49%)	20 (41%)	0.53
On lactulose?	5 (42%)	31 (61%)	29 (59%)	0.48
Lactulose dose (mL)	15.0 ± 19.2	23.0 ± 26.9	36.1 ± 49.0	0.11
Other laxatives	4 (33%)	2 (4%)	8 (16%)	0.01
Fiber	1 (8%)	6 (12%)	7 (14%)	0.83
Opioid use	3 (25%)	4 (8%)	5 (10%)	0.30
Antibiotics	1 (8%)	2 (4%)	2 (4%)	0.35

BMs, bowel movements, BSS, Bristol stool scale, HE, hepatic encephalopathy; MELD, model for end-stage liver disease.

in the interim. No change in BSS (4.3 ± 1.3 vs 4.4 ± 1.5, $P = 0.73$) or BMs (2.4 ± 0.9 vs 2.7 ± 1.6, $P = 0.19$) were found between the 2 time points (Figure 3).

DISCUSSION

Our results show that the BSS is complementary and additive to BM frequency in modulating several important outcomes in outpatients

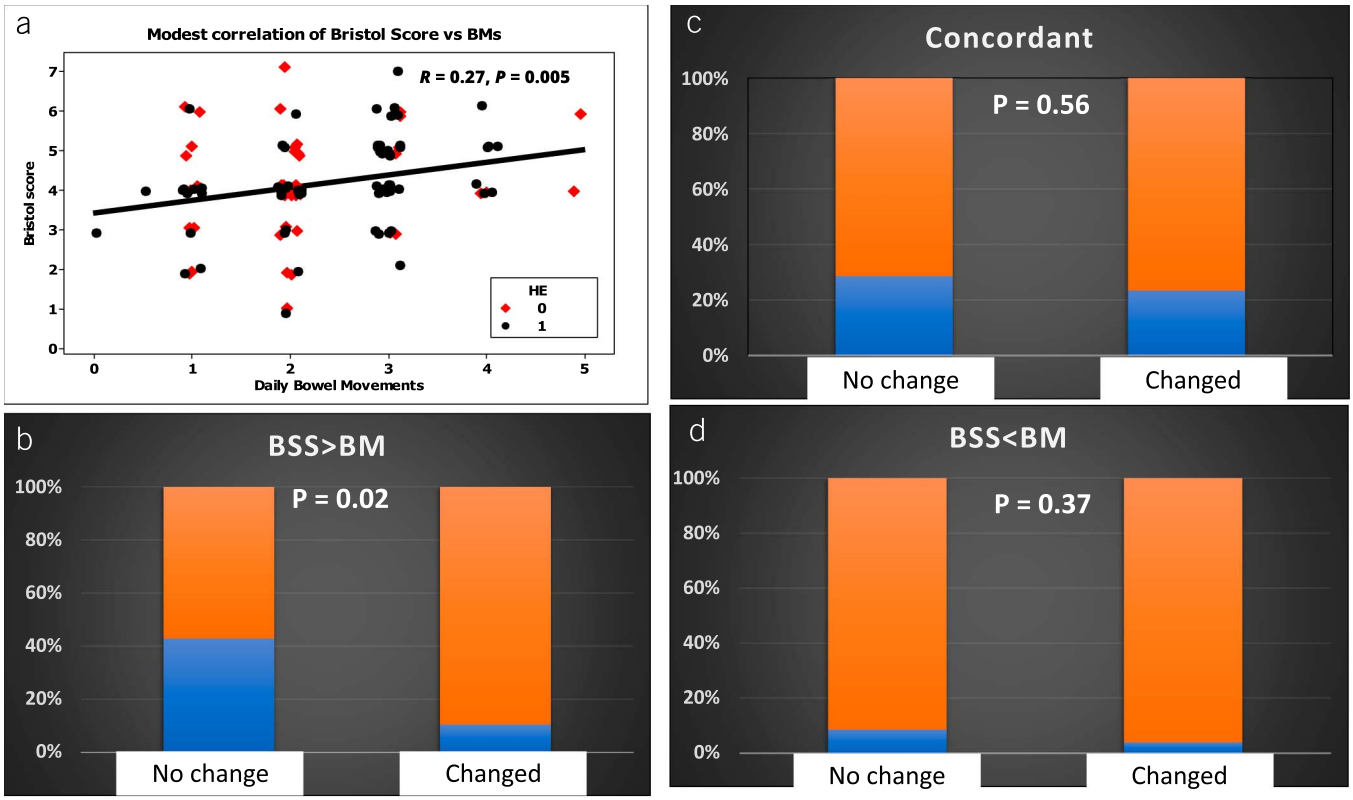

Figure 2. (**a**) Modest correlation of BSS and daily BMs in outpatients with red diamonds indicating those with previous HE and black circles those without previous HE. (**b**) Proportion of patients with BSS > BMs (blue portion) vs the rest (orange) in those who required HE-related medication changes or not over the next 90 days was statistically significant. (**c**) Proportion of patients with concordant BSS and BMs (blue portion) vs the rest (orange) in those who required HE-related medication changes or not over the next 90 days was statistically similar. (**d**) Proportion of patients with BSS < BMs (blue portion) vs the rest (orange) in those who required HE-related medication changes or not over the next 90 days was statistically similar. BMs, bowel movements, BSS, Bristol stool scale, HE, hepatic encephalopathy.

Table 3. Comparison of medications, BSS, and BMs

	Daily BMs			BSS		
Outpatients (n = 112)	Without	With	*P* value	Without	With	*P* value
Previous HE	2.1 ± 0.9	2.4 ± 0.9	0.07	4.1 ± 1.3	4.2 ± 1.1	0.82
Lactulose yes/no	2.1 ± 1.1	2.5 ± 0.9	0.05	4.0 ± 1.3	4.3 ± 1.1	0.27
Rifaximin yes/no	2.1 ± 1.0	2.7 ± 0.9	0.001	4.1 ± 1.2	4.3 ± 1.1	0.36
Opioids	2.4 ± 1.0	2.1 ± 1.0	0.39	4.2 ± 1.2	4.3 ± 1.4	0.84
Other laxatives	2.4 ± 0.9	2.2 ± 1.5	0.69	4.2 ± 1.2	4.1 ± 1.4	0.78
Fiber	2.3 ± 1.0	2.5 ± 1.2	0.55	4.2 ± 1.2	4.1 ± 1.1	0.72
Antibiotics	2.3 ± 1.0	3.2 ± 1.1	0.14	4.2 ± 1.2	4.0 ± 2.0	0.85

Comparison of bowel movements and BSS between those with/without the conditions or those on or not on medications listed on the left column.
BMs, bowel movement, BSS, Bristol stool scale, HE, hepatic encephalopathy.

with cirrhosis. BSS and BM frequency are modestly correlated, and almost half of the patients exhibit discordance between these stool consistency as measured by BSS and daily stool frequency.

Patients with cirrhosis, especially those with HE, are prescribed lactulose under the assumption that achieving a set number of BMs implies efficacy (1,8). However, this dogma is being increasingly challenged with the recent publication from our group determining that regardless of HE or lactulose use, cognitive impairment was not associated with BM frequency (4). The focus on number of BMs and driving doses of lactulose beyond that would be tolerable to most Western patients often leads to readmissions due to nonadherence (3,9). HE remains the major cause of readmissions, many of which are driven by medication nonadherence to lactulose (10–12). In addition, performing cognitive testing routinely even using simple tests remains beyond the logistic workflow of most practices (13,14). Therefore, we need other therapeutic targets and modalities that can improve this approach. The 2 outpatient cohorts were relatively balanced regarding most factors that affect BMs and BSS, and the BM frequency and cirrhosis severity were comparable. We included patients regardless of lactulose use and recorded data pertaining to other laxatives, fiber use, antibiotics, and opioids to make the results generalizable (15). All these could affect BMs and BSS and are often used in patients with cirrhosis regardless of HE. The modest correlation and major discordance between daily BMs and BSS are striking. This shows that inquiring only BM frequency only gives an incomplete picture, especially because discordance could have clinical implications such as changes in HE-related medications.

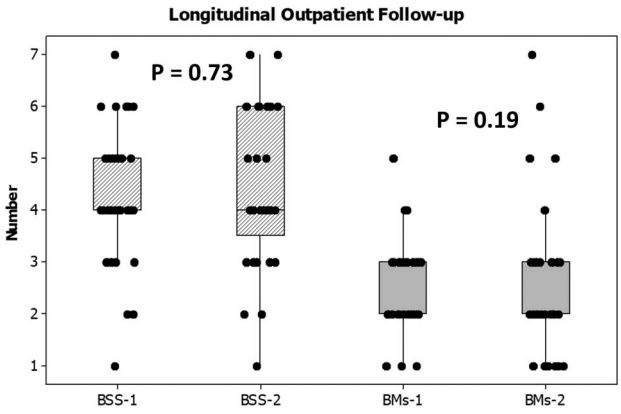

Figure 3. Longitudinal follow-up in outpatients showed no significant difference in BSS (hashed bars) or bowel movements (plain gray bars) at visits 1 or 2. Data are presented as median and 95% confidence interval with individual values. BSS, Bristol stool scale.

Of more importance, we observed a striking reduction in admissions over 6 months, especially related to HE, when BSS was incorporated into the decision-making compared with when only daily BMs were used. The only difference between the 2 cohorts was the knowledge of the medical teams of the BSS because the medications available, cirrhosis severity and complications, and clinical practices were similar in both cohorts. The proximate impact of BSS incorporation was reflected in a greater stability of the HE-related medication regimen compared with the cohort in whom only BMs was used as a biomarker of medication efficacy. This could have tempered the push by the clinicians to increase the lactulose dose based on inputs from both metrics, which could potentially prevent recurrence due to nonadherence or hospitalizations due to dehydration, hypernatremia, acute kidney injury, or electrolyte abnormalities due to overuse. This was further confirmed by a greater stability of HE-related medication changes in patients whose BSS > BMs. This demonstrates that higher BSS could counteract the relatively low BMs/d, and further increasing lactulose or initiating lactulose in these patients may not add more to the clinical efficacy of medications. Moreover, daily BMs and BSS in patients seen over a month apart were relatively stable that mirrored their disease course. This increases confidence in the stability of this metric in outpatients.

Although it is unclear why the BM consistency could have an impact on cirrhosis outcomes other than HE, previous studies have shown that BSS is a major contributor toward stool microbiota change that could help in cirrhosis-related outcomes (16,17). Therefore, it could be likely that the reduction in admissions over time could be extended to causes other than HE. Although other measures such as acidification, laxative, and prebiotic action of lactulose have been considered, the modulation of BSS without necessarily changing BM frequency could result in a potential microbiome-related benefit that could improve the outcomes without the need to push for higher daily BMs and their attendant problems (18,19). Further studies are needed to examine these changes.

We chose BSS because of the relative familiarity of clinicians with this instrument and the pictorial interface that enhances patient communication with minimal time and effort (20). BSS has been used extensively in intestinal disorders, but we expanded this into the cirrhosis and HE field (6,7,20–22). We also wanted to encourage greater patient participation in their care by focusing on BM consistency and frequency, which could integrate BSS as a

patient-reported outcome that informs the treating teams (23). The results show that within the liver specialty clinics, there was a high uptake of BSS incorporation that portends well for general GI practices who could be more likely to inquire about the BM frequency and consistency in all patients rather than those on lactulose alone compared with liver-focused practices (6,21).

Our study is limited because of the relatively modest sample sizes from 2 institutions and a cross-sectional design for the pre-BSS/post-BSS component. However, the longitudinal analyses add a valuable dimension. We also followed up outpatients for 6 months given the relative rarity of outcomes in outpatients.

We conclude that the BSS adds to BM frequency in our characterization of the impact of HE-related therapies in patients with cirrhosis in stable outpatient settings. BSS could be used to complement the information provided by BM frequencies in modulating complications of cirrhosis.

CONFLICTS OF INTEREST

Guarantor of the article: Jasmohan S. Bajaj, MD, MS, FACG.
Specific author contributions: N.K.D., S.S., J.S.B., D.P., O.S., A.F., Z.M., M.L.G., A.M.: collected data. N.K.D., J.S.B.: analyzed the data and produced the first draft. B.C.D.: provided critical revision and input. J.S.B.: conceptualized the study. All authors approved the final draft.
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Potential competing interests: None to report.

Study Highlights

WHAT IS KNOWN

- ✓ Lactulose is the first-line therapy for hepatic encephalopathy (HE) and is titrated to bowel movement (BM) frequency in clinical practice.
- ✓ Recent data suggest that bowel movement (BM) frequency is not associated with cognitive function in cirrhosis.
- ✓ Current practice based on the daily BM frequency alone could worsen adherence and outcomes in HE through lactulose overuse or underuse.
- ✓ Bristol stool scale (BSS) is a low-cost, quick, and noninvasive method to assess stool consistency, but it needs validation in patients with cirrhosis.

WHAT IS NEW HERE

- ✓ When clinic staff were trained to incorporate BSS in addition to daily BMs in their decision-making, there was a reduction in HE-related medication changes and all-cause and HE-related admissions when compared with a previous outpatient cohort where decision-making was based on BM frequency alone.
- ✓ Daily BM frequency and BSS were modestly correlated and remained stable over time in a separate group reevaluated without medication changes.
- ✓ Changes in HE-related medications was higher in those with BSS > BMs indicating an additive impact of BSS in reducing unnecessary medication alterations.
- ✓ Incorporation of the BSS with BM frequency may help to tailor treatment of HE to be more personalized and reduce medication changes and negative outcomes.

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