The Importance of Making an Accurate Diagnosis for Hepatic Encephalopathy

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Patient Case

A 43-year-old White male with metabolic syndrome presented with complaints of fatigue and feeling distracted. Blood work showed a mild increase in aspartate aminotransferase and alanine aminotransferase, and he was evaluated by his endocrinologist for suspected metabolic dysfunction-associated steatotic liver disease (MASLD). Based on the result of this evaluation (Fibrosis-4 Index of 3.3), he was referred to a local gastroenterologist.

The gastroenterologist excluded viral hepatitis and iron overload and ordered an ultrasound with elastography. These findings were reported as surface nodularity, mild ascites, and elastography scores suggesting portal hypertension (22 kPa). The patient denied any symptoms of liver disease. He was counseled about recommendations for further testing, including an upper endoscopy to screen for esophageal varices and liver cancer screening at 6-month intervals. He was advised to implement lifestyle modifications of metabolic factors, including a low-salt, high-protein diet and regular exercise to prevent sarcopenia. Routine evaluation was scheduled for 6 months.

Approximately 3 months later, the patient presented to the emergency department after his family found him confused and walking without a coat during a cold night in the neighborhood. A computed tomography scan of his head was normal. Blood work demonstrated abnormal liver chemistries and thrombocytopenia. Evaluation for infection (white blood cells, urine analysis, chest radiograph, and blood cultures) was unremarkable. On physical examination, he was sedated but arousable to stimulation. He refused to answer questions, only repeating his wife's name when asked questions. He did not have ascites on examination, so diagnostic paracentesis was deferred. Based on his severe degree of confusion, an ammonia level and toxicology screen were obtained, and he was admitted into the intensive care unit with a diagnosis of hepatic encephalopathy (HE). At this time, treatment was initiated with lactulose and rifaximin. His airway was protected, so intubation was not felt necessary. Within 6 hours, he began to become more alert and was able to leave the intensive care unit the following morning. After 5 days, he was discharged from the hospital with a recommendation to see his gastroenterologist in the next 2 weeks.

He attended his follow-up appointment with his wife, and both asked questions to understand the expectations and the prognosis of

Table 1. Blood Work Obtained at Hospital Follow-up

Test	Value
Total cholesterol	150 mg/dL
White blood cells	4.7×10^9/L
Platelets	67,000
Aspartate aminotransferase	76 U/L
Alanine aminotransferase	52 U/L
Alkaline phosphatase	137 U/L
Total bilirubin	2.4 mg/dL
Albumin	2.9 g/dL
PT/INR	1.3
Serum sodium	131 mEq/L
Serum creatinine	0.7 mg/dL
MELD/MELD-Na/MELD 3.0 scores[a]	13/18/17

MELD, Model for End-Stage Liver Disease; PT/INR, prothrombin time/international normalized ratio.

[a]These scores can be calculated at https://www.mdcalc.com/calc/10437/model-end-stage-liver-disease-meld.

the diagnosis. The gastroenterologist explained that this development indicated that his liver disease was progressing and that his prognosis had worsened. The gastroenterologist informed the couple about the possibility of a liver transplant. However, the patient was very reluctant to discuss this, so the gastroenterologist provided him with a referral to a transplant center should he change his mind after further consideration. The gastroenterologist recommended that he continue treatment with lactulose and rifaximin. When the patient complained about the diarrhea and bloating he was experiencing, the gastroenterologist reduced the dose of lactulose but discussed the importance of adjusting it if the patient did not have 2 to 3 soft bowel movements a day and recommended blood work (Table 1) in a follow-up appointment in 2 weeks.

The gastroenterologist again reminded the patient and his wife regarding the importance of nutrition with a low-salt, high-protein diet. The patient had been trying to reduce his meat intake after reading that this might increase his ammonia levels, and his wife told the clinician that he was eating primarily fruit and toast. The gastroenterologist strongly recommended against a reduction of protein, but suggested changing the type of protein he consumes to increase the amount of foods enriched in branched-chain amino acids, such as fish and beans. The patient was also advised to avoid foods high in nitrogen concentration, such as liver and red meats.

Overview of Hepatic Encephalopathy

Patients with end-stage liver disease experience many symptoms that can be described as decompensated liver disease. A patient who develops cirrhosis can be asymptomatic for a prolonged period. However, as the cirrhosis progresses, that patient will begin to demonstrate signs of liver disease or liver failure. These signs may include coagulopathy (bruising/elevated international normalized ratio), elevated bilirubin, or signs of portal hypertension, such as ascites, edema, and encephalopathy. HE is a neuropsychiatric syndrome occurring in the context of acute or chronic liver disease, although most cases occur in patients with cirrhosis as a result of both portal hypertension leading to spontaneous portal systemic shunting as well as hepatic synthetic dysfunction.[1] The greater the degree of portal hypertension, the higher the risk for HE. Thus, as liver disease progresses, the risk of developing HE increases. Any complication of end-stage liver disease is associated with a decrease in survival and worse quality of life (QoL). Indeed, patients with cirrhosis who develop HE have a poor prognosis and a reduced health-related QoL.[2-4]

In patients with cirrhosis, the prevalence of minimal HE is approximately 40% to 60%.[5,6] However, subclinical HE greatly increases the risk of developing overt HE. Within 1 year, approximately one-third of patients with cirrhosis and minimal (or covert) HE progress to clinically manifested HE. Additionally, approximately 10% to 15% of patients with cirrhosis show clinically manifested HE at the time of diagnosis. Although there are well-defined triggers for HE, HE is often a recurrent condition, with multiple episodes occurring within 6 months.

An assessment of Medicare data was used to calculate the risk of and associations with HE in a population of patients with cirrhosis. This assessment found that patients with HE are older (median of 65 years of age), have a high proportion of nonalcoholic fatty liver disease (now referred to as MASLD), have multiple comorbidities, and frequently experience polypharmacy.[7] In this population, incident HE was diagnosed at a rate of 11.6 per 100 person-years of follow-up. Although MASLD was a common etiology of liver disease, individuals with alcohol-related cirrhosis had a higher incidence of HE than those with hepatitis C virus–related cirrhosis (17.6 per 100 person-years vs 14.3 per 100 person-years) or nonalcoholic/nonviral cirrhosis (8.1 per 100 person-years). HE incidence was highest in individuals with portal hypertension (26.1 per 100 person-years). Indeed, individuals with severe liver disease (symptomatic cirrhosis from complications of portal hypertension) experienced an incidence rate of 27.11 hospitalizations per person-years, compared with 4.25 hospitalizations per person-years for individuals without severe liver disease. This resulted in an incidence

Table 2. West Haven Criteria for Grading Mental State in Patients With Cirrhosis

	Grade	Neurologic findings
Covert HE	0	No abnormalities detected
	1	Trivial lack of awareness, euphoria or anxiety, shortened attention span, impairment of addition or subtraction
Overt HE	2	Lethargy or apathy, disorientation concerning time, obvious personality change, inappropriate behavior
	3	Somnolence to semistupor, responsive to stimuli, confused, gross disorientation, bizarre behavior
	4	Coma, unable to test mental state

HE, hepatic encephalopathy.

Adapted from Conn HO. Quantifying the severity of hepatic encephalopathy. In: Conn HO, Bircher J, eds. *Hepatic Encephalopathy: Syndromes and Therapies*. Bloomington, IL: Medi-Ed Press; 1994:13-26.[24]

rate ratio of 6.38 (95% CI, 6.27-6.51).

HE is associated with cognitive and neuromuscular disturbances, which may present at varying degrees of severity. Patients tend to show disruptions in personality, self-reliance, and activities of daily living. Unlike the alarming symptoms of worsening liver disease, such as variceal bleeding, jaundice, and ascites, the initial development of HE can be very subtle. Subclinical HE may be difficult for a patient or their caregiver to recognize, but can be established through extensive neurocognitive testing. There are validated tools to assess for HE, however; even playing cognitive games and apps on a patient's smartphone can be used as tools. A reduction in performance on a game may be a sign that a patient should seek a follow-up appointment or consider adjusting their medication.

Eventually, HE will progress to less subtle symptoms of encephalopathy that the patient or the family will likely notice. It is also not unusual for many of these clues to be overlooked or dismissed until more extreme manifestations are present. In clinical practice, the grade of HE is determined using the West Haven criteria, which evaluate alterations in consciousness, intellectual function, personality/behavior, and neuromuscular abnormalities (Table 2). The West Haven criteria grade HE as 0 (no abnormalities), minimal HE (no clinical signs, abnormal psychometry), HE 1 (mild recognizable clinical signs), HE 2 (disorientation), HE 3 (somnolence but arousable confusion), and HE 4 (coma-like). Minimal HE and HE 1 are grouped as covert HE, whereas HE 2, HE 3, and HE 4 are grouped as overt HE.[8]

It is preferable to detect HE as early as possible in order to address reversible factors such as nutrition and polypharmacy and to prevent progression and symptoms, as the symptoms of HE can be quite frightening and impactful for both the patient and their family. There are several interventions that can be implemented to change that trajectory, which becomes much harder to accomplish during the more severe stages of HE.[9]

The psychometric hepatic encephalopathy score is considered the gold standard test to assess cognition in patients with HE.[10] The EncephalApp Stroop tool has been validated against the psychometric hepatic encephalopathy score; however, the user needs to complete an approximately 10-minute assessment. Recently, a shortened version of the EncephalApp, referred to as QuickStroop, was found to be promising in the detection of covert HE while requiring only 1 minute of patient contact.[11] The QuickStroop tool can predict time to development of overt HE as well as overt HE–related hospitalizations, all-cause hospitalizations, and death among outpatients with cirrhosis.[12]

Pathogenesis of Hepatic Encephalopathy

The pathogenesis of HE is considered complex and likely multifactorial. However, the buildup of toxins (including ammonia) owing to impaired liver function is considered a primary cause. In this context, ammonia, a neurotoxin primarily produced by cell metabolism in the gastrointestinal tract, then enters the circulation via the portal vein. Normally, a healthy liver is effective in clearing these toxins; however, portal hypertension can lead to the development of portosystemic shunts, which allows the blood to be shunted away from the liver. As a result, this blood does not enter the liver and is therefore not effectively detoxified. Other complicating factors in the pathogenesis of HE may include sarcopenia, renal dysfunction, cerebral edema, oxidative stress, and inflammatory mediators.[13]

Burden of Hepatic Encephalopathy

HE can have significant physical, financial, and emotional impact on both the patient and the caregiver. It can also

Table 3. Treatment Options for HE

Drug name	Description	Availability	Dose	FDA approval/status for use in HE
First line				
Lactulose	Poorly absorbed disaccharide	• Decreases blood ammonia concentration • Promotes elimination of NH_3 • Fermentation by bacteria acidifies the colon and prevents absorption • Reduces urease-producing bacteria	20-30 g orally 3-4 times per day. Maintenance dose adjusted to achieve 2-3 soft stools per day	Approved
Rifaximin	Nonaminoglycoside semisynthetic, nonsystemic antibiotic	• Decreases blood ammonia concentration • Broad-spectrum antibiotic; results in a change in bowel flora • May cause downregulation of intestinal glutaminase activity	550 mg BID	Approved
Second line				
Lactobacillus, Bifidobacterium	Probiotic	• Modulates fecal flora • Reduces generation of ammonia	9 billion CFU	Not approved
Metronidazole	Synthetic antiprotozoal/ antibacterial agent	• Modulates fecal flora • Reduces generation of ammonia • Associated with neurotoxicity	250 mg BID	Not approved
Neomycin	Aminoglycoside antibiotic	• Decreases blood ammonia concentration • Inhibits intestinal glutaminase • Association with ototoxicity and nephrotoxicity • Should not be used in clinical practice	4-12 g orally per day in divided doses	Approved
Polyethylene glycol 3350	Cathartic	• Increases excretion of ammonia in the stool	4 L orally or via nasogastric tube	Not approved
Sodium benzoate and/or sodium phenylacetate	Nitrogen-binding agents	• Promotes renal excretion	5 g BID	Not approved
Valine, leucine, isoleucine	BCAAs	• Correct plasma ratio of BCAAs to aromatic amino acids • May reduce catabolism and muscle breakdown and prevent synthesis of false neurotransmitters	1.2-1.5 g/kg/day	Not approved

BCAAs, branched-chain amino acids; BID, twice daily; CFU, colony-forming units; FDA, US Food and Drug Administration; HE, hepatic encephalopathy.

Adapted from Reau NS, Brown RS, Flamm SL, Poordad F. A step-by-step approach to the diagnosis and management of hepatic encephalopathy in the United States. *Gastroenterol Hepatol (N Y)*. 2016;12(12 suppl 5):4-16.[13]

have a large and negative impact on patient independence; for example, it is generally recommended that patients with HE do not drive, which impacts autonomy and employment.

An analysis from 2011 evaluated 104 patients with cirrhosis and their caregivers; of these 104 patients, 46 had prior HE.[4] In this group, prior HE showed an adverse effect on multiple measures of financial status, although these differences did not reach statistical significance. For example, previous HE demonstrated an impact on median yearly family income ($35,000 to $49,999 for patients with prior HE vs $50,000 to $74,999 for patients with no prior HE; *P*=.17). The amount of cash patients had after asset liquidation was also markedly lower for patients with prior HE vs patients with no prior HE ($5000 to $9999 vs $20,000 to $49,999; *P*=.44).

The caregivers of patients with severe previous HE reported a significantly higher burden than caregivers of patients who had either previous HE that was controlled or no previous HE.[4] The Zarit Burden Interview short form scores were significantly higher (indicative of a higher burden) among the caregivers of patients with previous HE (19 vs 12; *P*=.005), as were the Perceived Caregiver Burden scale scores (indicative of a higher burden; 85 vs 68; *P*=.008). Within the Perceived Caregiver Burden scale, caregivers of patients with severe previous HE reported negative impacts on schedule and personal health, as well as a sense of entrapment.

A more recent study examined the psychological impact of HE on 15 patients and their respective caregivers, using 2 summary scores from the 36-Item Short Form Survey: a physical component score (PCS) and a mental component score (MCS).[14] For each, a higher score is indicative of a better QoL. Both the patients and the caregivers had markedly impaired QoL indicators compared with values from the reference population. Notably, the QoL values among caregivers were similar or only slightly higher than the QoL values among the patients. Within the PCS, the following mean values were reported for patients: role physical (32±12), physical functioning (34±11), bodily pain (39±10), and general health (35±8). The mean PCS values for caregivers were: role physical (47±11), physical functioning (51±6), bodily pain (47±12), and general health (47±9). Both sets of PCS values were lower than the reference values from a controlled series of adult subjects: role physical (7±41), physical functioning (66±30), bodily pain (68±30), and general health (60±21). Within the MCS, the following mean values were reported for patients: role emotional (43±14), social functioning (42±13), vitality (37±10), and mental health (43±6). The mean MCS values for caregivers were: role emotional (43±14), social functioning (42±13), vitality (48±14), and mental health (43±6). Both sets of MCS values were lower than the reference values: role emotional (85±33), social functioning (79±28), vitality (60±25), and mental health (68±22).

Management Strategies for Hepatic Encephalopathy

Guidelines for the clinical management of HE have been published jointly by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases.[8] Overall, the management of HE in patients with cirrhosis involves prophylaxis as well as treating HE episodes.

When a person with cirrhosis is newly found to have confusion, a 4-pronged approach is needed.[8] This includes (1) protecting the patient from complications that are associated with confusion (such as aspiration and falls); (2) immediately starting treatment for HE, which can be stopped if HE is ruled out; (3) searching for infections or other triggers of confusion that might have caused this episode of HE; and (4) searching for other mimickers or concomitant conditions (eg, a subdural bleed in a person who had a fall). Many other conditions can overlap and also be responsible for confusion, such as uremia, electrolyte abnormalities, and hyponatremia.

Most agents used in the management of HE act to reduce the levels of nitrogenous substances produced in the gut, although they may have additional mechanisms of action. Using agents from different classes with complementary mechanisms of action may improve patient outcomes. Several agents are available for patients with HE (Table 3), although the guidelines advocate for lactulose as first line and rifaximin after the first episode over any of the other agents.[8]

The goal of primary prophylaxis is to prevent the occurrence of a first HE episode.[1] Treatment in this setting is often controversial. If formal neurocognitive testing is abnormal, lactulose is often used in this setting, although tolerability is an issue. The agent is a sweet syrup that requires teaching to make tolerable for many patients. Suggestions include adding it to something sour, working with the pharmacy on additive flavoring, and drinking it cold. Side effects of excessive flatulence and diarrhea can also occur, which can be addressed with dose modification. These issues frequently lead to poor adherence.

Acute HE is often managed in the hospital. Patients hospitalized with high-grade HE require interventions such as prevention of airway obstruction and aspiration pneumonia, mitigation of potential harms caused by the patient's disorientation, care of intravenous lines, liquid balance, and monitoring of vital signs, urine output, renal function, pH, blood gases, electrolytes, and glucose. Exacerbating factors are addressed, and lactulose is first-line therapy. For these patients, the poorly absorbed antibiotic rifaximin can be added to lactulose, especially if there has been a prior episode of HE. Nutritional considerations are also important, as protein-calorie malnutrition is associated with a lower capacity for ammonia detoxification.

Secondary prophylaxis is implemented in patients following recovery from an HE episode, with the goal of reducing the risk of recurrence. Rifaximin is the only agent approved by the US Food and Drug Administration to reduce the risk of HE recurrence with or without lactulose. Because HE is a combination of synthetic dysfunction and portal hypertension, after onset of encephalopathy it is important to continue the medications prescribed to control the initial symptoms.

Addressing disease progression in patients with HE is

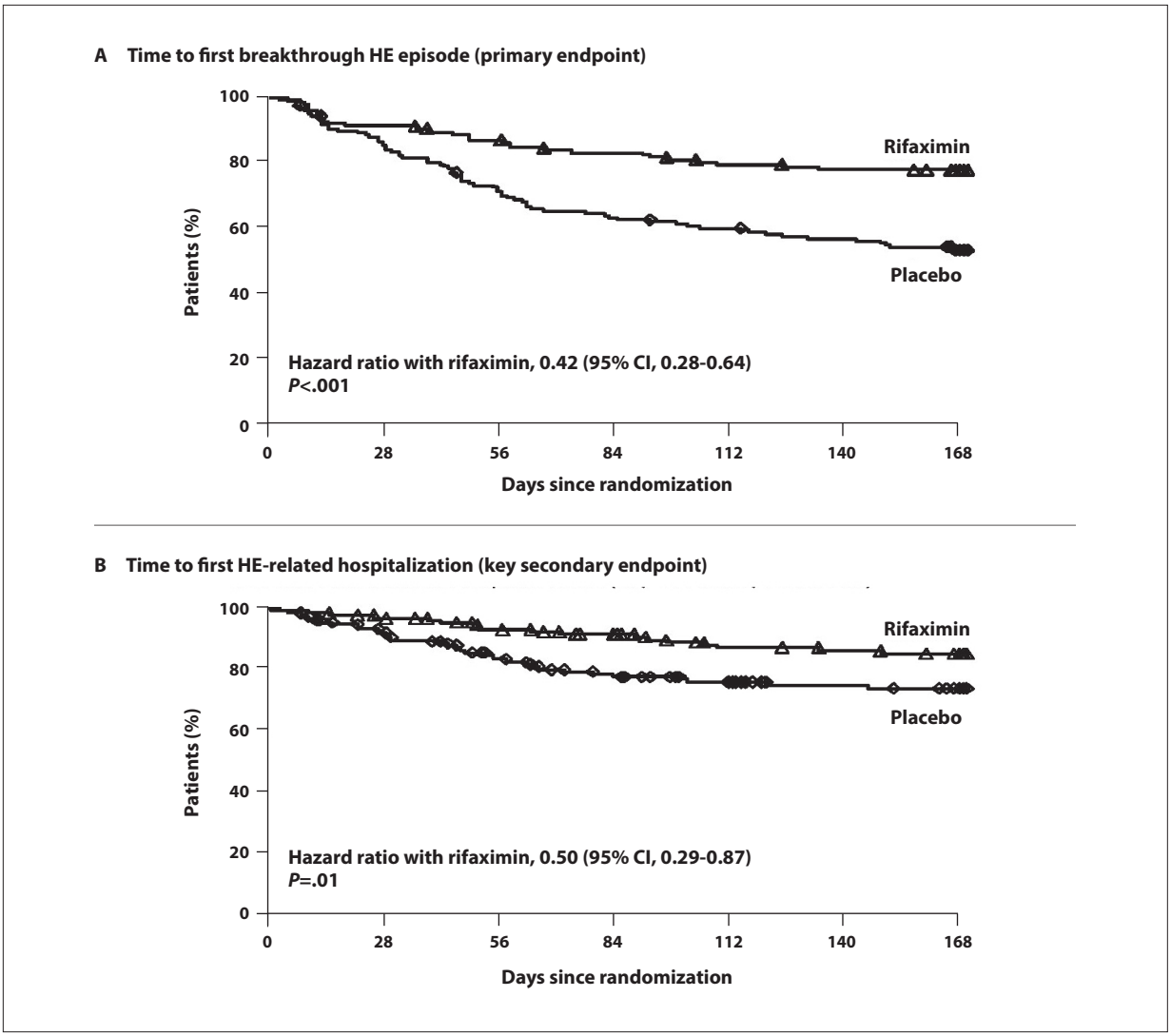

Figure 1. Kaplan-Meier estimates of efficacy endpoints in the intention-to-treat population with HE treated with rifaximin vs placebo.

HE, hepatic encephalopathy.

Adapted from Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;362(12):1071-1081.[16]

also imperative. For example, in patients with viral hepatitis, treatment should be initiated to eradicate or suppress the virus. Patients with MASLD should have their metabolic comorbid conditions addressed and be encouraged to engage in lifestyle modifications to prevent disease progression and malnutrition.[15] The risk of HE increases in patients who are malnourished and who have marginal renal function. Thus, it is important to communicate to the patient the need for a low-salt, high-protein diet, and physical activity to reverse sarcopenia.

Patients with HE or at risk for developing HE should have their medication burden carefully evaluated. Triggers for HE can include sedating medications and drug-drug interactions. Insomnia and sleep-wake reversal can be an early symptom of HE, and sometimes patients will take sedating medications to treat this. Cirrhosis also impacts drug metabolism, making the half-life of sedating drugs such as benzodiazepines less predictable and thus can contribute to confusion. Infections are a common cause of both new-onset and recurrence of HE. Certain bacteria can produce a relatively high degree of ammonia, and infections in general can increase the risk of an episode of HE. Patients with stable liver disease who become infected are also at an increased risk for HE. Another trigger of HE is gastrointestinal bleed, owing to the high production of nitrogen.

Particularly in patients with HE that is difficult to control, zinc deficiency should be considered. In patients not responding to standard therapy, large spontaneous shunts around the liver should also be considered, as HE may result in the accumulation of waste not appropriately processed by the liver. In conjunction with interventional radiology, these shunts may require closure to increase blood flow through the liver for appropriate metabolism.

Rifaximin for Hepatic Encephalopathy

The efficacy and safety of rifaximin for HE was established in a phase 3, multicenter, randomized, double-blind, placebo-controlled study that occurred over 6 months.[16] In this study, a total of 299 patients were randomized to receive either rifaximin or placebo; concomitant lactulose administration was permitted in both arms. The primary endpoint was the time to the first breakthrough episode of HE, which was used to determine the efficacy of rifaximin for maintenance of remission from episodes of HE in outpatients with a recent history of recurrent, overt HE. At baseline, a similar percentage of patients were receiving lactulose (91.4% in the rifaximin arm and 91.2% in the placebo arm). Within the 6 months prior to study enrollment, 69.3% of patients in the rifaximin arm and 69.8% in the placebo arm had experienced 2 HE episodes, and 30.7% of patients in the rifaximin arm and 29.6% in the placebo arm had experienced more than 2 HE episodes.

Significantly fewer patients in the rifaximin arm experienced a breakthrough episode of HE compared with the placebo arm (22.1% vs 45.9%; hazard ratio [HR], 0.42; 95% CI, 0.28-0.64; $P<.001$) (Figure 1).[16] These data show a relative reduction in the risk of a breakthrough episode by 58% with rifaximin vs placebo over the 6-month study period, and suggest that 4 patients would need to be treated with rifaximin for 6 months to prevent 1 episode of overt HE. HE-related hospitalizations were also reduced with rifaximin compared with placebo (13.6% vs 22.6%; HR, 0.50; 95% CI, 0.29-0.87; $P=.01$). A similar incidence of adverse events (80.0% with rifaximin and 79.9% with placebo) was reported in both groups, as were the various serious adverse events that occurred during the study period.

Coding for Hepatic Encephalopathy

Appropriate coding is imperative not just for justification of clinical care but also for quality assessment. Administrative data sources have been useful in studying the population burden of HE.[17] Several databases in the United States are available to provide such administrative data, namely from the US Department of Veterans Affairs, the Organ Procurement and Transplant Network, and the National Inpatient Sample. However, until recently, an International Classification of Diseases (ICD) code specific for HE was not available.

In October 2022, a new ICD, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis code took effect. This new code, K76.82, is specific for HE.[18] Prior to the publication of K76.82, providers used several codes to classify HE, including G93.40 or G93.49 (encephalopathy), K72.90 (hepatic failure), K72.91 (hepatic failure unspecified with coma), a liver disease K code plus G93.40 or G93.50, and K76.6 (portal hypertension). However, according to a survey of more than 400 providers, use of these different codes may have led to issues with treatment reimbursement and follow-up upon transition of care.[19] For example, improper diagnostic coding for HE can result in issues with payer coverage and prior authorization rejections. Combined with a patient's inability to pay out-of-pocket costs and/or lack of insurance coverage, these issues may form barriers for patients to receive their needed treatment and prescriptions after hospital discharge.

An analysis of patients with Child-Pugh class A or B cirrhosis and portal hypertension but no current or prior history of HE from 2016 to 2017 evaluated the sensitivity and specificity of the nonspecific diagnostic codes for their ability to predict HE.[20] These patients had a median age of 60 years (range, 52-66), were predominantly male (56.3%), and 70% were categorized as Child-Pugh class A. All patients had portal hypertension, most had varices (76%), and a history of ascites was prevalent in 41% (with most cases well controlled). The study investigators found that the ICD-10 code K72.90 (hepatic failure) identified patients with HE with suboptimal sensitivity (0.41; 95% CI, 0.30-0.53). These findings were extended to a validation cohort composed of patients identified from a US Department of Veterans Affairs database, again showing poor sensitivity with the K72.90 code (0.46; 95% CI, 0.31-0.62). However, this study also found that recorded use of lactulose or rifaximin from medical records could accurately identify patients with HE, with a sensitivity of 0.94 (95% CI, 0.85-0.98).

A similar analysis was recently published from the same group, evaluating the sensitivity of the new K76.82 code that is specific for HE.[21] Multiple patient cohorts were evaluated, with K76.82 showing sensitivities of 0.80 (95% CI, 0.74-0.85), 0.93 (95% CI, 0.86-0.97), and 0.68 (95% CI, 0.61-0.74). The investigators concluded that this code improved identification of HE compared with K72.90 across 2 of the 3 cohorts analyzed, and noted that variations in the third cohort could be owing to differences in local coding decisions among different institutions. Again, the investigators found that recorded use of lactulose or rifaximin from medical records could

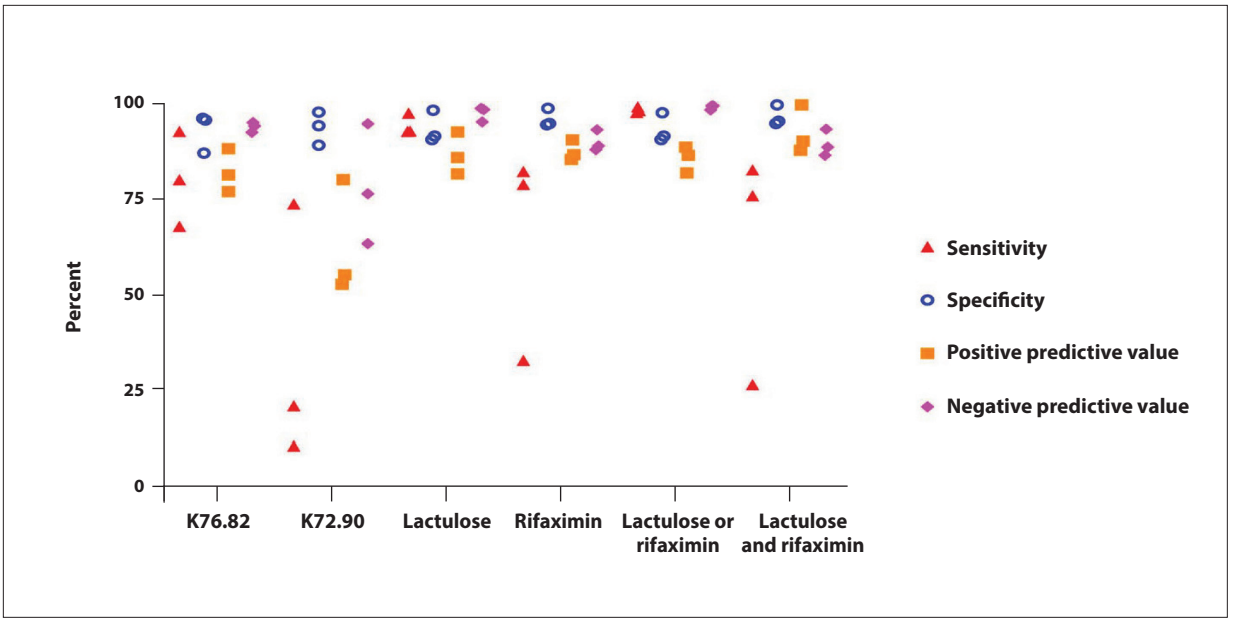

Figure 2. Diagnostic performance of various administrative data for identification of hepatic encephalopathy.

Adapted from Ozturk NB, Jamil LH, Tapper EB. Diagnostic performance of the ICD-10 code K76.82 for hepatic encephalopathy in patients with cirrhosis [published online November 1, 2023]. *Am J Gastroenterol*. doi:10.14309/ajg.0000000000002560.[21]

accurately identify those patients with HE (Figure 2).

The new K76.82 code allows for more simplified prior authorization, as it aids in the justification of prescriptions for HE. This is particularly important in the case of requesting rifaximin for HE, as this drug has multiple uses and different doses and schedules for each indication.[22] For example, when rifaximin is used for the treatment of traveler's diarrhea caused by noninvasive strains of *Escherichia coli*, it is administered for a very short course (3 days). For the treatment of irritable bowel syndrome with diarrhea, rifaximin is given for 14 days. In contrast, rifaximin is administered indefinitely as a treatment for HE. Likewise, the dosage of rifaximin is different in each of these indications: 200 mg 3 times daily for traveler's diarrhea, 550 mg 3 times daily for irritable bowel syndrome with diarrhea, and 550 mg twice daily for HE. Thus, providing an exact code for a patient with HE will aid in successful prior authorization as well as ensure that the pharmacy provides the correct dosage.

Further, precise coding of HE will increase the likelihood that a patient discharged with a diagnosis of HE will receive prompt clinical follow-up. A patient hospitalized with new-onset encephalopathy or recurrent encephalopathy should ideally see their clinical team within 1 to 2 weeks after discharge. Otherwise, medication prescriptions may not be filled correctly, or the prior authorization may not be completed. Without a clinical evaluation shortly after discharge, the patient with HE is much more likely to experience another episode of encephalopathy and rehospitalization or be ill at home. Thus, the correct coding facilitates both effective management of the condition and approval and availability of the appropriate therapies.

The prevalence of cirrhosis is expected to increase significantly over the next decade, given the increase in prevalence of MASLD and alcohol-related liver disease.[23] Patients with cirrhosis tend to be treated by a multidisciplinary care team. When incorrect diagnostic codes are applied to patients with HE, medical issues are more likely to be lost in the continuity of care, and procedures and interventions may not be approved by the payer.

Another important result of correctly applying a diagnostic code of HE to patients is an improvement in the epidemiologic understanding of this condition. This more exact diagnostic code will allow clinicians to better understand the impact of the changing prevalence of HE as well as demographics of conditions causing HE. This in turn will lend greater insight into how to manage these patients, the impacts on and cost of these patients, and factors affecting the patients' QoL. These issues will greatly impact our health care systems and shared medical management.

Gastroenterologists, hepatologists, and other clinicians who regularly care for patients with liver disease are likely already familiar with the new code for HE. However, it is important for other clinicians to be aware of the

appropriate coding for HE, especially because a hospital discharge summary will dictate the outpatient follow-up and management of that patient. Correct application of the appropriate diagnostic code for HE will help ensure that the inpatient-to-outpatient transition is smooth and properly supports the patient.

Disclosures

Dr Reau has done consultation for Salix.

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