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REVIEW

Hospitalized patients with cirrhosis: Addressing gaps in care

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In the last 3 years, all major hepatology and gastroenterology societies (American Association for the Study of Liver Diseases—AASLD, American Gastroenterological Association—AGA, American College of Gastroenterology—ACG, European Association for the Study of the Liver—EASL) have published detailed guidance regarding the management of patients with cirrhosis. Those recommendations include evidence-based practices relevant for hospitalized patients, from treating several complications of cirrhosis such as ascites/spontaneous bacterial peritonitis,[1] acute kidney injury/hepatorenal syndrome,[2,3] variceal bleeding,[4,5] HE,[6] acute-on-chronic liver failure,[7,8] to integration of palliative care[9,10] and optimal management of malnutrition.[11] This shows the highly complex care required to appropriately take care of patients with cirrhosis. While therapeutic advances are certainly benefiting our patients, consistent guideline-driven clinical practice remains challenging. In addition, transitions of care and appropriate transfer/referral for liver transplantation are critical for providing patient-centered quality hospital care. We hope that the following considerations will help hospital-based practitioners with variable experience in hepatology to address these gaps in the management of hospitalized patients with cirrhosis and deliver high-value inpatient care.

ALIGNING CLINICAL PRACTICE WITH GUIDELINE RECOMMENDATIONS

Successful implementation of practice guidelines is variable across hospital systems.[12,13] To promote value improvement in cirrhosis care by reliably measuring and tracking the health care provided, AASLD has developed a standardized set of quality measures, including process measures, clinical, and patient-reported outcomes.[14] Table 1 summarizes the AASLD quality measures applicable for the inpatient management of cirrhosis and relevant major society guidelines. Higher adherence to certain quality measures was associated with lower overall mortality and lower inpatient health care use,[15] but further research is needed to evaluate the full impact of process measures on clinical outcomes.

Given increased interest and publications on quality improvement (QI) in cirrhosis, there is now substantial data assessing the efficacy of several initiatives to align real-world practice with guidelines-based management. Various QI interventions in cirrhosis targeted higher compliance to recommended process measures with the goal of achieving superior clinical outcomes (survival, decreased rate of complications) and avoiding unwarranted hospital service utilization (preventable admissions/readmissions, unjustified length of hospital stay). To overcome the knowledge gap due to time restrains and difficulty for hospital practitioners to keep up to date with the latest guidelines, many QI trials have used easy-to-access and time-efficient tools to reduce variation in clinical practice: handheld checklists,[16] templated notes,[17] best practice alerts/decision support,[16] and clinical pathways/order sets.[18,19] More resource-intensive solutions have addressed institutional logistics and culture changes but require high commitment across all shareholders: “best practice” in

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; EASL, European Association for the Study of the Liver; ER, emergency room; LT, liver transplant; QI, quality improvement.

TABLE 1 AASLD quality measures and relevant major society guidelines, as applicable for inpatient management of cirrhosis

Selected AASLD quality measures	Ascites/acute kidney injury	Variceal bleeding	HE	Nutrition
Process measures	Patients with ascites who are admitted to the hospital for evaluation and management of symptoms related to ascites or encephalopathy should receive a diagnostic paracentesis during the index hospitalization	Patients who are admitted with or develop GI bleeding should receive antibiotics within 24 h of presentation. Antibiotics should be continued for at least 5 d	Patients with previous overt HE should be counseled regarding the risks associated with driving	Patients with cirrhosis should be assessed for frailty using a systematic screening method
	Hospitalized patients with ascites, with an ascitic fluid PMN $\geq$ 250 cells/mm^3, should receive empiric antibiotics and albumin within 12 h (1.5 g/kg D1, 1.0 g/kg D3)	Patients with cirrhosis who present with upper GI bleeding should receive upper endoscopy within 12 h of presentation	Patients with HE should have a search for evidence of precipitating factors documented in the chart	
	Patients undergoing large-volume paracentesis ($>$ 5 L removed) should receive i.v. albumin (6–8 g/L removed)	Patients with cirrhosis who are found to have bleeding esophageal varices should receive EVL or sclerotherapy at the time of index endoscopy	Patients who are hospitalized and have an acute episode of overt HE should receive lactulose	
	Patients who undergo paracentesis should not receive fresh frozen plasma or platelets	Patients with cirrhosis who survive an episode of acute variceal hemorrhage should receive a combination of EVL and beta-blockers	Patients who are discharged after an acute episode of HE should receive secondary prophylaxis with lactulose and/or rifaximin	
	Patients with ascites and/or hepatic hydrothorax should be managed with both sodium restriction and diuretics	—	—	—
Clinical outcomes	—	First variceal bleeding Variceal rebleeding	—	—
	Overall: liver-related hospitalization, rehospitalization within 7 or 30 d			
Patient-reported outcomes	Fluid in the legs/belly	—	Confusion, concentration/memory	
	General: medication side effects/muscle cramps, falls			
Relevant guidelines	2021 AASLD ascites/SBP/HRS 2022 AGA AKI, 2024 AGA vasoactive drugs/ HRS	2024 AASLD portal hypertension /varices 2023 AASLD TIPS/RTO variceal bleed	EASL HE	2021 AASLD malnutrition/ frailty
	General: ACLF (ACG, 2022, EASL 2023), Palliative care (AGA 2021, AASLD 2022)			

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ACG, American College of Gastroenterology; ACLF, acute-on-chronic liver failure; AGA, American Gastroenterological Association; AKI, acute kidney injury; EASL, European Association for the Study of the Liver; EVL, endoscopic variceal ligation; GI, gastrointestinal; HRS, hepatorenal syndrome; PMN, polymorphonuclear cells; RTO, retrograde transvenous obliteration; SBP, spontaneous bacterial peritonitis.

emergency room focusing on timely interventions,[20] dedicated teams to perform emergency room or inpatient paracentesis,[21] bundled interventions to ensure timely performance of diagnostic paracentesis (education + workflow support/ultrasound/premade kits + alert + orderset)[22] or postdischarge care management programs.[23,24]

Despite the increase in compliance with practice guidelines, the results of QI initiatives have varied in terms of sustainability and impact on clinical outcomes (survival, length of stay, and readmissions), sometimes leading to undesired effects (increased length of stay due to electrolyte disturbances secondary to excessive lactulose use).[19] Nevertheless, they provide useful ideas that should be tailored to the local institutional needs and practices. Optimal QI in cirrhosis should integrate clinical practice with an iterative QI process, ideally based on a learning health system paradigm, continuously assessing the efficacy of interventions and responding to clinical challenges.[25]

NUTRITION MANAGEMENT FOR THE HOSPITALIZED PATIENTS WITH CIRRHOSIS

There is a high prevalence of malnutrition among patients with cirrhosis, exceeding 90% in some study populations.[26] Both macronutrients and micronutrients/trace elements may be deficient,[27–30] with important implications for the hospitalized patient. For patients with alcohol use disorders and cholestatic disorders, malnutrition may be present to a significant degree prior to the onset of cirrhosis and can worsen as the liver disease progresses.[29,31] Imposed fasting states, such as preprocedure or pretesting "nil per os" periods, exacerbate this caloric deficit, which may be particularly relevant in the inpatient setting. Malnutrition in cirrhosis is associated with sarcopenia, infection, and frailty and thus contributes to an increased risk of mortality.[32–35] This risk extends to patients who receive a liver transplant (LT); malnutrition is a risk factor for poor transplant outcomes.[36]

Despite the consequences of malnutrition, it tends to be under-assessed and under-diagnosed, even by subspecialty providers.[26,37] However, addressing and treating malnutrition in patients with cirrhosis can both improve quality of life and extend survival.[38,39] Therefore, in the hospitalized patient with cirrhosis, nutritional status should be assessed at admission and may need repeated assessment if a hospital stay is prolonged.[11,26,35] Ideally, this assessment should involve a multispecialty team with a gastroenterologist/hepatologist and a dietician.[11,26,35] Choosing the correct screening tools can be challenging, as the majority of validated nutritional screening and assessment instruments are not specific for liver disease. Furthermore, their use in the inpatient setting can be limited by expense, the need for specialized equipment, and patient factors such as hypervolemia.[35,40] For example, the presence of ascites can mask abnormally low body mass index.[41] True obesity, far from reassuring the clinician that malnutrition is not present, can also obfuscate the presence of sarcopenia as well as other nutrient deficiencies.[34,42] The Royal Free Hospital-Nutritional Prioritizing Tool can be used at the bedside by nonspecialist staff as a screening tool,[43] though further, more specific testing may later be needed.

Several general nutritional principles can be applied in the inpatient setting. In situations where patients with cirrhosis present with significant ascites and/or edema, a low salt diet, defined as $\leq$2000 mg/24 hours of dietary sodium, is recommended.[43] This should be differentiated from a "no salt added" diet, which for US adults is typically 3400 mg/24 h of dietary sodium, most of which comes from processed foods.[44] Patients with cirrhosis typically have elevated protein needs, requiring 1.2–1.5 g/kg/d of protein.[45] There is no role for protein restriction to prevent HE,[46] and there is insufficient evidence to recommend animal-based or plant-based protein sources specifically for the prevention of HE.[47] Oral nutritional supplementation may be beneficial in the hospital setting; although a recent meta-analysis has not supported an overall mortality benefit from supplementation use, subgroup analyses support its use in hospitalized patients.[11,48] Given the prevalence of micronutrient deficiencies within this population, some societies have suggested the use of an empiric multivitamin.[11] In addition to minimizing times of nil per os, small frequent meals and the implementation of evening snacks are additional strategies[40,49,50] that can be employed to maximize nutrition in the inpatient with cirrhosis.

Patient education regarding nutrition and dietary strategies remains crucial. Many patients with cirrhosis have a limited understanding of their disease state, including nutrition goals,[51] and an inpatient hospital stay provides a potential opportunity for patient and family education.

TRANSITIONS OF CARE FOR THE HOSPITALIZED PATIENTS WITH CIRRHOSIS

There is limited data on best practices for transitions of care for hospitalized patients with cirrhosis. This represents a significant information deficit, as patients with cirrhosis have a high rate of hospitalization, which has been increasing within the United States.[52] A timely transfer to a LT center is an important part of an optimal transition of care for patients who are critically ill and need to undergo their LT evaluation in an

"expedited" fashion. Delayed referrals were associated with worse outcomes.[53,54] While discussions about LT are typically deferred to gastroenterology/hepatology team, hospital providers responsible for the inpatient care of patients with cirrhosis should have a basic understanding of indications for LT and be comfortable to initiate the transfer to a transplant center for an expedited evaluation especially if their local access to inpatient specialty care is limited. Barring a specific contraindication to LT, patients hospitalized for complications of cirrhosis, such as portal hypertensive bleeding, HE, ascites, spontaneous bacterial peritonitis, or hepatorenal syndrome should be considered for transplant evaluation.[55–57] Model for End-Stage Liver Disease–Sodium score $\geq$15 has also been used as a threshold for LT referral[56]; however, it is important to note that patients with cirrhosis may have a low Model for End-Stage Liver Disease–Sodium score and still demonstrate elements of decompensation; transplant referral should not be withheld based on a low Model for End-Stage Liver Disease–Sodium score.

Multiple barriers to initiation of LT referral and evaluation have been identified. These include incorrect provider understanding of transplant contraindications,[53] patient socioeconomic status,[58] perceived complexity of referral process,[59] and geography.[60] Parameters for defining contraindications to LT, especially psychosocial contraindications, have changed since the inception of transplant care. Severe acute alcoholic hepatitis, previously considered a contraindication to LT, is now accepted as an indication for LT at an increasing number of centers within the United States[61] and should not preclude referral. While transplant centers within the United States are encouraged to develop program-specific criteria for patient evaluation, a recent Organ Procurement and Transplantation Network white paper[62] has recommended that neither patient chronologic age nor immigration status should serve as the sole criteria for determining eligibility for transplant.

Finally, patient education and facilitation of post-hospital discharge follow-up remain critical points in the transitional care of patients with cirrhosis from hospital to home or from local hospital to transplant center. Patients and their caregivers have reported significant educational deficiencies regarding the process of LT.[63] Lack of patient education from the multidisciplinary team has been identified as a risk factor for medication-related problems in patients with cirrhosis[64] and for poor medication adherence post-LT.[65] Multimodal education presentations (eg, both written and verbal) have been identified as helpful.[63] Provision of educational tools regarding cirrhosis in general has demonstrated utility,[66] though further studies on the type and timing of educational interventions are needed. The increased use of telehealth platforms has also shown promise in decreasing hospital readmission for patients with cirrhosis and improving outcomes.[67,68]

PALLIATIVE CARE CONSIDERATIONS FOR THE HOSPITALIZED PATIENTS WITH CIRRHOSIS

The lack of including palliative care in the 2019 AASLD quality measures in cirrhosis is rather proof of a rapidly growing field, as both AASLD and AGA published recent guidance[9,10] regarding the importance of primary and specialty palliative care in the management of patients with advanced liver disease. Both documents highlight the unmet demand for palliative care and include great resources that hospital providers can use in their practice, from introducing the benefits of palliative care to their patients to improving their palliative care skills specifically to address the needs of patients with cirrhosis.

There is reluctance to start palliative care discussions in the inpatient setting as likely there is no longitudinal relationship between patient and providers, but hospitalizations and transitions of care, especially escalation of care to medical intensive care unit, are sentinel events that should prompt goals of care conversations.[10] Hospitalized patients with cirrhosis must cope with unexpected deteriorations in their disease course, new or worsening cirrhosis complications, frequent readmissions, invasive procedures, medication side effects, and they should be given the opportunity to reassess if the medical care they receive remains concordant with their wishes.

All providers caring for patients with cirrhosis should feel comfortable applying primary palliative care principles within their practice (assess/treat symptoms, foster communication around goals of care, and advance care planning) and collaborate with gastroenterology/hepatology specialists regarding prognosis and LT candidacy.[10] As specialty palliative care is more available inpatient rather than outpatient in most health care systems, patients with complex needs (eg, difficult goals of care discussions and family dynamics, management of refractory symptoms) could access palliative care consultation during hospitalization, but this requires active involvement of the hospital team to explore the need to involve palliative care consultants.

In summary, the management of hospitalized patients with cirrhosis is increasingly complex. High-value inpatient care requires adherence to best practices, and integration of QI processes with clinical care keeps us accountable to achieve and maintain a higher standard of health care delivery.

CONFLICTS OF INTEREST

The authors have no conflicts to report.

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