REVIEW ARTICLE

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Treatment of Patients with Cirrhosis

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Cirrhosis is the irreversible fibrosis of the liver, the end stage of a final shared pathway in chronic damage to a major vital organ. It is the 8th leading cause of death in the United States and the 13th leading cause of death globally, with worldwide mortality having increased by 45.6% from 1990 to 2013.[1] The pathophysiological features of cirrhosis involve progressive liver injury and fibrosis resulting in portal hypertension and decompensation, including ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, variceal hemorrhage, the hepatorenal syndrome, and hepatocellular carcinoma. This article reviews the practical treatment of patients with cirrhosis, with a focus on recent developments. Our recommendations are based on results from clinical trials, when available, and on current clinical practice when controlled trials have not been conducted.

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EPIDEMIOLOGY AND DIAGNOSIS

The major causes of cirrhosis include chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, alcoholism, and nonalcoholic steatohepatitis. HCV infection and nonalcoholic steatohepatitis are the causes that are primarily responsible for the growing burden of cirrhosis in health care. Owing to the increasing prevalence of nonalcoholic fatty liver disease, cirrhosis related to nonalcoholic steatohepatitis is predicted to surpass HCV-related cirrhosis as the most common indication for orthotopic liver transplantation in the United States. Chronic injuries to the liver are synergistic; it is not unusual to see patients with cirrhosis that is due to a combination of chronic viral hepatitis, obesity, and alcoholism.

A diagnosis of compensated cirrhosis is associated with a risk of death that is 4.7 times as high as the risk in the general population, and decompensated cirrhosis is associated with a risk that is 9.7 times as high.[2] The average life expectancy of a patient with compensated cirrhosis is 10 to 13 years, and the average life expectancy may be as low as 2 years if there is decompensation.[3] Among patients with alcoholic cirrhosis, 65% of the patients who abstain from drinking alcohol are alive at 3 years, as compared with 0% who continue drinking alcohol.[4]

The economic burden of cirrhosis in the United States is substantial, with annual direct costs exceeding $2 billion and indirect costs exceeding $10 billion.[5] Annual costs increase with decompensation, with costs of $2,400 for the treatment of diuretic-sensitive ascites, $24,800 for the treatment of diuretic-refractory ascites, $25,600 for the treatment of variceal hemorrhage, $16,400 for the treatment of hepatic encephalopathy, and $44,200 for the treatment of hepatocellular carcinoma.

An algorithm for the clinical diagnosis of cirrhosis is provided in Figure 1, and in Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org. In patients with compensated cirrhosis, the 10-year probabilities of ascites, hepatic encephalopathy, and gastrointestinal bleeding are 47%, 28%, and 25%, respectively.[6] These are ominous landmarks; 15% of patients who

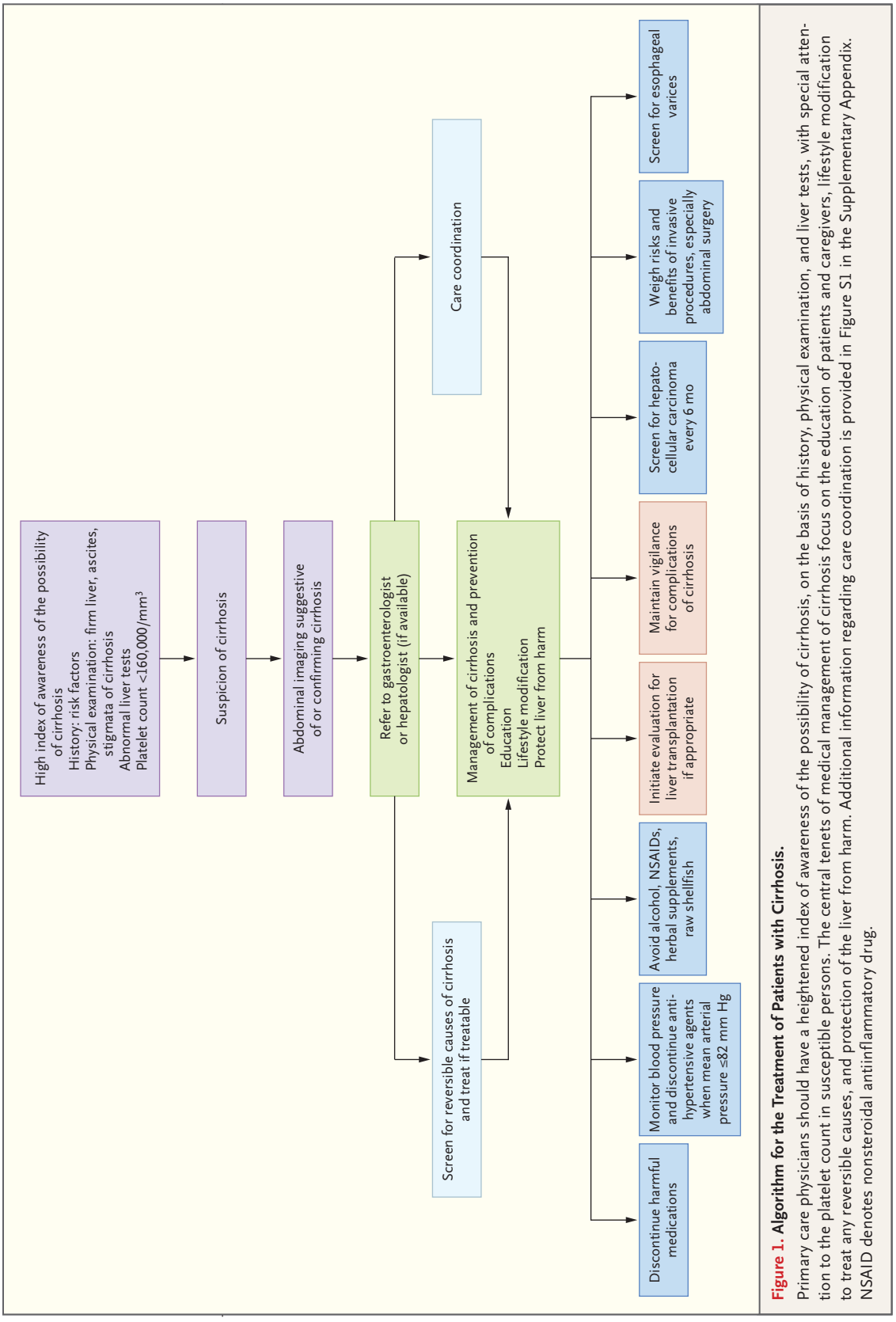

Figure 1. Algorithm for the Treatment of Patients with Cirrhosis.

Primary care physicians should have a heightened index of awareness of the possibility of cirrhosis, on the basis of history, physical examination, and liver tests, with special attention to the platelet count in susceptible persons. The central tenets of medical management of cirrhosis focus on the education of patients and caregivers, lifestyle modification to treat any reversible causes, and protection of the liver from harm. Additional information regarding care coordination is provided in Figure S1 in the Supplementary Appendix. NSAID denotes nonsteroidal antiinflammatory drug.

receive a diagnosis of ascites die within 1 year, and 44% within 5 years.[7] Esophageal varices develop in more than one third of patients with cirrhosis within 3 years after diagnosis.[8] The annual incidence of hepatocellular carcinoma is 5%. The median survival among patients with limited hepatocellular carcinoma is approximately 2 years, and the median survival among those with advanced hepatocellular carcinoma is approximately 6 months.[9]

NUTRITION

Malnutrition occurs in 20 to 60% of patients with cirrhosis, and current guidelines recommend a daily protein intake of 1.0 to 1.5 g per kilogram of dry body weight.[10] High-protein diets are well tolerated and are associated with sustained improvement in mental status, whereas restriction of protein intake does not have any beneficial effect in patients with acute hepatic encephalopathy.[11] Therefore, we avoid protein restriction in patients, regardless of whether they have a history of hepatic encephalopathy.

Because of a hypermetabolic state, overnight fasting contributes to muscle depletion in patients with cirrhosis. Late-evening meals may improve nitrogen balance without exacerbating hepatic encephalopathy. A randomized trial involving patients with cirrhosis who received two cans of high-protein nutritional supplement (474 ml per can) nightly showed that nocturnal supplementation resulted in sustained increases in total body protein.[12]

A 2000-mg limit in daily sodium intake is mandatory in the treatment of ascites. Dietary counseling is particularly useful for patients and the people who cook for them. We recommend fluid restriction only when the serum sodium concentration is less than 120 mmol per liter. Successful fluid restriction requires that the fluid intake be less than urinary volume, but the urinary volume is typically so low in patients with cirrhosis that adequate fluid restriction is nearly impossible to achieve.

MEDICATIONS

ANTIHYPERTENSIVE AGENTS

With cirrhosis, the risks of medications must be weighed against the benefits (Table S2 in the Supplementary Appendix). Patients with cirrhosis who have a history of hypertension gradually become normotensive and eventually hypotensive as cirrhosis progresses (Fig. 2). Studies of blood pressure in patients with cirrhosis and ascites showed that a mean arterial pressure of 82 mm Hg or less was the single variable that was most strongly correlated with a reduced probability of survival.[13] The probability of survival among patients with a mean arterial pressure of 82 mm Hg or less was 20% at 24 months and 0% at 48 months, as compared with 70% at 24 months and 50% at 48 months among patients with a mean arterial pressure of more than 82 mm Hg. In a similar study, hypotension with a cardiac index below 1.5 liters per minute per square meter of body-surface area predicted the development of the hepatorenal syndrome and a decreased probability of survival among patients with cirrhosis and ascites.[14] Because of these hemodynamic changes, antihypertensive agents should be discontinued in patients who have decompensated cirrhosis with ascites or hypotension.[8,15]

BETA-BLOCKERS

Nonselective beta-blockers reduce portal pressures and are used in the primary and secondary prophylaxis of variceal hemorrhage.[16,17] However, various studies caution the use of beta-blockers in situations such as decompensated cirrhosis with refractory ascites,[18,19] spontaneous bacterial peritonitis,[20] and severe alcoholic hepatitis.[21]

These studies led to the "window hypothesis," which postulates that beta-blockers are associated with higher rates of survival only within a clinical window (Fig. 3).[8] In patients who have early cirrhosis without moderate-to-large varices, beta-blockers do not prevent the development of varices and also result in adverse effects.[22] The clinical window opens when moderate-to-large esophageal varices develop, with or without variceal bleeding, and beta-blockers are indicated for primary and secondary prophylaxis of variceal bleeding.[16,17] Increasingly, evidence suggests that the clinical window for beta-blockers closes and that they are no longer effective when refractory ascites, hypotension, the hepatorenal syndrome, spontaneous bacterial peritonitis, sepsis, or severe alcoholic hepatitis develops, owing to unfavorable hemodynamic effects in advanced cirrhosis.[8,15,18-21]

The use of invasive measurement of the hepatic

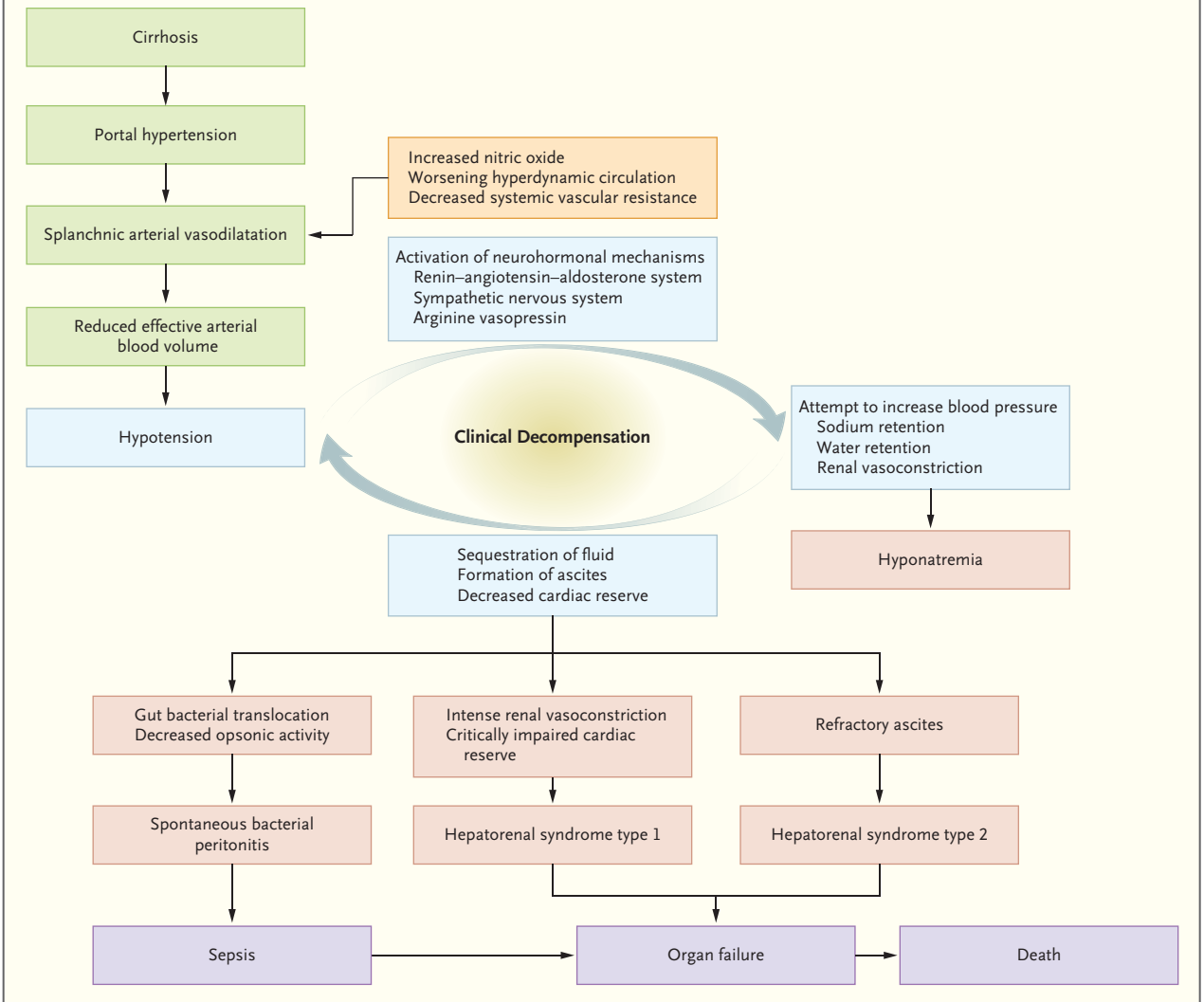

Figure 2. Pathophysiological Features of Hypotension in Patients with Cirrhosis.

The peripheral arterial vasodilatation hypothesis states that as cirrhosis progresses, systemic vasodilatation from reduced systemic vascular resistance and the sequestration of fluid into the peritoneal cavity result in arterial underfilling and activation of salt-retaining neurohormonal mechanisms such as the sympathetic nervous system and the renin–angiotensin–aldosterone system to counteract low arterial blood pressures. Consequently, although plasma and blood volume are increased, effective arterial blood volume is decreased. These circulatory changes, along with the development of sodium and water retention and the formation of ascites, are an adaptive compensatory response aimed at maintaining adequate cardiac output and organ perfusion.

venous pressure gradient to guide beta-blocker use may predict clinical efficacy and provide useful prognostic information.[22] However, its routine use is not necessary in the decision to initiate beta-blocker therapy, and its clinical indications in the practical treatment of patients with cirrhosis are limited.[23]

In patients with stable hypotension, midodrine may improve splanchnic and systemic hemodynamic variables, renal function, and sodium excretion. The combination of octreotide and midodrine is used for the treatment of type 1 hepatorenal syndrome.[24] In patients without the hepatorenal syndrome, midodrine was shown to increase urinary volume, urinary sodium excretion, and mean arterial pressure and was associated with a reduction in overall mortality.[25] It remains to be studied whether the simultaneous use of beta-blockers for the prophylaxis of variceal bleeding and midodrine for the

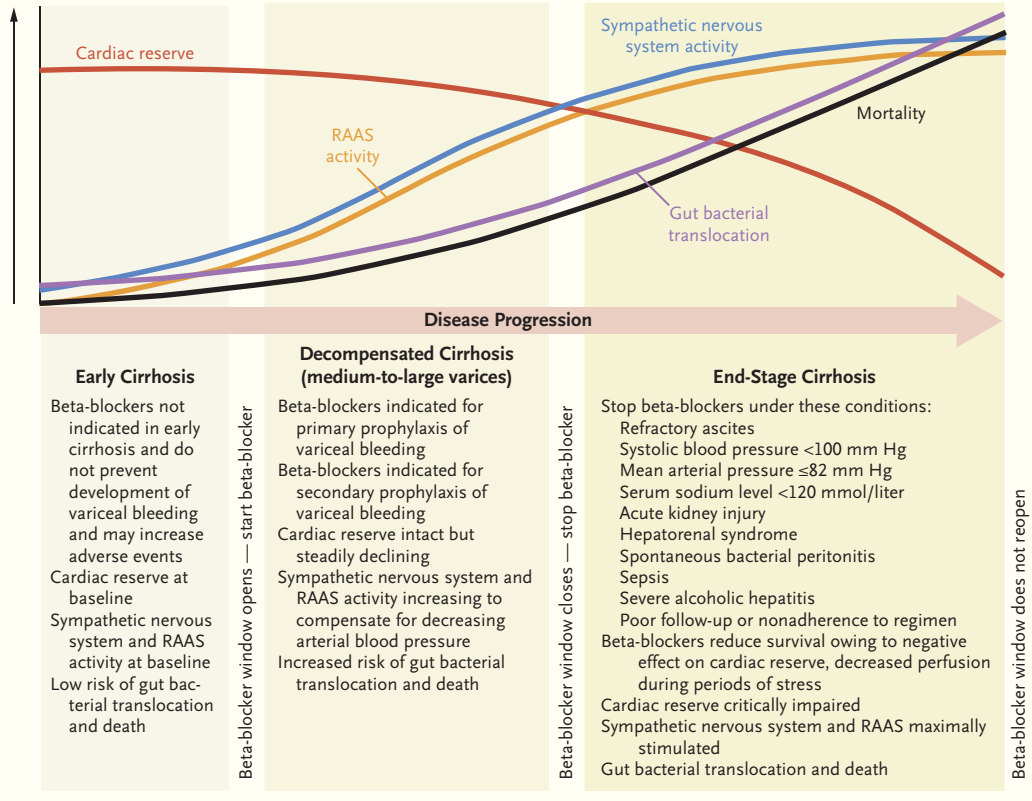

Figure 3. Window Hypothesis.

Adapted, with permission, from Krag et al.[8] The "window hypothesis" postulates that beta-blockers increase the survival rate only within a clinical window. In patients who have early cirrhosis without moderate-to-large varices, beta-blockers do not prevent the development of varices and may result in adverse effects. The clinical window for beta-blockers opens when patients have moderate-to-large esophageal varices with or without variceal bleeding, and beta-blockers are indicated for primary and secondary prophylaxis of variceal bleeding. The clinical window for beta-blockers closes when patients have refractory ascites, hypotension, the hepatorenal syndrome, spontaneous bacterial peritonitis, or sepsis, owing to unfavorable hemodynamic effects in advanced cirrhosis. RAAS denotes renin–angiotensin–aldosterone system.

improvement of hemodynamic variables may be beneficial in selected patients.

Although the role of beta-blockers in patients with end-stage cirrhosis remains controversial, there is increasing awareness of the role of blood pressure in the survival of patients with cirrhosis.[15] The most recent Baveno VI consensus guidelines regarding portal hypertension recommend the discontinuation of beta-blockers when the systolic blood pressure is less than 90 mm Hg, the serum sodium concentration is less than 120 mmol per liter, or acute kidney injury has developed.[23] Our practice is to discontinue beta-blockers when the systolic blood pressure is less than 100 mm Hg, because a blood pressure of 100/73 mm Hg is required to obtain the mean arterial pressure of 82 mm Hg that has been described to correlate with survival.[13]

PAIN MANAGEMENT

Analgesic agents must be carefully selected in patients with cirrhosis. Because of the risk of acute renal failure and gastrointestinal bleeding, nonsteroidal antiinflammatory drugs are contraindicated, except for low-dose aspirin in patients in whom the severity of cardiovascular disease exceeds the severity of cirrhosis. Opiates should be used cautiously or avoided, because they may precipitate or aggravate hepatic encephalopathy. Tramadol is safe in low doses, and topical medications such as lidocaine patches are generally safe.

Acetaminophen is effective and safe in patients with liver disease, provided that the patient does not drink alcohol. The Food and Drug Administration has recommended limiting the total daily dose of acetaminophen to 4 g in all patients. Although this dose is theoretically safe in patients with cirrhosis,[26] many hepatologists limit acetaminophen to a dose of 2 g daily.

PROTON-PUMP INHIBITORS

Proton-pump inhibitors are vastly overprescribed in hospitalized patients with cirrhosis, often without any documented indication. A large study involving patients with cirrhosis who were hospitalized with an initial infection showed that the risk of subsequent infection was increased among patients taking proton-pump inhibitors and those receiving long-term antibiotic agents as prophylaxis for spontaneous bacterial peritonitis.[27] Indiscriminate use without appropriate indications should be avoided.

SEDATIVES

Benzodiazepines should be avoided in patients with hepatic encephalopathy. For patients with alcoholic hepatitis or cirrhosis in whom severe symptoms of acute alcohol withdrawal develop, short-acting benzodiazepines such as lorazepam and oxazepam are preferred in order to minimize the risk of oversedation. For patients with insomnia, hydroxyzine at a dose of 25 mg at bedtime may be a reasonable alternative and has been studied in a small, randomized trial.[28] We have prescribed trazodone at a dose of 100 mg at bedtime with greater success than hydroxyzine for the treatment of insomnia.

STATINS

3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) can be safely started and continued in patients with cirrhosis. Statins have established cardiovascular benefits in the treatment of nonalcoholic fatty liver disease.[29] Large trials lasting for 5 to 10 years have shown that the incidence of major cardiovascular events is 33% lower among patients who take statins than among those who receive placebo.[30] The overall rate of statin-induced acute liver failure is 0.2 to 1 cases per million persons taking statins, although estimates of patients who do not receive statins because of concerns about hepatotoxicity range from 10 to 30%.[31] Data from the Drug-Induced Liver Injury Network corroborated the exceedingly low likelihood of hepatic injury due to statins, with only 22 cases of drug-induced liver injury being attributed to statins over an 8-year period.[32] Routine monitoring of the alanine aminotransferase level in patients who use statins is no longer recommended.

VAPTANS

Selective vasopressin V_2–receptor antagonists (vaptans) have been evaluated for use in hyponatremia and ascites. A large, placebo-controlled study involving patients with cirrhosis and ascites showed that although satavaptan alleviated hyponatremia, mortality was higher among patients with recurrent ascites who were receiving satavaptan than among those who were receiving placebo.[33] Because of these findings as well as hepatotoxicity reported with respect to tolvaptan,[34] the use of vaptans in patients with cirrhosis and ascites is not recommended.

INVASIVE PROCEDURES

INTRAABDOMINAL SURGERY

In patients with cirrhosis, the risks of invasive procedures must be weighed against the benefits (Table S3 in the Supplementary Appendix). Intraabdominal surgery should be avoided in patients with decompensated cirrhosis unless the procedure confers more benefit than risk, as is the case with orthotopic liver transplantation. Cholecystectomy in particular is associated with high morbidity and mortality among patients with decompensated cirrhosis.

The Model for End-Stage Liver Disease (MELD) score can be used to predict 30-day postoperative mortality among patients who are planning to undergo nontransplantation surgical procedures. A MELD score of more than 14 (on a scale from 6 to 40, with higher scores indicating more advanced liver disease) is better than Child–Pugh class C in predicting a high risk of death associated with abdominal surgery.[35] A study of surgical mortality estimated an increase in mortality of 1 percentage point per MELD point among patients with a MELD score of less than 20 and an additional increase in mortality of 2 percentage points per MELD point among those with a MELD score of more than 20, with an overall mortality of 23.9% among patients undergoing nontransplantation intraabdominal surgery.[36]

A large study involving patients undergoing major digestive, orthopedic, or cardiac surgery

showed on multivariate analysis that MELD score, age, and the American Society of Anesthesiologists classification were independent predictors of surgical mortality.[37] An online surgical risk calculator has since been developed that uses these predictors (www.mayoclinic.org/medical-professionals/model-end-stage-liver-disease/post-operative-mortality-risk-patients-cirrhosis).

ENDOSCOPY

Endoscopic procedures are relatively safe in patients with cirrhosis, and antibiotic prophylaxis is not indicated for routine endoscopy, except for specific clinical scenarios such as acute gastrointestinal hemorrhage.[38] However, percutaneous endoscopic gastrostomy is associated with a high risk of death among patients with ascites and is contraindicated in that population.

PARACENTESIS

Paracentesis is particularly helpful in all patients with new-onset ascites, in patients with existing ascites who are admitted to the hospital, and in patients with clinical deterioration (fever, abdominal pain, hepatic encephalopathy, leukocytosis, renal failure, or metabolic acidosis). Spontaneous bacterial peritonitis is diagnosed when the neutrophil count in ascitic fluid is at least 250 cells per cubic millimeter and secondary bacterial peritonitis is ruled out.

Paracentesis is relatively safe, even in patients with marked coagulopathy, including an international normalized ratio as high as 8.7 and a platelet count as low as 19,000 per cubic millimeter.[39] Bloody ascitic fluid is typically due to a traumatic paracentesis, but excessive blood is suggestive of ruptured hepatocellular carcinoma; this condition is often associated with hemodynamic instability and requires urgent embolization.

In patients with diuretic-sensitive ascites, the removal of 5 liters of fluid is sufficient to reduce intraabdominal pressure, at which point sodium restriction and diuretics are continued. With diuretic-refractory ascites, the goal is to remove as much fluid as possible. Patients in whom more than 8 liters of fluid must be removed every 2 weeks are frequently found to be nonadherent to the prescribed dietary regimen.

It is important not to delay paracentesis in patients with suspected spontaneous bacterial peritonitis. One study showed that diagnostic paracentesis that was performed within 12 hours after the time of first encounter with a physician was associated with increased short-term survival rates. Delayed paracentesis was associated with a risk of death that was 2.7 times as high as the risk associated with early paracentesis.[40] Each hour of delay was associated with a 3.3% increase in in-hospital mortality.

Although colloid replacement is not necessary after paracentesis of less than 5 liters of fluid, it is recommended that 6 to 8 g of albumin should be given per liter of fluid removed in the case of larger-volume paracentesis.[41] In patients with spontaneous bacterial peritonitis, it is recommended that albumin at a dose of 1.5 g per kilogram be given within 6 hours after diagnosis, with another 1 g per kilogram administered on day 3.[42] The use of albumin in patients with spontaneous bacterial peritonitis can be restricted to patients who have a higher risk of death (serum creatinine level, >1 mg per deciliter [90 μmol per liter]; blood urea nitrogen, >30 mg per deciliter [10.5 mmol per liter]; or bilirubin level, >4 mg per deciliter [68 μmol per liter]), because the probability of survival is not higher when albumin is given to patients who have a low risk of death.[43]

COMPLICATIONS

Major complications from cirrhosis are described in Table 1, and lesser complications and miscellaneous symptoms are described in Table S4 in the Supplementary Appendix. Many lesser "nuisance" symptoms of cirrhosis are underreported by patients, are underrecognized by clinicians, decrease quality of life, and can be challenging to manage.

Elevated portal pressures have been observed in one third of patients with nonalcoholic fatty liver disease without cirrhosis, correlating with the severity of steatosis.[44] Weight loss may reduce portal pressure. Obesity, diabetes, nonalcoholic steatohepatitis, and nonalcoholic fatty liver disease are independently associated with an increased risk of hepatocellular carcinoma,[45] although hepatocellular carcinoma occurs primarily in patients with cirrhosis.[46] Nonalcoholic steatohepatitis can recur rapidly after orthotopic liver transplantation. Obesity is present in 17 to 43% of patients 1 year after orthotopic liver transplantation,[47] and cirrhosis related to nonalcoholic steatohepatitis can recur as early as 76 weeks after transplantation.[48] Combined orthotopic liver

Table 1. Major Complications of Cirrhosis.*

Complication	Presentation	Comments	Prevention
Ascites	Accumulation of fluid within peritoneal cavity owing to multiple circulatory, vascular, functional, biochemical, and neurohormonal abnormalities	Treated with combination of diuretics and sodium restriction; may require paracentesis or TIPS if refractory	Low-sodium diet; fluid restriction is often not beneficial
Cirrhotic cardiomyopathy	Normal-to-increased cardiac output and contractility; blunted response to cardiac stress	Alcoholism and hemochromatosis may have additional contribution	None
Hepatic encephalopathy	Sleep disturbance (common early symptom), asterixis, altered mental status, hyperactive deep-tendon reflexes, or coma; disorder can be clinically diagnosed when overt, although subclinical cases may be detected by the Trail Making Test	Treated with lactulose and rifaximin; measurement of ammonia is unreliable and should not be used to initiate or guide treatment	Avoid sedatives and opiates; protein restriction is not beneficial
Hepatic hydrothorax	Movement of ascitic fluid into pleural space through defect in diaphragm, usually on the right side	Avoid chest tubes because of risk of protein depletion, infection, and bleeding	Low-sodium diet; control of ascites
Hepatocellular carcinoma	Frequently asymptomatic; should be suspected when decompensation suddenly develops in a patient with previously compensated cirrhosis; other signs and symptoms include pain, early satiety, jaundice, and palpable mass; may rupture and cause life-threatening hemoperitoneum	May develop in absence of cirrhosis in patients with HBV infection and nonalcoholic steatohepatitis or nonalcoholic fatty liver disease; highest risk occurs among patients with HBV or HCV infection, nonalcoholic steatohepatitis, or hemochromatosis	Imaging every 6 mo with abdominal ultrasonography, CT, or MRI; addition of alpha-fetoprotein increases effectiveness of surveillance
Hepatopulmonary syndrome	Triad of liver disease, increased alveolar–arterial gradient while the patient is breathing ambient air, and evidence of intrapulmonary vascular dilatations	No effective medical therapy; liver transplantation is necessary for treatment	None
Hepatorenal syndrome	Arterial vasodilatation in splanchnic circulation; end result of a sequence of reductions in renal perfusion induced by increasing hepatic injury	Volume depletion can mimic all the findings of hepatorenal syndrome	Avoid nephrotoxic agents; discontinue beta-blockers and antihypertensive agents in patients with refractory ascites or spontaneous bacterial peritonitis
Portal hypertensive gastropathy	Uncommon cause of substantial bleeding; diffuse mucosal oozing with no other lesions to account for bleeding and anemia	Severity is related to degree of underlying portal hypertension	None
Portal-vein thrombosis	Frequently asymptomatic; should be suspected when decompensation suddenly develops in a patient with previously compensated cirrhosis; may be associated with hepatocellular carcinoma	Anticoagulation is controversial and not currently recommended because of elevated bleeding risk among patients with cirrhosis	Prophylactic enoxaparin has been studied but is still controversial and not currently recommended
Portopulmonary hypertension	Pulmonary hypertension, associated with fatigue, exertional dyspnea, chest pain, syncope, or orthopnea	Difficult to treat with medical therapy; high perioperative mortality with liver transplantation	None
Spontaneous bacterial peritonitis	Fever, abdominal pain, abdominal tenderness, altered mental status, and sepsis	Early paracentesis is important; inoculate blood-culture bottles with ascitic fluid at bedside	Prophylactic antibiotics in selected situations (i.e., gastrointestinal bleeding, low protein ascites, history of spontaneous bacterial peritonitis)
Variceal hemorrhage	Abrupt major gastrointestinal bleeding, including hematemesis and melena	Treat with endoscopic band ligation; refractory bleeding can be treated with TIPS; transfuse to hemoglobin goal of 7 to 8 g per deciliter	Prophylactic endoscopic band ligation; nonselective beta-blockers may prevent bleeding but not the development of varices

* CT denotes computed tomography, HBV hepatitis B virus, HCV hepatitis C virus, MRI magnetic resonance imaging, and TIPS transjugular intrahepatic portosystemic shunt.

transplantation and sleeve gastrectomy may result in effective weight loss and fewer post-transplantation metabolic complications than liver transplantation alone, although long-term studies are needed.[49]

CLINICAL APPROACH

PROTECTING THE LIVER FROM HARM

Aside from the management of decompensation, the fundamental principles in the management of cirrhosis focus on education, lifestyle modification, protecting the liver from harm (Fig. 1), and care coordination. The liver has considerable regenerative potential, and "recompensation" and reversal of cirrhosis have been described in patients with alcoholic cirrhosis who abstained from alcohol, patients with HBV infection who underwent antiviral therapy, and patients with nonalcoholic steatohepatitis who underwent bariatric surgery.[50] A study involving patients with decompensated HCV cirrhosis who received direct-acting antiviral therapy showed that a sustained virologic response at 12 weeks after the completion of treatment was associated with decreases in the Child–Pugh class and MELD score.[51] Antiviral therapy in patients with HBV cirrhosis may reduce the risk of hepatocellular carcinoma.[52]

Public education efforts are needed to discourage obesity, needle sharing, and excessive alcohol consumption. Screening is very useful in high-risk groups. A study of screening for HBV infection revealed that 8.9% of Asian Americans in California were chronically infected, often unknowingly.[53]

It is recommended that patients undergo endoscopy for variceal screening and subsequently follow established guidelines for endoscopic surveillance.[54] Endoscopic band ligation is preferred in patients with medium-to-large esophageal varices. A nonselective beta-blocker can be considered if the patient does not have refractory ascites, spontaneous bacterial peritonitis, severe alcoholic hepatitis, or hypotension.

It is recommended that all patients with cirrhosis undergo surveillance for hepatocellular carcinoma with the use of abdominal ultrasonography or computed tomography every 6 months.[55] Serum measurement of the alpha-fetoprotein level in conjunction with abdominal ultrasonography may improve the effectiveness of surveillance for hepatocellular carcinoma.[56] Current guidelines do not support surveillance for hepatocellular carcinoma in patients without cirrhosis who have HCV infection, nonalcoholic fatty liver disease, or nonalcoholic steatohepatitis.

Antibiotic prophylaxis may reduce the risk of bacterial infection (including spontaneous bacterial peritonitis) and increase survival rates in selected scenarios. Among patients with a history of spontaneous bacterial peritonitis or among hospitalized patients with an ascitic-fluid protein level of less than 1.5 g of protein per deciliter of ascitic fluid, selective intestinal decontamination with trimethoprim–sulfamethoxazole or ciprofloxacin increases the rate of short-term survival and reduces the overall risk of bacterial infection[57,58]; norfloxacin is no longer available in the United States. Among patients with acute gastrointestinal bleeding, ceftriaxone at a dose of 1 g daily for 7 days is effective in the prophylaxis of bacterial infections, including spontaneous bacterial peritonitis.[38] It is important that routine antibiotic prophylaxis be otherwise avoided to minimize the risk of antibiotic-resistant infection.[27]

Patients with alcoholism are prone to relapse because of cravings and anxiety. We recommend baclofen for the suppression of alcohol cravings. A randomized trial involving patients with alcohol dependency and cirrhosis showed that 71% of patients receiving baclofen were able to maintain abstinence, as compared with 29% of patients receiving placebo.[59]

Patients with decompensated cirrhosis may ultimately require orthotopic liver transplantation. Evaluation for transplantation is indicated when the MELD score is 17 or more.

CARE COORDINATION

Patients with cirrhosis are plagued by frequent hospital readmissions for fluid overload, hepatic encephalopathy, or gastrointestinal hemorrhage. Such readmissions are costly, moderately predictable, frequently preventable, and associated with a risk of death. One study showed that 69% of patients had at least one nonelective readmission, including 14% who were readmitted within 1 week after discharge and 37% who were readmitted within 1 month.[60] The average rate was three hospitalizations per person-year, and 22% of the readmissions were potentially preventable. One patient was readmitted 40 times.

Care coordination is an increasingly popular

concept to improve quality and clinical outcomes while reducing readmission rates and expenditures. Care coordinators facilitate inpatient-to-clinic transitions, reconcile medications, call patients to prevent unnecessary visits to the emergency department, place "smart scales" in homes to monitor body weight remotely, facilitate interaction with other health care professionals, and arrange referrals to nursing facilities or hospice (Fig. S1 in the Supplementary Appendix). A recent study compared a traditional system involving family physicians and punctual consultation with a coordinated system involving a specialized team of nurses and hepatologists.[61] The results favored care coordination: 30-day and 12-month readmission rates were lower, as was 12-month mortality, and expenditures were 46% lower with care coordination than with the traditional system.

As health care expenditures continue to grow, the management of cirrhosis must involve prevention and mitigation of risk factors, accurate and timely diagnosis, appropriate nutritional support, avoidance of harmful medications and procedures, public education, and care coordination. We hope that by shifting our mentality from treating the complications of decompensated cirrhosis to preventing their development, the burden of cirrhosis will progressively decline.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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