Care of the Cirrhotic Patient

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KEYWORDS

• Cirrhosis • Antimicrobial therapy • Viral hepatitis • Hepatic decompensation

KEY POINTS

- The clinical manifestations of cirrhosis encompass a broad spectrum of conditions that reflect the consequences of increased portal pressures secondary to fibrosis and diminished hepatic synthetic function.
- Decompensated liver disease traditionally reflects the occurrence of ascites, gastrointestinal hemorrhage, or encephalopathy in the patient with cirrhosis.
- Antimicrobial management of patients with decompensated cirrhosis includes oral prophylaxis for bacterial peritonitis, nonabsorbable oral rifaximin for hepatic encephalopathy, and preemptive intravenous antibiotics in the face of acute gastrointestinal hemorrhage.
- After the development of hepatic decompensation, current hepatitis C antiviral therapy is no longer an option; such therapy is therefore strongly recommended in well-compensated patients with cirrhosis, and successful treatment may lead to improvement of liver function.
- Evaluation for liver transplantation should be initiated after the onset of clinical decompensation (ascites, encephalopathy, bleeding varices); onset of liver cancer; or after the Model for End Stage Liver Disease score exceeds 15.

INTRODUCTION

Cirrhosis occurs when chronic hepatocyte or bile duct injury causes progressive diffuse hepatic fibrosis with the development of regenerative nodules.[1] It is often difficult to label a patient as cirrhotic, because there may only be subtle changes in laboratory parameters. Current imaging modalities in the United States have variable sensitivity for detecting cirrhosis.[2] Physical and laboratory examination may aid in establishing the diagnosis including such signs as palmer erythema, spider angiomata, or splenomegaly, and thrombocytopenia and hypoalbuminemia. However, cirrhosis may occur in the absence of these examinations or laboratory findings, and these parameters are not pathognomonic.

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Cirrhosis can be presumed in patients with known chronic liver disease and evidence of decompensation including ascites, varices, or hepatic encephalopathy. Liver biopsy remains the gold standard when the clinical, laboratory, and imaging parameters are normal or equivocal. Liver biopsy as an assessment of fibrosis aids in identifying individuals at risk for developing further progressive liver disease. Liver biopsy is most useful in diagnosis with a validated fibrosis staging system, such as Ishak (0–6) or Metavir (0–4) scores.[2] Persons with minimal fibrosis (Metavir 0–1, Ishak 0–2) have low risk for complications and death during 10 to 20 years of follow-up, whereas the presence of bridging fibrosis (Metavir 3, Ishak 4) often predicts imminent progression to cirrhosis (Metavir 4, Ishak 5–6).[3] The risk of cirrhosis development in viral hepatitis C ranges from 5% to 25% during a 25- to 30-year period after virus acquisition.[4–6]

CIRRHOSIS AND ITS COMPLICATIONS

Evaluation of Cirrhosis

The Child-Turcotte-Pugh (CTP) score was initially developed for quantifying the risk of portal caval shunt surgery among alcoholic patients with cirrhosis but has subsequently been validated in patients with other forms of liver disease, including hepatitis C. It assesses the prognosis of chronic liver disease based on degree of abnormalities in bilirubin level, albumin level, the international normalized ratio for prothrombin time (INR), and the degree of hepatic encephalopathy and ascites. More than 30% of patients with CTP scores of 10 or more (class C) can be expected to die within 1 year.[4] In contrast, patients with CTP scores of 7 to 9 (class B) have an 80% chance of surviving 5 years, and those with CTP scores of 5 to 6 (class A) have a 90% chance of surviving more than 5 years without transplant.[7]

The Model for End-Stage Liver Disease (MELD) score was originally developed by investigators at Mayo Clinic to assess prognosis among patients undergoing transjugular intrahepatic portosystemic shunts.[8] The MELD score is computed-based on serum bilirubin (S-bilirubin); serum creatinine (S-creatinine); and INR.[9] The result is a score from 6 to 40, with respective 3-month survival from 90% to 7%.[8] This model assesses prognosis (survival estimates) in patients with cirrhosis, and in the United States is used to prioritize patients for donor allocation.[10,11] The MELD score is useful in predicting short-term survival and the risk of postoperative mortality.[4,5]

DECOMPENSATED CIRRHOSIS

Patients with cirrhosis with Child-Pugh scores less than seven or MELD scores less than 15 who do not have complications caused by hepatic dysfunction are said to have compensated disease.[12] The occurrence of ascites, gastrointestinal hemorrhage, or encephalopathy signals the onset of decompensation in a patient with cirrhosis. Patients with advanced fibrosis (Metavir score of F3 or F4) progress to decompensated liver disease at a rate of approximately 5% per year, progress to hepatocellular carcinoma (HCC) at a rate of 1% to 2% per year, and progress to death at a rate of 3% to 4% per year.[13–16] The 5-year survival of patients with decompensated cirrhosis is 50% compared with 91% in those with compensated cirrhosis.[14]

Many of the physiologic consequences and clinical sequelae of decompensated liver disease are related to alteration in blood flow through the liver. A buildup of fibrotic scar tissue and intrahepatic vasoconstriction in the liver with decrease in nitric oxide can cause reduction of blood flow into the liver. This phenomenon causes blood to back up into the many vessels within the splanchnic circulation that, in turn, results in many of the complications related to decompensation.[17,18]

A patient should be considered for transplantation after the onset of clinical decompensation or after the MELD score exceeds 15.[19] Cirrhotic complications that represent manifestations of decompensation may include the following[20]:

- Ascites
- Hepatic encephalopathy
- Hepatorenal syndrome (resulting from vasoconstriction of the renovascular system leading to renal insufficiency)
- Hepatic hydrothorax (ascitic fluid seeping into the pleural space caused by negative pressure and the porous diaphragm)
- Spontaneous bacterial peritonitis (SBP) caused by dysfunction of the intestinal barrier leading to infection in the low-protein ascitic fluid
- Portopulmonary hypertension caused by thrombotic remodeling of the pulmonary vasculature leading to resistance to flow into the lungs
- Hepatopulmonary syndrome with vasodilatation of the pulmonary arteries leading to shunting and poor oxygenation
- Development of HCC that also, by convention, represents a manifestation of decompensation.

VARICES

A response to reduced blood flow into the liver is the development of collateral vessels. These vessels grow mostly in mucosal junctions with potential resultant varices in the esophagus, stomach, and rectum. Variceal bleed represents the most common lethal complication of cirrhosis. Independent predictors of varices include elevated MELD score; low platelet count (<93,000/mm^3); elevated aspartate aminotransferase (>1.34 times upper limit of normal); and total bilirubin higher than 1 mg/dL.[21] A total of 40% of compensated patients with cirrhosis and 85% of patients with decompensated cirrhosis have varices.[22] Esophageal varices develop in 35% to 80% of patients with cirrhosis, and bleeding occurs in 25% to 40% of those with varices.[23] Patients with advanced fibrosis should be monitored periodically for varices using esophagogastroduodenoscopy (EGD).[24] Those with no varices should have repeat EGD performed at 3 years for well-compensated liver disease and at 1 year for decompensated disease. Patients with small varices may be observed with repeat EGD in 2 years for well-compensated disease and at 1 year for decompensated disease. Patients with medium (<30% of esophageal circumference) or large (>30%) varices who have no red wales (indicating impending bleeding) should receive β-blocker treatment with consideration for endoscopic band ligation.[25,26] Any patient with red wales should be given β-blocker treatment and be treated with esophageal band ligation. Repeat EGD interval for patients undergoing band ligation should be every 2 to 3 weeks until elimination.[25,26]

Patients with bleeding esophageal varices have a 90-day mortality of 30%.[13,23] Acute bleeding episodes are managed with splanchnic vasoconstriction with intravenous octreotide and endoscopic band ligation of varices.[27] Transjugular intrahepatic portosystemic shunt is used as a means of managing bleeding refractory to endoscopic attempts at bleeding control. The procedure is a means of stenting from the portal to the hepatic vein, reducing the resistance created by the cirrhotic liver to relieve pressure in venous collaterals/varices.[28] Patients whose hepatic vein portal gradient is decreased to less than 12 mm Hg have a lower probability of developing recurrent variceal hemorrhage, and a lower risk of developing ascites, SBP, and death. At the same time, such a shunt may increase the probability of hepatic encephalopathy,[29,30] and

posttransjugular intrahepatic portosystemic shunts mortality increases with higher MELD scores.

ASCITES AND SBP

Lymphatic drainage is supplemented by blood flow from the peritoneal space into the splanchnic circulation leading to decreased fluid absorption along the peritoneal surface, resulting in ascites.[31] Complications of ascites include hepatorenal syndrome, hepatic hydrothorax, and SBP. Because of the potentially lethal nature of SBP, a diagnostic paracentesis is indicated with any change in a cirrhotic's health status including any hospitalization, a rapid increase in ascites, abdominal discomfort, fever or relative leukocytosis, change in mental status, or gastrointestinal bleeding. Therapeutic taps should be performed only in the case of discomfort or shortness of breath caused by fluid overload and not for cosmetic reasons. A strict low-salt diet (<2000 mg/day) and gentle up-titration of diuretics must be emphasized to prevent excessive reliance on paracenteses.

SBP is diagnosed by examining the ascitic fluid: greater than 250 polymorphonuclear cells/mL, or a positive culture result are indicative of SBP. Paracentesis at the time of hospital admission is important because a high proportion of patients with ascites have SBP at the time of admission, whether or not fever or abdominal discomfort is present, and SBP is associated with marked morbidity and mortality. Paracentesis is very safe regardless of the patient's degree of coagulopathy. There is no need to transfuse fresh frozen plasma or platelets before undergoing the procedure, because these measures do not reduce the low bleeding risk associated with paracentesis.[32]

Cell counts on the fluid should be performed and fluid should be injected directly into bedside culture bottles, because false-negative results occur in 40% to 50% with improper culture technique. Albumin replacement is required if the patient's creatinine level is elevated or if more than 5 L of fluid is removed, because such replacement significantly reduces the morbidity and mortality associated with postparacentesis circulatory dysfunction.[33]

Literature from 20 years ago suggested that less than half of those in whom SBP develops can be expected to survive 1 year.[34,35] The ascitic fluid polymorphonuclear leukocyte count is more rapidly available than the culture and seems to be accurate in determining the need for empiric antibiotic treatment.[36,37] Delaying antimicrobial treatment until the ascitic fluid culture grows bacteria may prove lethal because of overwhelming infection.

Therapy consists of a 5-day course of intravenous cefotaxime or other cephalosporin.[38–40] For β-lactam allergy, ciprofloxacin can be considered although the incidence of fluoroquinolone resistance is increasing and alterations in therapy may be needed based on ascitic fluid cultures. Recent studies emphasize an increased resistance to cephalosporins and suggest that first-line therapy should include meropenem or piperacillin-tazobactam.[41,42]

The current algorithm for therapy remains initial empiric therapy with cefotaxime or a similar third-generation cephalosporin, with modifications in this initial empiric therapy only if the patient has a prior history of peritonitis with resistant organisms. Similarly, such empiric therapy requires modification pending cultures that demonstrate resistant bacteria or continued evidence of infection (persisting white cell count elevation or persistent bacteria on repeat paracentesis) necessitating the use of broad-spectrum antibiotic regimens. Repeat paracentesis should be performed 72 hours after treatment initiation to check for white blood cell response; absence

of response may suggest the presence of an organism with drug resistance or an alternate diagnosis.[40]

Early onset albumin infusions have been shown to reduce mortality through reduction of renal impairment. One study showed a reduction in 60-day mortality from 29% with cefotaxime alone to 10% with cefotaxime plus 1.5 g/kg albumin administered within 6 hours of SBP diagnosis, followed by 1 g/kg on Day 3.[37]

Primary and Secondary SBP Prophylaxis

Antibiotic prophylaxis with ciprofloxacin (750 mg/week) has been shown to prevent SBP in patients with ascites, with one classic study showing a 6-month incidence of SBP of 4% with ciprofloxacin versus 22% with placebo.[43] When first described, the mortality of SBP exceeded 90%; however, with early recognition of the disease and prompt and appropriate antibiotic therapy, mortality has been reduced to around 30%.[41] Alternative antibiotics for prophylaxis are norfloxacin and trimethoprim-sulfamethoxazole. The potential detriment of prophylaxis is a demonstrated increased incidence of fluoroquinolone resistance among patients with cirrhosis patients.[42] The guidelines by the American Association for the Study of Liver Diseases weigh the benefits and risk of antibiotic prophylaxis[44]; there is a strong recommendation for prophylaxis in patients after an occurrence of SBP, yet stopping short of a strong recommendation for primary prophylaxis in patients with cirrhosis with ascites and low ascitic protein (<1 g/dL) who do not have a prior history of infection. Primary prophylaxis studies found no significant difference in the incidence of infections, including SBP, with norfloxacin or ciprofloxacin treatment but significantly lower incidence of gram-negative infections.[45] Intermittent or weekly dosing may select resistant flora more rapidly.[46] Daily dosing of this drug combination is recommended rather than intermittent dosing.[44] Pharmacologic acid suppression with proton pump inhibitors has been demonstrated to increase the incidence of SBP.[47]

ANTIBIOTIC PROPHYLAXIS IN GASTROINTESTINAL BLEED

Antibiotic therapy is an integral part in the management of patients with cirrhosis and gastrointestinal bleeding, because several randomized controlled trials and two meta-analyses have demonstrated a significant reduction in bacterial infections and overall mortality and mortality with this intervention.[48,49] Gastrointestinal hemorrhage is the most frequently overlooked indication for antibiotic prophylaxis.[50] Intravenous ceftriaxone for 7 days or twice-daily oral norfloxacin for 7 days should be given to prevent bacterial infections in patients with cirrhosis and gastrointestinal hemorrhage.[44] Ceftriaxone is the preferred agent because of an increase in quinolone-resistant bacteria in the cirrhotic population. Intravenous ceftriaxone was far superior to oral norfloxacin in the prophylaxis of spontaneous bacteremia or SBP in patients with advanced cirrhosis and hemorrhage.[51]

BACTERIAL INFECTIONS IN CIRRHOSIS

Infection-related mortality ranges from 7% to 40%.[52] Polymorphonuclear leukocyte dysfunction is a crucial multifactorial parameter leading to infection predisposition. Complement deficiency has been attributed to decreased production from a failing liver and to increased consumption because of a constant acute phase response observed in cirrhosis, related to the endotoxin load.[53,54] C3 deficiency is a significant predictor of mortality.[55]

The death rate for bacteremia and sepsis in patients with cirrhosis is higher than noncirrhotics and highest in alcoholic patients with cirrhosis.[56,57] Mortality after septic

shock ranges from 55% to 100% and is closely related to the development of renal failure.[58,59] Mortality from respiratory infections is more than 40% with increased Child-Pugh stage representing a risk factor for mortality.[45] Fatality rate for meningitis exceeds 50% with the most common pathogens including *Streptococcus pneumoniae*, *Escherichia coli*, and *Listeria monocytogenes*.[60,61]

The most common bacteria leading to infection in cirrhosis are gram-positives including *Staphylococcus aureus*. These occur most commonly in compensated patients with cirrhosis. Methicillin resistance is progressively more common in the presence of decompensation.[62] *E coli* is the most common cause of infection in Childs C patients, accounting for 20% of urinary infections, with mortality from infections of 48%.[63,64] *Clostridium* infections occur with a higher incidence and a worse prognosis in patients with cirrhosis compared with noncirrhotics (54%–65% vs 19%).[65] *Mycobacterium tuberculosis* has an increased incidence, poorer prognosis, and an increased rate of resistance in patients with cirrhosis, with fatality up to 48%.[66]

In patients with cirrhosis, adrenal insufficiency may develop during sepsis.[67] The 250-μg adrenocorticotropic hormone stimulation test or direct free cortisol measurement or its surrogates may be useful measurements to define adrenal insufficiency in patients with cirrhosis, but further studies are needed to clarify this observation. One smaller study concluded that hydrocortisone (50 mg intravenously every 6 hours) administration in patients with cirrhosis with sepsis was associated with a significantly higher frequency of shock resolution and a higher survival rate.[68]

HEPATIC ENCEPHALOPATHY

The original detection of overt hepatic encephalopathy was diagnosed by the observation of hand asterixis (also known as liver flapping or flapping tremor). It is caused by the shunting of gut-derived neuroactive substances that cross the blood-brain barrier; these substances are mostly nitrogen based and act as inhibitory neurotransmitters. Precipitating factors for hepatic encephalopathy include gastrointestinal bleeding; infection (including SBP); vascular thrombosis; HCC; and narcotics/sedating medications.[69] Traditional but non–Food and Drug Administration approved treatments for hepatic encephalopathy include lactulose or other nonabsorbable sugars, which cause osmotic diarrhea and movement of nitrogen compounds out of the gut; and use of antibiotics, such as neomycin and metronidazole, which change the gut flora.

A recent phase III trial showed that, compared with placebo, the nonabsorbable antibiotic rifaximin administered at 550 mg twice daily was associated with a statistically significant reduction in episodes of breakthrough hepatic encephalopathy in patients in remission from recurrent hepatic encephalopathy (breakthrough episodes occurred in 22.1% of patients taking rifaximin vs 45.9% with placebo; $P < .001$).[70] More than 90% of patients in the trial received concomitant lactulose therapy. Rifaximin is now Food and Drug Administration approved for the treatment of hepatic encephalopathy, and treatment is associated with a significant reduction in frequency of hospitalization for hepatic encephalopathy (13.6% hospitalization rate with rifaximin vs 22.6% with placebo; $P = .01$).

HEPATOCELLULAR CARCINOMA

Although primary hepatic resection has long been considered the treatment of choice for HCC, 5-year tumor-free survival rates are less than 50%.[71] Furthermore, most patients referred for resection are declined, because the tumor is unresectable or because hepatic reserve is considered inadequate.[72] Even in patients with

well-compensated cirrhosis, there is an increase in mortality after surgical resection if patients have evidence of portal hypertension or elevated serum bilirubin values.[73] Radiofrequency ablation and percutaneous alcohol injection are effective in tumors smaller than 3 cm but are far less successful for larger tumors.[74,75] In selected patients with otherwise untreatable tumors but relatively well-preserved liver function, chemoembolization has been shown to improve survival; however, these patients have much lower survival rates than those who are candidates for surgical or ablative therapy.[76–78]

Optimal results after transplantation can be achieved in patients with a single lesion less than 5 cm, or no more than three lesions, the largest of which is less than 3 cm in size, and no radiographic evidence of extrahepatic disease.[79] The allocation policy for donor livers in the United States was modified to give such patients enhanced priority for deceased donor organs. Since implementation of this modification, the time on the donor waiting list for patients with HCC has decreased from a mean of 2.3 years to 0.7 months.[80]

Patients with chronic hepatitis B, chronic hepatitis C, and nonalcoholic steatohepatitis are at particularly high risk for HCC.[81] Viral eradication reduces but does not eliminate the risk of HCC. Liver cancer has been reported to occur after viral cure in hepatitis B and C.[82,83] Consequently, the American Association for the Study of Liver Diseases (AASLD) guidelines recommend that patients with cirrhosis should remain on surveillance programs aimed at the early diagnosis of HCC, with imaging of the liver every 6 months.[84]

TREATMENT OF HEPATITIS C IN PATIENTS WITH CIRRHOSIS

Hepatitis C therapy in patients with cirrhosis is approached with the goal of sustained virologic response (SVR) representing eradication of the virus and thereby, in theory, the prevention of liver-related deaths caused by the development of decompensated cirrhosis and HCC.[85–87] Eliminating hepatitis C has been shown to prevent progression to potentially fatal complications by ameliorating portal hypertension, by decreasing the risk for development of HCC, and by leading to fibrosis regression.[87–90] A total of 70% to 88% of patients chronically infected with HCV do not undergo treatment because of poor health access, medical contraindications including psychiatric or cardiac disease, and patient preference.[91–95]

Guidelines strongly recommend antiviral treatment for patients with more advanced fibrosis and cirrhosis given their increased risk of liver-related complications.[96,97] Patients with compensated HCV related liver disease should be treated provided serum albumin is greater than 3.4 g/dL; bilirubin less than 1.5 mg/dL; INR less than 1.5; platelet count greater than 75,000/mm^3; hemoglobin (Hb) greater than 12/13 g/dL (males 12 g/dL, females 13 g/dL); and S-creatinine less than 1.5 mg/dL. However, the SVR is generally lower and adverse events necessitating dose reductions are higher in patients with cirrhosis.[98,99]

Ideal hepatitis C cirrhosis candidates for therapy remain Child-Pugh class A patients whose virologic response rate is reasonably high and in whom the risk of side effects is almost identical to that of control subjects.[100] Antiviral therapy is currently not indicated in Child-Pugh class C patients (or MELD >18) because of the high risk of sepsis during treatment and a low SVR rate. In Child-Pugh class B patients, treatment should be discussed on a case-by-case basis according to baseline factors for a potential response: genotype non-1, low viral load, good-response IL28B genotype, treatment naive, or patients who have relapsed from previous antiviral therapy. Antiviral therapy can be discontinued after 4 or 12 weeks if there is no virologic response.[101]

The safety of peginterferon therapy is a major concern in patients with advanced or decompensated cirrhosis. The incidence of bacterial infection (either SBP or spontaneous bacteremia) in people with cirrhosis is higher in treated patients (25%) than in control subjects (6%) ($P = .01$).[102] The development of sepsis is not necessarily related to neutropenia. Splenomegaly caused by portal hypertension increases the risk for cytopenia, especially anemia (35%), neutropenia (38%), and thrombocytopenia (24%).[103,104] The reported rates of neutropenia, thrombocytopenia, anemia, and episodes of infection or liver decompensation during interferon based therapy are 50% to 60%, 30% to 50%, 30% to 60%, 4% to 13%, and 11% to 20%, respectively.[105–107]

The reported rate of clinical decompensation in compensated patients with cirrhosis enrolled in randomized controlled trials is negligible (0%–3%; median, 1.5%)[108] likely reflecting a careful selection of patients with the exclusion of those with advanced liver disease who were at heightened risk of decompensation (rate, 14%).[109] In a prospective controlled trial in patients with decompensated cirrhosis, peginterferon and ribavirin were administered in 66 patients for 24 weeks after patients achieved clinical recompensation (Child-Pugh <9; MELD <15) compared with 63 patients refusing therapy.[110] SVR was 44% for genotypes 2/3 and 7% for genotypes 1/4. Treatment was associated with a risk of infections (odds ratio = 2.43) and death related to infections (odds ratio = 1.97). There was a lower rate of decompensation and reduced mortality in responders.

Guidelines now recommend the addition of a protease inhibitor (boceprevir or telaprevir) to peginterferon and ribavirin for treatment of hepatitis C, genotype 1.[111] These triple therapy regimens yield higher SVR rates, although the SVR rates in patients with cirrhosis are still uncertain because of low numbers of patients with established cirrhosis in the published studies.[112–117] In phase 3 trials, in treatment of naive patients with cirrhosis (6% of study patients), SVR was obtained in 62% of patients treated with telaprevir (12 weeks) compared with 33% with the standard treatment regimen.[116] SVR was achieved in 52% of patients with Metavir score 3 or 4 (around 10% of study patients) treated with boceprevir (44 weeks) compared with 38% with the standard regimen.[115]

In patients with cirrhosis who were previously treated with PEG/ribavirin therapy, SVR was achieved (1) in 84% of those who had relapsed and were now treated with telaprevir compared with 13% who were retreated with the PEG/ribavirin regimen; (2) in 34% of those with a previous partial response treated with telaprevir compared with 20% with PEG/ribavirin; and (3) in 14% of those with a previous nonresponse (reduction of less than 2 $\log_{10}$ in hepatitis C virus [HCV] RNA after 12 weeks) treated with telaprevir compared with 10% with PEG/ribavirin.[118] Interestingly, SVR rates among patients with cirrhosis with prior relapse were comparable with those without cirrhosis in the triple therapy arm, in contrast to the null responders with cirrhosis who did extremely poorly.

In previously treated patients with prior partial response and a baseline Metavir fibrosis score of 3 or 4, SVR was achieved in 83% of those who had relapsed and were treated with boceprevir (44 weeks) compared with 20% with PEG/ribavirin and in 46% of those with a previous nonresponse treated with boceprevir (44 weeks) compared with 0% with PEG/ribavirin.[119] There is no published experience on the efficacy and safety of telaprevir or boceprevir in patients with decompensated cirrhosis and this use is not recommended.[107]

A recent French study investigating telaprevir and boceprevir use in compensated patients with cirrhosis with a history of prior treatment failure supported the increased risk of morbidity and mortality of this therapy in patients with cirrhosis, with serious

adverse events (31%–50%) far higher than previously reported.[120] Additional details regarding this unique and important cohort of patients are awaited.

LIVER TRANSPLANTATION

Liver transplantation remains the definitive management for decompensated liver disease.[121] Decompensated cirrhosis caused by HCV accounted for 30% to 50% of the transplants performed in the United States and Europe.[122,123] Survival rates 1, 5, and 10 years after liver transplantation in the United States are 88.9%, 73.6%, and 60.4%, respectively.[124] Patients with a MELD score of 15 or more and a CTP score of 7 or more can be expected to achieve improved survival with liver transplantation.[4,5]

Recurrence of HCV after liver transplantation is universal and follows a more aggressive course than pretransplant HCV infection.[4,5] Most patients with hepatitis C develop recurrent liver injury.[125,126] Postoperative survival in early studies seemed to approximate that of patients transplanted for other conditions.[127] Significant strides have been made in posttransplant therapy for hepatitis B including improved oral antiviral suppression aiding graft survival. With newer direct-acting antivirals for hepatitis C, the hope is that likewise further improvement in graft survival may be achieved in patients with hepatitis C, both pretransplant and posttransplant. Although many patients do well with minimal liver damage despite persistently high levels of circulating virus, presently about 10% of patients develop rapidly progressive fibrosis and cirrhosis within the first few years after transplantation.[128–130]

SUMMARY

The hallmark of liver failure in the patient with cirrhosis, defined as hepatic decompensation, clinically represents the development of ascites, encephalopathy, gastrointestinal bleeding, and carcinoma. Literature from the past decade demonstrates that the infectious disease specialist is instrumental in the appropriate management of the patient with advanced liver disease. Antimicrobial treatment of the patient with cirrhosis in 2012 that reduces complications and improves survival now encompasses SBP diagnosis and prophylaxis, encephalopathy treatment and prophylaxis, and prevention of infection during gastrointestinal bleeding. Careful management of hepatitis antiviral therapy is of paramount importance in patients with cirrhosis patients. Liver transplantation, with subsequent immunosuppression, represents definitive management when medical therapy fails to achieve hepatic compensation.

Principles of management for cirrhotic patients

Principles of Management for Patients with Cirrhosis	Refs.
Antibiotic prophylaxis against bacteria during gastrointestinal hemorrhage	44
Antibiotic prophylaxis after any episode of SBP	44
Albumin infusion at diagnosis and 3 days after SBP	37
Rifaximin 550 mg twice daily with lactulose titration for hepatic encephalopathy	41
Abdominal imaging every 6 months in all patients with cirrhosis	82–84
Hepatitis C therapy in advanced fibrosis with no contraindication	96
Consideration for liver transplant listing for MELD >15 or decompensation	4
Band ligation or β blockade for large varices or varices with red wales	26

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