When to Consider Liver Transplant During the Management of Chronic Liver Disease

Rena K. Fox, MD, FACP

KEYWORDS

• Liver transplantation • Chronic liver disease • Cirrhosis • Referral • Timing
• Clinical practice • Primary care • Evaluation

KEY POINTS

- The increasing prevalence of chronic liver disease and increasing prevalence of cirrhosis and hepatocellular carcinoma will bring an increasing demand for liver transplantation.
- Improved education and a simple guide for primary physicians are necessary for a timely referral of patients for liver transplant evaluation.
- Long-term management of patients with cirrhosis should include a regular repeated calculation of the Model for End-Stage Liver Disease (MELD) score to continually assess the appropriate time for transplant referral.
- Patients with a MELD score of 15 or greater should be referred for transplant, and ideally at a score of 10 or greater to allow adequate time for evaluation.
- Any patient with cirrhosis should be referred for liver transplantation evaluation at the time of their first decompensating event, regardless of MELD.

INTRODUCTION

The rising prevalence of cirrhosis in the United States is alarming. Models predict that within 40 to 50 years, the peak incidence of end-stage liver disease due to hepatitis C virus (HCV) will be 38,000 and the peak prevalence of cirrhosis due to HCV in the US will be 1 million, and that by 2060, one-third of the HCV infected population will die of HCV if untreated. These estimates only refer to liver disease due to HCV, so including other causes of liver disease make these numbers even higher.[1,2] In the United States, liver cirrhosis is currently the 12th most common cause of death (9.5/100,000 individuals). Examining these statistics, it is predicted that over the next several decades there will

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Division of General Internal Medicine, Department of Medicine, University of California, San Francisco School of Medicine, 1545 Divisadero Street, Suite 307, San Francisco, CA 94143-0320, USA
E-mail address: rfox@medicine.ucsf.edu

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be a rapid increase in the demand for liver transplantation (LT). At present, HCV infection is the leading indication for LT in the United States,[3] and as the HCV population is aging and the number of patients developing cirrhosis from HCV increases, the demand for LT as a result of HCV is expected to increase.[1] However, with the rising prevalence of the metabolic syndrome, it is staggering that approximately 30% to 40% of the United States population[4,5] is estimated to have nonalcoholic fatty liver disease (NAFLD). Although NAFLD has a much more benign course compared with HCV for most patients, approximately 30% with isolated steatosis will progress to nonalcoholic steatohepatitis (NASH). Of those with NASH, a small but significant proportion will progress to more serious liver disease. It is estimated that 20% of NASH patients will develop cirrhosis and approximately one-third of the cirrhotics will decompensate.[6,7] NAFLD has already grown to be the fourth most common reason for LT.[8] It is anticipated that NASH will potentially become the leading indication for transplantation as more effective treatments for HCV become available and the prevalence of cirrhosis from NAFLD increases.[8,9] Although local access to subspecialists has been shown to be associated with the likelihood of receiving a transplant,[10] with the astounding prevalence of the metabolic syndrome and diabetes,[11] many more of these patients will be managed in the primary care setting and may not have access to gastroenterology and hepatology specialists locally. One can thus expect primary care physicians to be increasingly making the diagnosis of chronic liver disease or cirrhosis, and the decision of when to refer their patients for LT evaluation.

KEEPING AN EYE ON TRANSPLANT TIMING DURING LONG-TERM MANAGEMENT OF CIRRHOSIS

Every chronic liver disease can eventually progress to cirrhosis, although some liver diseases are more likely than others to lead to cirrhosis. Because patients with chronic liver disease are almost always asymptomatic, physicians must actively watch for and recognize cirrhosis when it develops. The diagnosis of cirrhosis is not always straightforward[12]; and it is often misunderstood. Mistakenly, many physicians rely on serum aminotransferase levels, although both alanine aminotransferase and serum bilirubin have been shown to be nonpredictive of a diagnosis of cirrhosis.[12] Regularly reassessing all patients with chronic liver disease for any signs of cirrhosis is a major task for the primary care clinician, and education and understanding of the early signs and symptoms is lacking.[13] Patients and physicians may not be aware of development of cirrhosis during asymptomatic phases.

Cirrhosis itself is a progressive disease that results ultimately in death unless transplant is available (**Fig. 1**).[14–17] The median survival of patients with compensated cirrhosis is greater than 12 years and the median survival of those with decompensated cirrhosis is approximately 2 years.[17] The transition from a compensated to a decompensated phase occurs at a rate of approximately 5% to 7% per year and can be divided into stages. Stage 1 cirrhosis is characterized by an absence of esophageal varices and ascites. Stage 2 cirrhotics have developed esophagogastric varices without bleeding, but still have an absence of ascites. The presence of ascites signals stage 3 disease, which may or may not be associated with varices without bleeding. Stage 4 cirrhotics have developed gastrointestinal bleeding with or without the presence of ascites. Stages 1 and 2 are compensated stages, whereas stages 3 and 4 are decompensated stages. Ascites is the most common first presentation of decompensation. The mortality rate in stage 1 is 1% per year; however, patients progress from stage 1 at a cumulative rate of 11.4% per year, moving into either stage 2 or directly to stage 3. The mortality rate in stage 2 cirrhosis is 3.4% per year, progressing to either