Hepatitis Viruses and Liver Transplantation

Evolving Trends in Antiviral Management

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KEYWORDS

• Liver transplant • HCV • HEV • HBV • Antiviral therapy

KEY POINTS

- Viral hepatitis-related end-stage liver disease and hepatocellular carcinoma (HCC) remain the most common indications for liver transplant (LT) throughout the world.
- The profound improvement in post-LT outcomes in patients with hepatitis B virus (HBV) due to the development of effective antiviral strategies is one of the most dramatic success stories in liver transplantation.
- The management of LT recipients with hepatitis C virus (HCV) is evolving rapidly.
- The ideal strategy to prevent recurrence of HCV after LT would be antiviral treatment with cure while on an LT waitlist, thus potentially eliminating the risk of recurrent HCV.

Viral hepatitis-related end-stage liver disease and HCC remain the most common indications for LT throughout the world. This review focuses on recent updates in antiviral management of 3 viral hepatidities: hepatitis C, B, and E. Each of these potentially chronic viral infections is in a different phase of understanding of their impact on the LT population and the ability to prevent recurrent or progressive disease. The profound improvement in post-LT outcomes in patients with HBV due to the development of effective antiviral strategies is one of the most dramatic success stories in liver transplantation. By comparison, peri-LT treatment of HCV is in its infancy, although rapidly accumulating data on novel and interferon (IFN)-free direct-acting antiviral (DAA) regimens will soon permanently alter the natural history of HCV in LT recipients. Finally, data have emerged that hepatitis E virus (HEV) is more common in LT recipients throughout the world than previously understood, and although HEV can cause chronic hepatitis and progressive graft failure in this setting, the incidence, natural history, and optimal treatment strategy for HEV in this setting remain uncertain.

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ANTIVIRAL MANAGEMENT OF HEPATITIS C VIRUS IN LIVER TRANSPLANT RECIPIENTS

The management of LT recipients with HCV is evolving rapidly. Despite marked improvements in the ability to cure patients of HCV infection, HCV-related end-stage liver disease remains the leading indication for LT, and, due to recurrence of HCV in the liver allograft, death and graft failure are more common in this population compared with HCV-negative recipients (Fig. 1).[1] Successful antiviral treatment with sustained virologic response (SVR) improves post-LT survival (Fig. 2),[2–4] but, until now, HCV treatment in patients on a waitlist to prevent recurrence or on immunosuppression after LT was hindered by significant toxicities and disappointing response rates. There is a variety of new DAAs recently approved or in clinical trials that will soon lead to a marked improvement in SVR rates with shorter duration of therapy. Although these agents are not yet well tested or approved for use in waitlisted or post-LT patients, strategies to eradicate the virus in the pre- and post-LT setting will play a key role in improving outcomes and are now included in the recently published joint American Association for the Study of Liver Disease (AASLD) and Infectious Diseases Society of America (IDSA) recommendations for the treatment of HCV.[5]

The Diagnosis of HCV Recurrence

The natural history of HCV-related liver disease is accelerated in the post-LT setting, including rapid progression to cirrhosis (10%–25% of patients within 5–10 years), rapid decompensation once cirrhosis occurs (40% with clinical decompensation within 1 year), and thus poor survival.[6] The overall 1-, 3-, and 5-year survival rates United States national data between 1997 and 2010 were recently reported to be 87%, 78%, and 70%, respectively.[7]

Risk factors for severe or rapid recurrence of advanced fibrosis include most prominently donor age, with an increase in risk of graft loss with donors as young as in their fourth decade.[1] Additional risk factors include graft characteristics, such as the donor risk index[8] and HCV serostatus[9]; recipient characteristics, such as female gender[10] and race/ethnicity[11,12]; and post-LT factors, including biliary complications,[13] treated

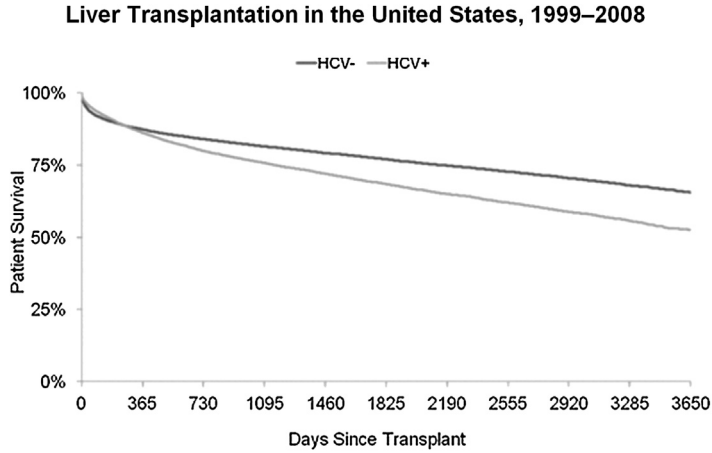

Fig. 1. Patient survival in HCV-positive and HCV-negative recipients from a report on the Scientific Registry of Transplant Recipients (SRTR) database for liver transplantation between 1999 and 2008. (*From* Thuluvath PJ, Guidinger MK, Fung JJ, et al. Liver transplantation in the United States, 1999–2008. Am J Transplant 2010;10:1003–19; with permission.)