Management of Viral Hepatitis in Solid Organ Transplant Recipients

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KEYWORDS

• Hepatitis B virus • Hepatitis C virus • Hepatitis E virus • Liver transplantation
• Kidney transplantation • Thoracic transplantation

KEY POINTS

- Hepatitis B virus (HBV) has declined as an indication for liver transplant in North America, but remains a common indication in Asia. Outcomes following transplant are now excellent in liver and nonliver recipients with chronic HBV infection with modern management strategies including potent antiviral therapy with or without hepatitis B immunoglobulin tailored to patient risk.
- Hepatitis C virus (HCV) remains a leading indication for liver transplant globally. However, direct-acting antiviral therapy can now cure virtually all liver and nonliver transplant candidates and recipients with excellent short-term results, although the optimal timing of therapy remains controversial.
- The use of organs from donors who are either hepatitis B surface antigen or HCV RNA positive has been increasingly described in case series and with modern antiviral therapy seems to be safe in selected cases, although the optimal use of such donors remains to be evaluated.
- Chronic hepatitis E virus infection is an emerging cause of chronic hepatitis and cirrhosis in immunocompromised hosts in the developed world. A high clinical suspicion is needed to make this diagnosis because signs and symptoms may be minimal and serology negative in up to 20%.

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INTRODUCTION

In recent years, strategies for the prevention and treatment of hepatitis B virus (HBV) and hepatitis C virus (HCV) in organ transplant candidates and recipients have evolved rapidly. Although these viral infections no longer threaten transplant outcomes, in either hepatic or nonhepatic transplantation, they continue to be a focus of research. Strategies are needed to optimize cost-effective management that improve survival and quality of life because viral hepatitis remains a leading cause of death globally from liver failure and hepatocellular carcinoma (HCC). Remaining controversies include the ideal timing of HCV antiviral therapy and the use of HCV viremic donors in hepatic and nonhepatic transplantation. Hepatitis E virus (HEV) is an emerging pathogen in organ transplantation, now recognized to be a cause of chronic hepatitis post-transplantation with a significant risk of progression to cirrhosis. This article reviews the current management of HBV, HCV, and HEV in organ transplantation, highlighting remaining priorities for research.

HEPATITIS B VIRUS

Liver Transplant

In 2015, an estimated 257 million people were living with chronic hepatitis B infection globally.[1] Despite a highly effective vaccine and potent antiviral medications for treatment, the global attributable mortality because of HBV increased between 1990 and 2013[2] with most deaths attributable to HCC, followed by liver failure. In the United States, and other Western countries, however, HBV-related liver disease has become an uncommon indication for liver transplant (LT), although it remains a common indication in Asian countries.[3,4] Before the introduction of hepatitis B immunoglobulin (HBIg) and the development of potent nucleos(t)ide analogues (NA) used to prevent HBV recurrence in the graft, early graft loss and mortality were common, but outcomes now for this indication are among the best.[5] Although early data with the use of lamivudine or adefovir in combination with HBIg demonstrated improved early outcomes and lower risk of HBV recurrence, potent NAs with a high barrier to resistance (entecavir [ETV], tenofovir disoproxil fumarate [TDF], or tenofovir alafenamide fumarate [TAF]) are now preferred.

The risk of recurrent HBV after LT is related to the HBV DNA load at the time of transplantation[6] and thus all patients on the LT waiting list with HBV-related liver disease should be treated with a potent NA and a goal of achieving an undetectable HBV DNA. After LT, all patients should receive the combination of HBIg and a potent NA, which reduces the risk of HBV recurrence to less than 5%.[7,8] The NA therapy should continue indefinitely in all; however, in those at low risk for recurrence, HBIg discontinuation is considered, generally after a minimum of 1 to 3 months, although in select patients, potent NA therapy alone, without HBIg has been shown to effectively prevent recurrence.[9,10] Conversely, in those with risk factors for recurrent HBV, including those with detectable HBV DNA at the time of transplant, those with HCC, and those with coinfection with human immunodeficiency virus or hepatitis delta virus, combination HBIg and potent NA therapy should continue indefinitely.

In addition to the potency of NAs, renal function and prior antiviral exposure should be considered in choosing the preferred agent. In those with renal dysfunction, ETV or TAF is preferred. In those with prior lamivudine exposure, TDF or TAF are preferred.[11] Although the risk of recurrence is low with prophylaxis, monitoring is recommended to pick up recurrent disease early and limit the impact on long-term outcomes. HBV recurrence is defined as the reappearance of hepatitis B surface antigen (HBsAg) after LT and quantifiable levels of DNA, although patients on antiviral prophylaxis may