Management of the Liver Transplant Recipient

Approach to Allograft Dysfunction

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KEYWORDS

• Liver transplantation • Allograft dysfunction • Acute cellular rejection • Hepatitis
• Immunosuppression

KEY POINTS

- Early recognition of liver allograft dysfunction is key to preventing graft failure.
- The differential diagnosis of allograft dysfunction depends on the timing after transplantation, with anatomic and infectious issues being most common in the first month.
- Acute cellular rejection occurs in approximately 15% of liver transplant recipients, with most episodes occurring between the third and twelfth month.
- Recurrent diseases, including hepatitis C and nonalcoholic fatty liver disease, are the most common causes of allograft dysfunction after the first year.

INTRODUCTION

Due to improved outcomes after liver transplant (LT) over the last 30 years, many patients with end-stage liver disease and acute liver failure have been granted a second chance at life. This improvement in survival post-LT is largely due to advances in surgical techniques, careful selection of donors and recipients, fine-tuned immunosuppression, and aggressive management of infections. With more than 6000 LTs performed annually in the Unites States, it can be estimated that with an increasing number of long-term survivors, primary care physicians will be seeing a larger number of LT recipients in their practice.[1,2] Primary care physicians must be able to recognize and optimally manage key complications, including detection of allograft dysfunction. This article provides an overview of issues pertinent to the diagnosis and management of allograft dysfunction in LT recipients.

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DEFINITION OF ALLOGRAFT DYSFUNCTION

Liver allograft dysfunction may be identified by either clinical or laboratory findings. In many instances, laboratory findings may be more specific (ie, abnormal liver function tests) and are detected earlier than clinical manifestations.[3] If liver enzymes (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase) or function tests (bilirubin, international normalized ratio [INR]) are elevated 1.5 or more times the upper limits of normal, further evaluation is warranted. Clinical manifestations include poor mental function, hypoglycemia, acidosis, jaundice, poor bile output when a T-tube is present, acholic stools, ascites, and bleeding. It is possible to have none of these clinical findings and yet for the LT recipient to have significant graft dysfunction. For this reason, diagnostic investigation should be pursued for any rise in or failure to normalize aminotransferase enzymes, alkaline phosphatase enzyme, serum bilirubin, and/or the coagulation profile (prothrombin time [PT] and INR).

DIFFERENTIAL DIAGNOSIS

Liver allograft dysfunction is a serious complication that can result in loss of the donor organ. Salvage of the organ depends on accurate diagnosis and prompt treatment. The approach to the patient with graft dysfunction is highly dependent on timing posttransplant (**Table 1**).

Less than 1-month Posttransplant

Early graft dysfunction

To offer grafts to as many LT candidates as possible, the transplant professional community has had to expand its organ pool. One of the main results of this is variability in early graft function.[4] Almost all LT recipients have significant laboratory elevations immediately posttransplant and some degree of early graft dysfunction is common. Laboratory trends in this period are especially important with regard to the aminotransferase enzymes. An early peak, usually in the first or second postoperative day, is expected and then a consistent decline to the normal range is the typical course.[5] Values in the aminotransferases greater than the 3000 range are worrisome that the injury causing the enzyme elevation may be too significant for the liver to reasonably recover. In instances in which this occurs within the first 2 days of transplantation, early diagnosis of primary nonfunction or hepatic artery thrombosis (HAT) must be considered. If either of these 2 conditions occurs within 1 week of transplant, the recipient may be relisted for a second transplant with the highest priority (United Network for Organ Sharing Status 1 listing).

Table 1
Common cause of liver allograft dysfunction depending on posttransplant period

<1 mo Post-LT	1–12 mo Post-LT	>1 y Post-LT
Early graft dysfunction	Rejection (acute or chronic)	Rejection (acute or chronic)
Vascular complications (ie, HAT, vascular impairment)	Recurrence of primary disease (ie, HCC, HCV)	Recurrence of primary disease (ie, HCC, HCV, alcoholism)
Biliary complications (ie, bile leak, strictures)	Vascular complications	Development of de novo liver disease (ie, NAFLD)
Infection (ie, sepsis)	Infection (ie, CMV)	—

Abbreviations: CMV, cytomegalovirus; HAT, hepatic artery thrombosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NALFD, nonalcoholic liver disease.