Liver Transplant for Cholestatic Liver Diseases

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KEYWORDS

• Cholestatic liver disease • Primary sclerosing cholangitis • Primary biliary cirrhosis
• Liver transplantation • Recurrence • Outcomes

KEY POINTS

- Cholestatic liver diseases are a heterogeneous of group of disorders that can progress to biliary cirrhosis.
- Disease-specific manifestations in each of these cholestatic liver diseases pose specific risks that significantly affect the morbidity and mortality of affected patients.
- Liver transplant (LT) is the only definitive therapy for patients in whom the condition has progressed to end-stage liver disease.
- In general, cholestatic liver diseases have the best posttransplant outcomes when compared with other indications of LT.
- Disease recurrence and extrahepatic manifestations of cholestatic liver diseases can significantly affect the quality of life, and long-term studies are needed to understand the natural history after LT.

PRIMARY SCLEROSING CHOLANGITIS

Primary sclerosing cholangitis (PSC) is considered a rare disease, but the average annual percentage incidence of PSC has increased by 5%.[1] The estimated 10-year survival is approximately 65%.[2] Despite the modest increase in incidence, the number of transplants has remained stable between 1995 and 2006.[3] PSC is the fifth most common indication for LT in the United States and the number one indication in Scandinavian countries.[4] PSC accounts for approximately 250 LTs or 5% of all LTs per year in the United States (United Network for Organ Sharing [UNOS]). The rates of LT in Europe, especially in the Scandinavian and Nordic regions, are higher than that in the United States (8%–16% per year) because of the lower incidence of viral and

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alcoholic liver disease and expanded selection criteria, which additionally include patients with PSC with high-grade biliary dysplasia and early cholangiocarcinoma (CCA). At present, there is no effective therapy for the management of PSC except for LT.[4–7]

LT Evaluation

Organ allocation for PSC is similar to that for other indications in the United States and is prioritized by the Model for End-stage Liver Disease (MELD) score, which is cause independent. Several prognostic models specific for PSC have been developed by combining demographic, serologic, and radiologic variables known to independently affect survival of patients with PSC. Nevertheless, these models are imprecise in predicting outcomes for individual patients, and no consensus exists about the optimal model. Thus, the American Association for the Study of Liver Disease recommends against using disease-specific models for predicting clinical outcomes in individual patients.[4]

Additional MELD (exception) points can be requested from the regional transplant review boards for specific manifestations of PSC such as intractable pruritus, recurrent or refractory bacterial cholangitis, and carefully selected limited-stage CCA,[4] which are granted on a case-by-case basis by determining risk of waitlist mortality, waitlist removal, and non–liver-related comorbidities.[5] According to current consensus recommendations, exception points are granted to patients with PSC with either 2 or more episodes of culture-proven bacteremia within a 6-month period or noniatrogenic septic complications of cholangitis with positive result of blood cultures, no identifiable correctable structural lesion, and the absence of biliary stents.[6] Data from the UNOS show that 12.2% of patients with PSC listed for LT between 2002 and 2011 received exception points and an overwhelming majority of them did not conform to established consensus recommendations.[7]

LT Evaluation for PSC with Cholangiocarcinoma

CCA is the second most common primary hepatic malignancy with a reported incidence 0.6% to 1.5% per year and a lifetime risk 7% to 17% in patients with PSC.[8,9] The prognosis of CCA is extremely poor with an average 5-year survival of 5% to 10%.[10] Surgical resection provides the only possibility of cure for localized CCA, and adjuvant chemoradiation should be considered in all cases.[11] LT for unresectable CCA is not considered a standard therapy at present, and some transplant centers even consider CCA as a contraindication for LT. Nevertheless, dismal survival rates initially reported (0%–20% at 5 years post-LT) have been challenged by more recent reports describing an improved 5-year survival rate of 30% to 55% after LT for unresectable CCA.[12,13] MELD exception points may be obtained only in selected patients with early unresectable hilar CCA who complete standardized protocols with neoadjuvant chemoradiation by an individual written petition, which must be approved by regional transplant review boards.[14] The Mayo Clinic protocol is one of the commonly followed protocols, which consists of external beam radiotherapy or brachytherapy plus chemotherapy and staging laparotomy.[14] Under this protocol, only patients with confirmed stage I or II disease are eligible for LT. Palliative options include biliary stenting, chemotherapy, chemoembolization, photodynamic therapy, and radiofrequency ablation.[15]

Post-LT Outcomes

Survival of patients with PSC after LT has increased markedly in the past few decades and is approximately 80% at 5 years.[16] Living donor LT (LDLT) and deceased donor LT