Liver Transplantation for Primary Biliary Cholangitis

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KEYWORDS

• Primary biliary cholangitis • Liver transplantation • Outcomes • Recurrence
• Ursodeoxycholic acid

KEY POINTS

- Although ursodeoxycholic acid (UDCA) has significantly improved the clinical course of primary biliary cholangitis (PBC), liver transplantation (LT) remains the only effective cure.
- PBC, which was once the most common indication for LT, is now the seventh most common indication for LT.
- Graft and patient survival following LT for PBC are among the highest of all indications for LT.
- Recurrent PBC (rPBC) occurs in 22%, 36%, and 50% at 3, 5, and 10 years post-LT, respectively, and is associated with decreased patient and graft survival.
- Prophylactic UDCA in post-LT PBC patients is associated with reduced risk of rPBC, graft loss, liver-related death, and all-cause mortality.

INTRODUCTION

Primary biliary cholangitis (PBC) is an autoimmune cholestatic liver disease that is characterized by the progressive destruction of small intrahepatic bile ducts resulting in hepatocellular injury, cholestasis, fibrosis, and biliary cirrhosis. With a worldwide prevalence of 19.2 to 402 per million population, PBC is the most common cholestatic autoimmune liver disease.[1] PBC is often a serologic diagnosis in the setting of persistently elevated alkaline phosphatase (ALP) in the presence of the antimitochondrial antibody (AMA) or other PBC-specific antinuclear antibodies (eg, gp210 and sp100). However, a liver biopsy is required when there is a high suspicion for PBC in the absence of AMA (AMA-negative PBC). The characteristic histologic findings of PBC include chronic, nonsuppurative cholangitis that affects mainly interlobular and septal bile ducts.[2] Although the use of ursodeoxycholic acid (UDCA) as first-line therapy has significantly improved biochemical indices, delays histologic progression, and improves transplant-free survival, liver transplantation (LT) remains the only effective cure for end-stage liver disease caused by PBC.

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NATURAL COURSE

Signs and Symptoms

Fatigue and pruritus are the most commonly reported symptoms by patients with PBC and have a negative impact on quality of life (QOL).[3] In a large UK registry study during the pre-UDCA era in which 770 PBC patients were followed for up to 28 years, 60% of patients with PBC were asymptomatic at time of diagnosis, but only 5% remained asymptomatic after 20 years with a median time from diagnosis to appearance of symptoms of 3 to 4 years.[4] Other signs and symptoms of PBC include decreased bone mineral density (BMD), hyperlipidemia, xanthelasma, and the presence of other autoimmune diseases, such as Sjogren's syndrome, Raynaud's syndrome, Hashimoto's thyroiditis, and/or rheumatoid arthritis.[5]

Fatigue

Fatigue is the most common symptom in PBC and is present in nearly 80% of the patients. Fatigue fluctuates independently of disease activity and severity and is not alleviated by UDCA.[6–8] Fatigue related to PBC is associated with inability to work, sleep disturbance, depression, decreased QOL, and increased mortality.[9–11] Fatigue often persists after LT and, therefore, is not a unique indication for LT in patients with PBC.

Pruritus

Pruritus, which is a common manifestation of all cholestatic liver diseases, is reported in 40% to 80% of patients with PBC. A population-based study of patients with PBC from England reported a cumulate risk for developing pruritus in previously asymptomatic patients at 1, 5, and 10 years was 13%, 31%, and 47%, respectively.[12] Although there are well-defined treatment strategies for cholestatic pruritus,[13] chronic pruritus can be severe and debilitating and is associated with prolonged wound healing, skin infections, sleep disturbance, and diminished QOL.[3,7,14] A so-called "premature ductopenic variant" has been described in which severe pruritus develops due to progressive cholestasis and profound ductopenia in the absence of advanced hepatic fibrosis or cirrhosis.[15] This variant, which is reported to affect 5% to 10% of patients with PBC, is typically unresponsive to UDCA therapy and can progress quickly to require LT.[15] Unlike fatigue, pruritus dramatically resolves after LT, often within the first 24 hours after LT.[16] Therefore, intractable pruritus is a justifiable indication for LT.

Abnormal bone mineral density

As seen in other etiologies of cholestatic liver disease, patients with PBC have a higher prevalence of metabolic bone disease before and after LT.[17,18] Specifically, osteoporosis is four times more common in patients with PBC compared with age and gender-matched controls.[17,18] There is an expected bone loss of 8% to 18% within the first 6 months after LT,[19,20] with a reported incidence of fractures within the first posttransplant year of 20% to 40%.[21,22] Osteoporotic fractures significantly impact morbidity and mortality, especially those with PBC. Therefore, reducing the burden of disease from osteoporosis before and after LT is essential in the overall management of PBC. According to current American Association for the Study of Liver Diseases (AASLD) guidelines, BMD should be evaluated every year for osteopenic patients for the first 5 years after LT and every 2 to 3 year for patients with normal BMD.[2] The screening and treatment thereafter depends on the progression of BMD.

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TREATMENT

Ursodeoxycholic Acid

Before the introduction of UDCA, LT was the only therapeutic option for PBC. The clinical course of PBC has significantly improved since the introduction of UDCA, which was formally approved by the Food and Drug Administration (FDA) in 1997 as the only first-line therapy for PBC. The clinical efficacy of long-term UDCA use is well established and characterized by improvement of liver biochemistries, slowing of histologic progression, delaying the onset of symptoms, and prolonging transplant-free survival.[23–27] However, up to 40% of patients treated with UDCA have an incomplete or absent biochemical response to therapy and such patients have significantly worse transplant-free survival than UDCA-responsive patients.[28–30]

Obeticholic Acid

Obeticholic acid (OCA), which is a potent activator of the nuclear farnesoid X receptor, was approved in 2016 by the FDA as a second-line therapy for use in combination with UDCA in patients with PBC patients with incomplete UDCA treatment response or as monotherapy in treatment-intolerant patients. There are emerging outcomes data that shown significant improvement in transplant-free survival for patients treated with OCA compared with two large well-established external PBC registry data sets, namely the Global PBC Study Group and UK-PBC registries.[31] Owing to reports of serious liver adverse events by the FDA in patients with advanced liver disease (Child-Pugh B or C), cautious dosing in accordance with the drug label is imperative. In the event of hepatic decompensation, OCA should be discontinued, and the patient should be referred for LT.

RISK ASSESSMENT

Multiple prognostic models were developed to assess the responsiveness to UDCA and estimate transplant-free survival specific to patients with PBC.[29,30,32–40] Of these, the GLOBE and UK-PBC scores, demonstrate superior predictive performance of biochemical response criteria compared with earlier models.

The GLOBE score was derived from an international, multicenter, prospective study of 2488 UDCA-treated patients with PBC and validated in an independent cohort of 1631 patients throughout Europe and North America.[37] The study showed that patients with risk scores greater than 0.30 had significantly shorter transplant-free survivals than matched healthy individuals ($P < .001$). Specifically, the 10-year transplant-free survival with a GLOBE score greater than 0.30 is 60%, compared with 92% with a GLOBE score ≤ 0.30.[37] Similarly, the UK-PBC score (http://www.uk-pbc.com/resources/tools/riskcalculator/) was derived and validated in a multicenter study including 3165 patients with UDCA-treated patients with PBC to estimate the risk of developing liver failure requiring LT within 5, 10, or 15 years from diagnosis.[33]

LIVER TRANSPLANTATION

The indications for LT for patients with PBC are similar for those with other forms of chronic liver disease. Unique to those with PBC, bilirubin greater than 6 mg/dL, Mayo risk score greater than 7.8, and intractable pruritus are other acceptable indications for LT.[35,41–43] Although the Model for End-Stage Liver Disease (MELD) score is widely used to estimate prognosis and for organ allocation in patients with end-stage liver disease of all etiologies, it remains a subject of debate as to how accurately

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the MELD score reflects mortality risk without taking into account the etiology of liver disease. Despite the perceived similarities of underlying autoimmune pathophysiology, PBC is often mistakenly compared with autoimmune hepatitis (AIH) and primary sclerosing cholangitis (PSC). In AIH, for example, corticosteroids and other immunosuppressive therapies can improve hepatic decompensation, even in patients previously thought to require lifesaving LT.[44] On the other hand, patients with PSC may be listed and subsequently transplanted due to recurrent cholangitis, for which they are eligible to receive MELD exceptions points on application to the National Liver Review Board (NLRB).[45] However, no such exception points exist for PBC. MELD exception points for intractable pruritus in PBC were previously granted on an individual basis by regional review boards; however, practices related to exceptions points varied widely by region.[46] Moreover, in an effort to provide a more efficient and equitable approach for waitlisted patients whose unique need for LT may not be adequately captured by their calculated MELD score, the NLRB was implemented in 2019 and replaced the prior system of 11 separate regional review boards. However, despite the high incidence of pruritus in PBC and its negative impact on QOL, the current guidance documents established by the NLRB explicitly state "there is inadequate evidence to support granting a MELD exception for pruritus in adult candidates with the typical clinical symptoms associated with this diagnosis."[45] Although intractable pruritus is a justifiable indication for LT, it is not a standard indication for MELD exception points, and therefore, it is a subject to appeal to the NLRB.

TRENDS IN LIVER TRANSPLANT FOR PRIMARY BILIARY CHOLANGITIS

Waitlist

The number of PBC patients listed for LT has declined in the United States and United Kingdom by nearly 50% since 1995.[47] The ratio of women: men with PBC waitlisted for LT decreased by 50%.[47] Although non-white patients are usually younger and with higher severity scores at time of listing compared with white patients, black and Hispanic patients remain underrepresented on the LT waitlist. Moreover, patients with PBC on the LT waitlist have a disproportionately higher waitlist mortality compared with other etiologies of chronic liver disease despite similar MELD scores.[48,49] Specifically, waitlisted patients with PBC had a higher overall and 3-month waitlist mortality when compared with patients with PSC (21.6% vs 12.7% and 5.0% vs 2.9%, respectively), despite a similar listing MELD score[49] In another study, Hispanic patients with PBC had the highest percentage of waitlist deaths (20.8%) of any ethnicity or race evaluated.[48] Compared with white patients with PBC, Hispanic patients with PBC had the lowest overall rate of undergoing LT with a significantly higher risk of death while on the waitlist and the highest proportion of waitlist removals due to clinical deterioration.[48] In fact, only patients with alcoholic liver disease combined with hepatitis C virus had a higher waitlist mortality. Waitlisted patients with PSC have a higher rate of delisting for clinical improvement than PBC (13% vs 3%).[50] As such, patients with PBC are historically considered to be disadvantaged with respect to LT due to higher waitlist mortality and lower transplant rates compared with other liver disease etiologies.

Transplant

According to data from the United Network for Organ Sharing (UNOS), other than cryptogenic cirrhosis, which accounted for 332 LT (19.4%), PBC was the most common identified indication for LT in the United States in 1988 accounting for 209 of all LTs (12.2%) compared with PSC (8.6%) and alcoholic cirrhosis (8.3%).[51] Despite an

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increase in the total number of LT performed in the United States by 169% since 1993, the number of LT performed for PBC decreased by 38.7% during the same time period (**Fig. 1**).[51] As a result of these trends, PBC has become a relatively uncommon indication for LT as it is now the seventh most common identified indication for LT accounting for 2.0% of all LTs in 2021, which is the lowest since such data were first collected by UNOS in 1988 (**Fig. 2**).[51] On the other hand, living donor LT (LDLT) accounted for 29 (15.9%) of all LTs performed for PBC in 2021, which was the most ever in 1 year for PBC since the first LDLT for PBC was performed in 1994.[51]

Despite the increasing overall prevalence of PBC,[52] the number of LT for PBC has declined in both North America and Europe.[2,53,54] This trend reflects the benefits of early diagnosis and treatment with UDCA as well as the availability of emerging alternative therapies for refractory disease, such as OCA.

Survival After Liver Transplant

Similar to other cholestatic liver diseases, survival rates following LT for PBC are among the highest of all indications for LT (**Table 1**). Specifically, following a more recent review of the UNOS database, the 1-year, 3-year, 5-year, and 10-year graft survival rates were 85.0%, 80.5%, 78.1%, and 71.9%, respectively, and the 1-year, 3-year, 5-year, and 10-year patient survival rates were 90.2%, 86.7%, 84.4%, and 79.0%, respectively.[55] Independent predictors of posttransplant mortality in patients with PBC included age, insurance, history of prior LT, and longer post-LT inpatient stay.[56] In a retrospective analysis of the UNOS database from 2002 to 2006, which included 99 patients with PBC who underwent LDLT, patient and graft survival following LDLT was similar to those following deceased donor liver transplant (DDLT).[57]

Disease Recurrence

Diagnosis

Recurrence of PBC after LT was originally described in 1982 by Neuberger and colleagues.[58] The diagnosis of recurrent PBC (rPBC) is often difficult because the diagnostic criteria for PBC before LT are obscured in the post-LT setting by multiple factors. First, many clinical and biochemical features of PBC that are present before LT are frequently absent in rPBC and, therefore, cannot be used alone for diagnostic

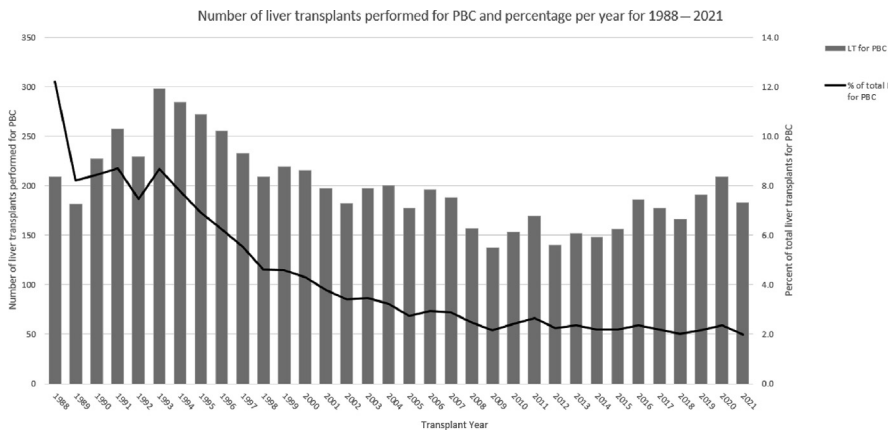


Fig. 1. Number of liver transplants performed for PBC and percentage per year for 1998 to 2021. (*Data from* https://optn.transplant.hrsa.gov/data/ (last access January 27, 2022).)

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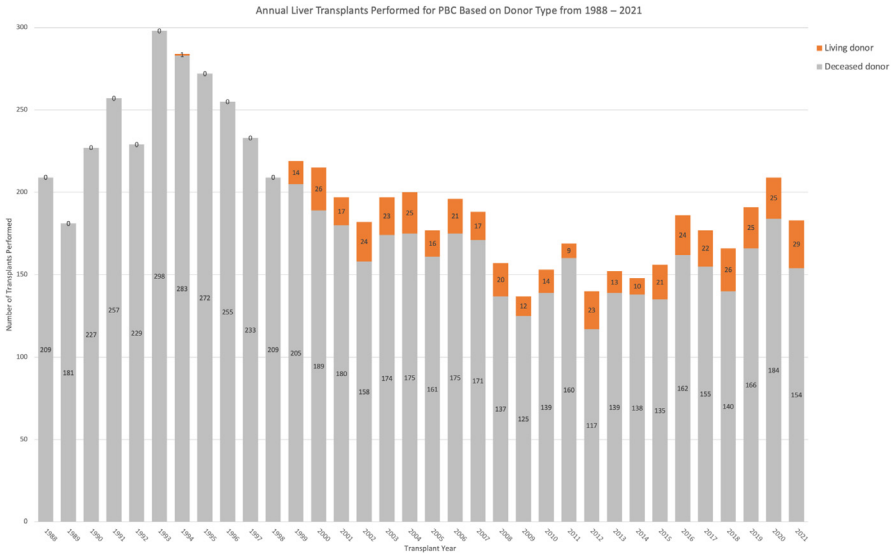


Fig. 2. Annual liver transplants performed for PBC based on donor type from 1998 to 2021. (*Data from* https://optn.transplant.hrsa.gov/data/ (last access January 27, 2022).)

purposes. In one study, only 12% of patients with rPBC reported potentially disease-related, but often nonspecific symptoms.[59] As is the case in pretransplant PBC, fatigue and pruritus were the most common symptoms, which were present in 50% of the patients with rPBC who experienced symptoms.[60] However, fatigue is nonspecific and may persist in many patients after LT unrelated to PBC.[61] Second, PBC-specific autoantibodies often persist after LT regardless of recurrence and, therefore, lose their diagnostic value for rPBC. Moreover, a cholestatic pattern of liver enzymes with an elevated ALP is also nonspecific after LT and can be found in many other clinical scenarios (**Table 2**). Owing to these limitations, histology is required to confirm the diagnosis of rPBC. In addition, the histologic features of PBC seen in the pretransplant setting, namely the immune-mediate lymphoplasmacytic injury of small bile ducts and bile duct paucity, may be mimicked in the post-LT setting by acute and chronic rejection. Therefore, the diagnosis of rPBC relies not only on the characteristic histologic features but also the exclusion of other causes of graft dysfunction (**Table 3**).[62,63]

Incidence of recurrent primary biliary cholangitis

The overall rates of rPBC are variable and range between 10% and 61% with the median time to rPBC between 3 and 5.5 years (**Table 4**).[60,64–74] The reported recurrence rates not surprisingly increase with time but vary in part due to non-standardized diagnostic criteria for rPBC with inconsistent use of protocol biopsies and variable follow-up. Using the largest PBC cohort to date, a recent study from the Global PBC Study Group reported recurrence rates of 22%, 36%, 50%, and 55% at 5, 10, 15, and 20 years, respectively.[70]

Risk factors for recurrent primary biliary cholangitis

Multiple risk factors for rPBC have been identified and are included in **Table 4**.[65,66,70,72,75,76] However, multiple previous studies reported inconsistent and contradictory results. Of all the baseline patient characteristics and immunosuppression regimens included in a recent meta-analysis included 3184 PBC patients who

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Table 1
Patient and graft survival after liver transplantation for primary biliary cholangitis

Registry	Year	Cohort Size	Graft Survival (%)						Patient Survival (%)					
			1 y	3 y	5 y	10 y	15 y	20 y	1 y	3 y	5 y	10 y	15 y	20 y
UNOS[68]	1994–2009	3052	85.0	80.5	78.1	71.9	—	—	90.2	86.7	84.4	79.0	—	—
ELTR, European Liver Transplant Registry[71]	1999–2009	1929	85.0	—	78.0	—	—	—	90.0	83.0	—	—	—	—
UNOS (DDLT)[70]	2002–2006	100	85.2	82.5	80.7	—	—	—	89.6	87.0	85.1	—	—	—
UNOS (LDLT)[70]	2002–2006	100	85.6	80.9	77.4	—	—	—	92.8	90.1	86.4	—	—	—
Japanese Liver Transplant Society[72]	1994–2010	444	—	—	—	—	—	—	—	—	76.6	71.0	52.6	—
University of Tokyo Hospital[73]	1996–2010	81	—	—	—	—	—	—	90.0	88.0	80.0	—	—	—
Global PBC Group[74]	1983–2016	785	—	—	94.0	90.0	86.0	77.0	—	—	90.0	81.0	70.0	53.0

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Table 2
Causes of cholestasis after liver transplantation

Early (≤6 mo)	Late (>6 mo)
Extrahepatic	Extrahepatic
Stricture: anastomotic, compressive	Stricture: anastomotic
Multiple strictures: ischemic or HAT	Multiple strictures:
Bile leak	ischemic, HAT, recurrent PSC
Cholangitis	Choledocholithiasis
Intrahepatic	Intrahepatic
Ischemia/reperfusion injury	Intrahepatic biliary strictures
ABO blood group incompatibility	Chronic rejection
HAT, hepatic artery thrombosis/stenosis	Recurrent disease
ACR	(PBC, PSC, HCV, hepatitis C virus)
Sepsis	ACR
DILI	DILI, drug-induced liver injury
Small for size CBD, common bile duct	De novo AIH
Post-LT infection	De novo viral hepatitis

underwent LT with underwent protocol or clinically driven liver biopsies, only tacrolimus and preventive UDCA were statistically and significantly associated with the risk of developing rPBC with pooled HRs of 2.62 (95% CI: 1.35–5.09; $P = .004$) and 0.40 (95% CI: 0.28–0.57; $P<.001$), respectively.[77]

Clinical impact of recurrent primary biliary cholangitis

Previous studies suggested that rPBC does not significantly affect long-term patient or graft survival.[60,67,74,78] In two previously reported cohort studies, a combined 5 out of 639 recipients required retransplantation.[60,79] rPBC after second and third LT has been described, but the proportion of graft failure due to rPBC remains low (7–14%).[67,80] However, the recently published Global PBC Study Group data challenge those conclusions. In addition to the identified risk factors for rPBC listed in **Table 4**, the study reported that rRBC was associated with graft loss and death with HR of 2.01 and 1.72, respectively.[70] For this reason, interventions to mitigate the risk of recurrent disease may play a significant role in improving posttransplant outcomes.[70]

Prevention and treatment of recurrent primary biliary cholangitis

Historically, the use of UDCA post-LT for PBC was more reactive than preventive. This approach was supported by previous data that showed the use of UDCA once rPBC was confirmed improved liver biochemistries, but did not influence patient or graft

Table 3
Proposed diagnostic criteria for recurrent primary biliary cholangitis after liver transplant

Inclusion Criteria	Exclusion Criteria
Diagnosis:	Acute and chronic rejection
Confirmed diagnosis of PBC from liver explant histology	Graft-vs-host disease
Serology"	Biliary obstruction or cholangitis
Persistence of AMA or AMA-M2	Vascular complications
Histology:	Viral hepatitis
Lymphoplasmacytic portal inflammation	DILI
Lymphoid aggregates	
Epithelioid granulomas	
Evidence of bile duct injury	

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Table 4
Frequency of and risk factors for recurrent primary biliary cholangitis after liver transplantation

Reference	Registry/Study	Year	Cohort Size	Frequency	Risk Factor(s)
Liermann Garcia et al[69]	Single center (Queen Elizabeth Hospital, Birmingham, UK)	1982–1999	400	17% (3 y)	Younger age at transplant Tacrolimus
Sylvestre et al[89]	Single center (Mayo clinic)	1985–1997	100	17% (4.7 y)	Not reported
Sanchez et al[73]	Single center (Baylor University Medical Center)	1985–1999	156	10.9% (6 y)	Tacrolimus (vs cyclosporine)
Neuberger et al[72]	Single center (Queen Elizabeth Hospital, Birmingham, UK)	1982–2002	485	23%	Recipient age Tacrolimus
Jacob et al[67]	Single center (Germany)	1989–2003	100	14% (median 61 mo)	Tacrolimus
Charatcharoenwitthaya et al[60]	Single center (Mayo Clinic)	1985–2002	164	32% (3.5 y)	Older age at transplant Male sex Tacrolimus
Montano-Loza et al[71]	Single center (Alberta, Canada)	1989–2008	108	13% (5 y) 29% (10 y)	Tacrolimus Mycophenolate mofetil
Bosch et al[64]	Multicenter French and Swiss study	1988–2010	90	27% (5 y) 61% (15 y) 47% (10 y)	No significant factors
Egawa et al[66]	Japanese Liver Transplant Society Registry	1994–2010	444 (LDLT)	9.6% (5 y) 20.6% (10 y)	Younger age at transplant (48 y) IgM, immunoglobulin M > 554 mg/dL Gender mismatch Cyclosporin A as initial immunosuppression
Morioka et al[90]	Single center (Tokyo)	1994–2004	50 (LDLT)	9%	Average tacrolimus trough level within first year of LT LDLT HLA-DR, Human Leukocyte Antigen-DR locus mismatching

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Table 4
(*continued*)

Reference	Registry/Study	Year	Cohort Size	Frequency	Risk Factor(s)
Kogiso et al[68]	Japanese Liver Transplant Society Registry	1994–2010	388 (LDLT)	14% (4.6 y)	Younger recipient age Higher serum IgM Donor sex mismatch Human leukocyte antigen B60 and DR8 Cyclosporin A as initial immunosuppression
Montano-Loza et al[70]	Global PBC Study Group	1983–2016	785	22% (5 y) 36% (10 y)	Biochemical cholestasis within first 6 mo after LT Age at diagnosis (<50 y) Age at LT (<60 y) Tacrolimus
Corpechot et al[65]	Global PBC Study Group	1983–2017	780	18% (5 y) 31% (10 y)	Tacrolimus

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survival.[60] However, recently published data from the Global PBC Study showed that preventive administration of UDCA (10–15 mg/kd/d) is associated with lower risk of rPBC, graft loss, liver-related death, and all-cause mortality compared with no treatment.[65] These findings strongly support the use of UDCA after LT to not only help prevent rPBC but also improve graft and patient survival.[65] These findings were confirmed in two subsequent meta-analyses.[77,81] Further studies are needed to determine the utility of second-line therapies, such as OCA, as an alternative therapeutic option for post-LT PBC patients.

Immunosuppressive therapy

The primary maintenance immunosuppressants used after LT in the United States and Europe are calcineurin inhibitors (CNIs) of which tacrolimus is the drug of choice. However, CNI use is often limited by numerous side effects, particularly those related to renal toxicity. As such, there is a growing trend toward the use of antimetabolites such as mycophenolate mofetil (MMF) on account of its more acceptable safety profile.[41,82,83] However, there are growing data to suggest these trends may not be the most efficacious when PBC is the indication for LT. Before two recently published multicenter studies by the Global PBC Study Group, many of the previous studies reported inconsistent findings on the impact of immunosuppressants after LT in patients with PBC. The first study by Motano-Loza and colleagues, reported that tacrolimus was associated with a higher risk of rPBC (HR 2.31, 95% CI 1.72–3.10, $P < .001$) compared with MMF (HR 1.56, 95% CI: 1.19–2.04; $P = .001$) and cyclosporine (HR 0.62, 95% CI: 0.46–0.82; $P = .001$).[70] The second study published by Corphechot and colleagues supported the use of cyclosporine A in post-LT PBC patients, whereas it confirmed the previous results reporting that tacrolimus significantly increased the risk of rPBC (HR 2.06, 95% CI: 1.44–2.94; $P < .001$).[65] In addition, the Global PBC Study Group also observed an additive beneficial effect of cyclosporine compared with tacrolimus, which strongly supports the use of cyclosporine and preventive UDCA combination therapy in post-LT PBC patients.[65] Although there is no universal immunosuppression protocol for all post-LT patients, these results support a more individualized immunosuppression regimen based on the indication, one that is based on the knowledge of risk factors for disease recurrence while balancing the risk of potential medication side effects, rejection, and graft and patient mortality. Based on the growing evidence that cyclosporine A reduces PBC recurrence, it should be considered over tacrolimus as the primary immunosuppressant after LT for PBC.

Rejection

Similar to other forms of autoimmune liver disease, PBC is associated with an increased risk of rejection after LT.[84]

Rates of acute cellular rejection (ACR) after LT for PBC range from 21.7% to 83.3%.[67,85,86] ACR is associated with decreased recipient and graft survival but may also play a negative role in the development of the rPBC.[86,87] In addition, 16% of patients with PBC who underwent LT are at risk of developing late onset acute cellular rejection (LAR). In addition to previous graft failure and younger recipient age, a history of PBC was identified as an independent negative predicator of LAR with odds ratio of 2.1 and is associated with worsened graft survival.[88]

SUMMARY

The number of LT performed for PBC has declined over the years, which likely reflects the benefits of earlier diagnosis and treatment. Nonetheless, LT remains an important

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option and the only cure for patients with progressive PBC despite medical therapy with survival rates among the highest of all indications for LT.

As such, patients are living longer and are at risk for developing clinically relevant recurrent disease and other complications related to chronic immunosuppression. The recent landmark publications from the Global PBC Study Group provide valuable insight into the changing landscape of PBC before and after LT. Although the incidence of rPBC is improved with preventive UDCA, rPBC is associated with decreased patient and graft survival.

CLINICS CARE POINTS

- Although intractable pruritus is a justifiable indication for liver transplantation (LT) for primary biliary cholangitis (PBC), it is not a standard indication for MELD exception points, and therefore, it is a subject to appeal to the National Liver Review Board (NLRB).
- Liver biopsy is required to confirm the diagnosis of recurrent PBC (rPBC).
- The preventive administration of UDCA after LT to not only helps prevent rPBC but also improves graft and patient survival.
- Based on the growing evidence that cyclosporine A reduces PBC recurrence, it should be considered over tacrolimus as the primary immunosuppressant after LT for PBC.

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