POST TRANSPLANT OUTCOMES IN PSC

Kidist K. Yimam, MD
Medical Director, Autoimmune Liver Disease Program
Division of Hepatology and Liver Transplantation
California Pacific Medical Center (CPMC)
PSC Partners 2018 Conference, Sacramento, CA
INDICATION FOR LT IN PSC

- Decompensated cirrhosis
- Cholangiocarcinoma (CCA): hilar, < 3cm, per neoadjuvant Mayo Clinic protocol
- Recurrent bacterial cholangitis
TRANSPLANT FOR PSC IN THE US

- 5% of all adult transplant recipients in the US each year have PSC as the primary etiology of liver disease necessitating a liver transplant.

- ~14% of transplant recipients with PSC receive a living donor liver transplant (LDLT), compared to 3.5–4% of transplant recipients with other forms of chronic liver disease
LT for PSC has been fairly stable with an average of 292 LT per year.
LT for PSC is highly successful, with 5-year patient survival rates in the United States exceeding 85%
POST LT OUTCOMES

- PSC have post-transplant graft and patient survival that is not different than other transplant recipients

- However, when considering only recipients of a living donor allograft in the US from 2002–2013, patients with PSC transplanted at an ‘experienced’ center (defined as having performed >15 living donor liver transplants) had superior post-transplant graft and patient survival even after adjusting for other factors.


RECURRENT PSC

- Recurrent PSC, is estimated to occur in the range of 15–35% of transplant recipients.

- Wide range of the estimated risk of recurrent PSC rests in part on the challenges in diagnosing recurrent PSC, as it is considered a diagnosis of exclusion.

### RECURRENT PSC RATES

<table>
<thead>
<tr>
<th>Reference</th>
<th>Time Period</th>
<th>Number of Patients</th>
<th>Recurrence Rate (%)</th>
<th>Median Time to Recurrence (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grazziadi et al, 1999</td>
<td>1985–1996</td>
<td>120</td>
<td>20 (8.3 based on both cholangiographic and histologic features)</td>
<td>36 mo (14–108 mo), histologic criteria; 8.6 mo (3–43 mo), cholangiographic criteria</td>
</tr>
<tr>
<td>Alabraba et al, 2009</td>
<td>1986–2006</td>
<td>230</td>
<td>23.5</td>
<td>4.6 y (0.5–12.9 y)</td>
</tr>
<tr>
<td>Goss et al, 1997</td>
<td>1984–1996</td>
<td>127</td>
<td>8.6</td>
<td>Not provided</td>
</tr>
<tr>
<td>Vera et al, 2002</td>
<td>1986–2000</td>
<td>152</td>
<td>37</td>
<td>36 mo (1–120)</td>
</tr>
</tbody>
</table>
RECURRENT PSC

- In post LT setting, characteristic of PSC can also be seen in patients who have developed a
  - Hepatic artery stenosis/thrombosis
  - Chronic ductopenic rejection
  - Cytomegalovirus infections of the biliary tract, and/or
  - Received a transplant from a donor with an incompatible blood type or from a donation after cardiac arrest

- For these reasons, the diagnosis of recurrent PSC is one of exclusion, and requires exclusion of conditions that can mimic recurrent PSC
## RECURRENT PSC

### Diagnostic criteria for recurrent primary sclerosing cholangitis following liver transplantation

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed diagnosis of PSC prior to liver transplantation</td>
<td>Hepatic artery stenosis or thrombosis on radiographic imaging or angiography</td>
</tr>
<tr>
<td>Cholangiography (MRCP or ERCP) performed ≥90 days after transplantation demonstrating intrahepatic and/or extrahepatic biliary structuring, beading, and/or irregularity, OR</td>
<td>Chronic ductopenic rejection on histologic evaluation of liver biopsy</td>
</tr>
<tr>
<td>Liver biopsy demonstrating fibrous cholangitis and/or fibroobliterative lesions, with or without biliary fibrosis or cirrhosis, and/or ductopenia</td>
<td>Isolated extrahepatic anastomotic strictures</td>
</tr>
<tr>
<td></td>
<td>Donor and recipient ABO incompatibility</td>
</tr>
<tr>
<td></td>
<td>Non-anastomotic strictures occurring prior to day 90 post-transplantation</td>
</tr>
</tbody>
</table>

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RISK FOR RECURRENT PSC

### Table 4
Risk factors for recurrent primary sclerosing cholangitis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-DRB1*08 (in Recipient or Donor)</td>
<td>Use of extended donor criteria grafts</td>
</tr>
<tr>
<td>Absence of donor HLA-DR52</td>
<td>Steroid-resistant ACR</td>
</tr>
<tr>
<td>Recipient-donor gender mismatch</td>
<td>Use of OKT3</td>
</tr>
<tr>
<td>Male recipient</td>
<td>Presence of UC after LT</td>
</tr>
<tr>
<td>Younger recipient age</td>
<td>Maintenance of steroid therapy for UC &gt;3 mo</td>
</tr>
<tr>
<td>Intact colon before LT</td>
<td>Presence of cholangiocarcinoma before LT</td>
</tr>
<tr>
<td>&gt;1 episode of ACR</td>
<td>Concurrent cytomegalovirus infection in recipient</td>
</tr>
<tr>
<td>First-degree related donors (LDLT)</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** ACR, acute cellular rejection; HLA, human leukocyte antigen.

Presence of ulcerative colitis

Acute cellular rejection (ACR)
TREATMENT FOR RECURRENT PSC

- There is no proven medical therapy for recurrent PSC (rPSC) after LT.
- Although ursodiol is used in most transplant centers and improves the liver biochemical profile, its effect on outcomes remains unclear.
- Prophylactic use of UDCA may be justified in patients with coexisting UC who may benefit from UDCA by reducing the risk of colon cancer.
- As in the nontransplant setting, biliary strictures may be managed by endoscopic or percutaneous methods.
Patients with PSC are commonly thought to have a higher risk of ACR compared with LT recipients with other primary liver diseases.

- Reported rates are variable
- Variable immunosuppressive regimens, inconsistent use of protocol biopsies, and histologic definition of ACR

- Conflicting evidence regarding concomitant IBD as risk of ACR
# ACR AFTER LT IN PSC

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Cohort Size</th>
<th>Rejection Rate (%)</th>
<th>Type of Rejection</th>
<th>Median (Range) Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milkiewicz et al, 2000</td>
<td>1982–1998</td>
<td>136</td>
<td>7</td>
<td>Chronic</td>
<td>Not provided</td>
</tr>
</tbody>
</table>
LATE ACR

- Late acute rejection (LAR), which is more common in PBC, PSC, and autoimmune hepatitis (AIH), is associated with worse patient and graft survival.

RETRANSPLANT FOR RPSC

- Long-term data indicate that rPSC significantly affects graft survival, rate of retransplant, and patient survival

- Retransplant is a viable option in patients who develop rPSC with subsequent graft loss.

- In a retrospective review of the United Network for Organ Sharing (UNOS) database, the rate of retransplant was significantly higher in patients with PSC compared with patients with primary biliary cholangitis (PBC) (12.4% vs. 8.5%) and PSC was identified as an independent predictor for retransplantation.

INFLAMMATORY DISEASE (IBD) COURSE AFTER LT FOR PSC

- In general, one-third of patients with PSC and IBD will have worsening of IBD symptoms post-liver transplantation.

- Choice of immunosuppression can impact post-transplant activity of IBD in patients with PSC.

- Specifically, combination therapy with tacrolimus and mycophenolate mofetil has been associated with worsening of IBD activity while combination cyclosporine and azathioprine was associated with fewer IBD flares after LT.


MANAGEMENT OF IBD AFTER LT

- Similar to pre-LT with increased risk of infection if biologics are added to standard LT immunosuppression
  - Consider Azathiopurine in moderate to severe IBD with tacrolimus
  - Severe cases—will need anti-TNF
RISK OF CRC OR DYSPLASIA

- The risk of developing colorectal cancer in patients with PSC and IBD persists after liver transplantation, thus continued yearly colorectal surveillance is recommended.

- In one study, the risk of cumulative incidence of dysplasia was 15% at 5 years and 21% at 8 years (comparable to pre-LT risk).

POUCHITIS

- A total of 63 PSC/ileal-pouch anal anastomosis (IPAA) patients were studied, including 19 patients with OLT and 44 patients without OLT.

- Fifty patients (79.4%) had chronic antibiotic-refractory pouchitis (CARP).

- In both univariable and multivariable analyses (adjusting for OLT status), none of the variables studied was associated significantly with CARP (P > .20).

- All 7 patients (100%) with IPAA-then-OLT were diagnosed as having CARP, of whom 4 developed CARP before OLT, which persisted after OLT, and 3 had CARP after OLT.
POUCHITIS

- Of 12 patients with OLT-then-IPAA, 7 (58.3%) developed CARP.

- The frequency of CARP in OLT-then-IPAA was statistically significantly lower than that in IPAA-then-OLT (58.3% vs 100%; P = .047).

- CARP is common in patients with ulcerative colitis and PSC.

- OLT in these patients may not affect the frequency of CARP in general and appears not to alter the disease course of pre-existing CARP.

- However, in a subset of patients, OLT might reduce the risk for the development of de novo CARP.
THANK YOU.