Percutaneous management of biliary strictures after liver transplantation: is there a definitive solution?

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Aims and objectives

Still considered the Achilles heel in hepatic transplantation, biliary complications can remain a major source of morbidity. Biliary strictures (which can be either anastomotic or non anastomotic) can be treated percutaneously or via endoscopy (in selected cases), decreasing the need for subsequent surgical intervention.

- Our main objective was to determine the efficacy and long term results of percutaneous treatment in patients with biliary strictures or cholangitis following liver transplantation (LT) and to establish the suitable interventional therapeutic modality for these patients
- Our secondary objectives were the presentation of the main complications which can occur after the percutaneous interventions and the presentation of an algorithm of diagnosis and treatment in this subset of patients
Methods and materials

Patients:

Between 1st of January 2011 and 1st of January 2015, in the Fundeni Clinical Institute, 225 liver transplantations were performed. We analyzed retrospectively the clinical data, imaging findings and interventional radiology protocols of 34 consecutive patients with biliary strictures or cholangitis following LT, treated with percutaneous interventional techniques. The mean age was 47 years (range 3-62 years), with 21 male patients included (male:female ratio= 1:1.6). In our study group, living donor split grafts (n=23) or deceased donor grafts were performed (n=11). The biliary anastomosis was either duct-to-duct(n=19) or bilio enteric (Y en Roux anastomosis) (n=15) Fig. 1 on page 5.

In our study group, the most frequent indication for transplantation was liver failure due to viral or alcoholic cirrhosis (n=25), with 1 case known with primary biliary cirrhosis.

Definitions:

Biliary stricture was diagnosed when the stenosis of the bile duct and the dilatation of the intrahepatic duct proximal to the stricture were observed on magnetic resonance cholangiography (MRCP), and the liver biochemical parameters, such as serum bilirubin, #-glutamyltransferase, and alkaline phosphatase were abnormal, whether or not the patient had symptoms of abdominal pain and fever.

A nonanastomotic biliary stricture was diagnosed when the intrahepatic bile ducts proximal to the anastomotic site show strictures or irregularities, with corresponding clinical and biochemical parameters sugesting cholangitis.

The recurrence of the biliary complications was defined as recurrence of clinical symptoms (jaundice, cholestasis), associated with imaging findings suggestive of biliary strictures or cholangitis.

The end point of the percutaneous transhepatic biliary drainage (PTBD) was placement of an internal drainage, followed by definitive repair with bilioplasty (dilatation or cutting balloon) or stent placement. The patients were followed for a mean period of 1 year after suppression of the biliary drainage.

Investigation protocol:
All patients with clinical signs of cholestasis were referred to ultrasound imaging to determine the presence of a mechanical obstacle or to define the presence of an arterial hepatic thrombosis. In the presence of biliary dilatation, the patients were referred to magnetic resonance cholangio pancreatography (MRCP) or to endoscopic retrograde cholangio pancreatography (ERCP); in case of failure of ERCP, a direct percutaneous cholangiography was performed to assess the biliary complications Fig. 2 on page 5.

**Percutaneous transhepatic cholangiography protocol**

- Conscious sedation
- 10 mL of 1% lidocaine HCl was locally infiltrated at the skin surface of the prepared puncture site.
- Ultrasound guided puncture of the biliary tree (either right or left branches), using a 21G Chiba needle, followed by injection of contrast media; a 0.018-inch microwire is passed in the biliary tree, which is used for the placement of a 5 F sheath and a 0.035-inch hydrophilic guidewire is introduced.
- Navigation with a 4F RDC catheter (Cook) through the stenosis and placement of a stiff Amplatzer type guidewire, progressive dilatation with 6 and 8F dilators with placement of an internal-external 8,5F drain (Cook). If the stricture is not passed, an 8F external drain is placed and 2 weeks after a new procedure for internalization of the drain was scheduled.
- 2 weeks after successful placement of the internal drainage, bilioplasty sessions were started or stenting was performed (either percutaneously or with ERCP rendez vous technique). The bilioplasty sessions were performed with either cutting balloons (Flextome- Boston Scientific, 4x10mm) or with regular dilatation balloons (Cook, 8x10mm). The stents were either plastic or bare metal.

A typical placement of a percutaneous transhepatic biliary drainage, followed by dilatation sessions is presented in Fig. 3 on page 6.

**Exclusion criteria:**

- Irreversible coagulopathies (INR >1,5, PLT<50.000)
- Renal failure (serum creatinin >2mg/dl)
- Presence of ascites
Fig. 1: Types of biliary anastomoses performed in hepatic transplantation.

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**Fig. 2:** Investigational protocol in hepatic transplant recipients who develop jaundice or clinical signs of cholangitis.

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Fig. 3: 53 year old patient, 1 month after OLT with duct-duct anastomosis, develops cholangitis and mild jaundice. Placement of a percutaneous transhepatic biliary drainage. Puncture of the non dilated biliary tree using a 21G chiba needle with cholangiogram showing an anastomotic stricture (arrow) (a). The stenosis is passed and a 5F Neff catheter is placed (b). Internal external biliary drainage is placed draining the entire biliary tree (c). Two weeks after, several dilatations are performed using a 10mm/8cm balloon, which lead to resolution of symptoms and removal of the drain (d).

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Results

The demographic and clinical features of the study group are presented in Table 1 on page 11. Almost a third of the patients presented with clinical signs of cholangitis; in this subset, 7 patients had no US signs of biliary tract dilatation, but presented with jaundice and fever.

According to the imaging diagnosis, we divided our group in patients with anastomotic strictures (n=25) and patients with non anastomotic strictures (n=9). Biliary anastomotic strictures were more frequently found in patients with bilioenteric anastomosis (8/12 cases).

PTBD was successfully placed in 32 cases in the first session, in 2 cases a second attempt was necessary in 5-7 days. In n=3 patients, the passage through the stricture was not achieved (even with multiple internalization attempts), hence an external drain was placed - see Fig. 4 on page 13.

In the n=31 cases with internal/external drainage, a definitive solution for the treatment of the strictures was attempted. Hence, n=22 patients followed several dilatation sessions (mean 5; min 4-max 8 sessions), of which 6 patients with cutting balloon and 16 with dilatation balloons. In the other n=9 cases, a stent was placed: plastic stents with ERCP rendezvous technique (n=7) and bare metallic stents (n=2) (see Table 2 on page 11). A case with bare metallic stent is presented in Fig. 5 on page 14 and a patient which benefited from ERCP rendezvous technique is presented in Fig. 6 on page 15; a pediatric case with cutting balloon dilatation is presented in Fig. 7 on page 16.

The 6 month and 1 year recurrence rates are presented in Table 3 on page 12. The aggregate 6 months and 1 year recurrence rate in the bilioplasty group was 32% and 45% respectively; in the stenting group was 0% at 6 months and 33% at 1 year.

Catheter displacement with choleperitoneum (n=4) was the most frequent complication, which necessitated catheter repositioning and upsizing (8-10F catheters)- see Fig. 8 on page 17. Other complications encountered were hemobilia (n=2 cases), which required only conservative treatment and 1 case of septic shock.

Discussions
• The risk of occurrence of a specific biliary complication is related to the type of biliary reconstruction performed at the time of liver transplantation, so a thorough knowledge of the anatomy is essential to the procedure's success (1). The coledoco-coledocian anastomosis (duct-to-duct) is the most common biliary reconstruction procedure performed during OLT; the procedure is technically easier, it preserves the function of Sphincter of Oddi and allows easy endoscopic access to the biliary system after the surgery. Also the use of T-tubes is controversial, since it has been associated with bile leak and cholangitis at the time of their removal. The bilioenteric anastomosis is usually recommended in patients with pre-existing biliary disease (such as primary sclerosing cholangitis, or prior biliary surgery) when there is a size mismatch between donor and recipient ducts; it also is a contraindication to ERCP due to lack of access (2,3). In our study there was predominance of the duct-to-duct anastomosis (favored in both OLT and LDLT)

• By comparison with OLT, complication rates (from bile leaks and strictures) are higher with LDLT (high as 35% in certain series). The biliary leaks reported in LDLT are from the cut surface and at the site of the anastomosis and the incidence ranges from 10 to 25%. (4) The incidence of strictures ranges from 8 to 35%. Preservation of the liver beyond 12 hours may result in a higher incidence of diffuse or non anastomotic strictures (5). In our study, the incidence of biliary strictures was comparable to the previously published studies

• Although the biliary catheter itself maintains the patency of the anastomosis while allowing repeated access to the stricture for evaluation and dilatation, due to high rate of complications and lack of patient compliance, a definitive solution is needed (6). These catheters also offer an advantage in management of strictures complicated by significant debris, as daily flushing can get rid of most debris. In patients who develop cholangitis, the catheter can be opened for gravity drainage to allow external decompression of the biliary system and resolution of symptoms (7).

• Although a low sample size was used, our study shows the superiority of stent placement over bilioplasty; of course a larger sample and longer evaluation intervals are needed for a better evaluation of the response. Li et al (8) have shown that PTBD with stenting and bilioplasty have good results on long term followup (mean followup 452 days), with less efficacy in the treatment of multifocal nonanastomotic strictures which are better treated with retransplantation

• In our study, several patients had non dilated biliary tree, which proved to be a technical challenge, due to the added difficulty of accessing the biliary tract. In general, due to ischemic fibrosis, the technical difficulty of biliary punctures is increased (9). The complications met in our study group were mostly related to catheter depositioning (due to patient noncompliance) and one case of septic shock in a patient with severe cholangitis.
• There are several factors impacting the success of the interventional techniques, such as prolonged ischemia which can lead to rapid biliary complications, often severe. In these cases a quick diagnosis and treatment of these cases (with endovascular or surgical techniques), lead to a significant decrease in morbidity (10). Other limiting factors are the presence of non anastomotic strictures, which require the placement of several drainage catheters and treatment of the local and general septic complications (11). The development of chronic biliary sepsis and calculous disease further hinder the success of our treatment (12).
**Table 1:** Clinical and demographic characteristic of the recruited patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male:female)</td>
<td>1:1.6</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>47 years (range 3-62 years)</td>
</tr>
<tr>
<td>Total serum bilirubin (mean; min, max)</td>
<td>9mg/dl (1-20)</td>
</tr>
<tr>
<td>Gamma GT</td>
<td>620 U/L</td>
</tr>
<tr>
<td>PLT count (mean)</td>
<td>180,000</td>
</tr>
<tr>
<td>INR</td>
<td>1.2</td>
</tr>
<tr>
<td>Duct to duct anastomosis (number of cases)</td>
<td>22/34</td>
</tr>
<tr>
<td>Cholangitis (number of cases; percentage)</td>
<td>13; 28%</td>
</tr>
<tr>
<td>No biliary tract dilatation (number of cases)</td>
<td>7/34</td>
</tr>
</tbody>
</table>

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Table 2: Number of patients which benefited from definitive correction (bilioplasty and stenting)

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<table>
<thead>
<tr>
<th>Procedure</th>
<th>6 months reccurrency rate (%)</th>
<th>1 year reccurrency rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon dilatation (n=16)</td>
<td>31</td>
<td>45</td>
</tr>
<tr>
<td>Cutting balloon (n=6)</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Plastic stent (n=7)</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>Metallic stent (n=2)</td>
<td>0</td>
<td>50</td>
</tr>
</tbody>
</table>

**Table 3:** 6 months and 1 year reccurrency rates in the bilioplasty and stenting groups.

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Fig. 4: 51 year old male, with LDLT, presenting with fever 7 days after transplantation. A) Axial T2FrFSE FATSAT revealing a fluid collection near the cut surface of the liver (arrow); no signs of biliary dilatation is seen. B) T tube cholangiography (arrow). Under CT guidance a drain is placed in the fluid collection; contrast administration through the T tube reveals no contrast media extravasation and no biliary dilatation. C) Portal phase CT. One week after T tube suppression, biliary dilatation occurs, seen in both anterior and posterior segments (arrow). D) Cholangiogram performed through the external drain. An external drain is placed with the internal loop at the level of the biliary confluence; the whole biliary tree is drained. Note small fistula between the anterior duct and the fluid collection previously drained (arrow)

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**Fig. 5:** 41 yr old patient, 40 days after LDLT cholestasis and cholangitis; bilio-entero anastomosis US: small-moderate intrahepatic dilatation. A) MRCP, Long TE sequence. Dilatation of mainly the anterior segmental biliary branch with decalibration at the level of the anastomosis (arrow). B) An internal/external drainage is performed, the cholangiogram showing no residual dilatation. C) An uncovered metallic stent is deployed with an external drain in its immediate vicinity which was removed after two weeks symptom free.

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Fig. 6: 45 year old male, OLT, duct to duct anastomosis presents cholangitis. A) MRCP, short TE coronal sequence. Multiple irregularities and strictures involving the intrahepatic and extrahepatic biliary tree, with dilatation of the left lobe duct (arrows). B) CT portal phase. An intrahepatic fluid collection is seen in the VIIIth segment (arrow) which is percutaneously drained. C) Cholangiogram performed through an internal external drain shows contrast extravasation (arrows) in the abces previously drained (arrow head). D) A stent is placed using ERCP rendezvous procedure after the resolution of symptoms (4 weeks after the internal/external drain was placed).

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Fig. 7: 3 year old patient with living donor left liver lobe transplantation, develops stenosis of the hepatojejunal anastomosis with jaundice and cholangitis. A. MRCP, long TE sequence reveals a short anastomotic stricture (arrow). B. CT low dose colangiography. External decompression biliary drainage is performed with placement of a 6 Fr catheter, with no passage of the contrast media into the jejunal anastomotic loops c. A surgical transjejunal stent is placed, with the distal end above the anastomosis (arrow), which is catheterized using a hydrophilic wire. D. An internal-external drainage is placed (arrow). E, F. Two weeks later, cutting balloon dilatation sessions are performed using a 6mm diameter/4cm length Flextom (Boston Scientific) balloon, which are repeated 4 times at 2 weeks interval. At the end of the dilatation sessions, the biliary drainage is suppressed, with no recurrence of symptoms at 1 year and 2 years respectively.

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Fig. 8: 58 yr old patient, progressive jaundice and cholangitis signs after 2 months after OLT; duct -duct anastomosis US: moderate dilatation of intrahepatic ducts. A) MRCP, long TE sequence. A short anastomotic biliary stricture (arrow) is seen at the level of the anastomosis, causing moderate dilatation of the biliary tree. B) ERCP failed to catheterize the stenosis. C) A 8 Fr internal/external drain was placed at the level of the anterior biliary ducts, draining the the whole biliary system; clear visualization of the stricture (arrow). D) 24 hours later, the patient complained of severe abdominal pain, the abdominal radiograph showing displacement of the drainage catheter with its internal loop near the lateral abdominal wall (arrow) and pneumoperitoneum. E) A 4 F RDC catheter (arrow) is succesfully maneuvered inside the biliary tract. F) A 10F internal catheter is deployed with complete remission of symptoms.

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Conclusion

- PTBD followed by bilioplasty or stenting can be a viable option in the treatment of biliary complications after LT, increasing the quality of life and decreasing the associated morbidities.
- Low complication rates, make these procedures safe to perform in these patients, but the added difficulty of the posttransplantation setting increases the difficulty of the initial procedures.
- An accurate and rapid imaging diagnosis is essential to the treatment options available.
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References


