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Management of biliary anastomotic strictures after liver transplantation

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A B S T R A C T

Biliary strictures constitute 40% to 60% of the biliary complications after liver transplantation. They are more common after living donor related liver transplantation (LDLT) than orthotopic liver transplantation (OLT). Balloon dilation followed by multiple plastic stent insertion leads to a mean resolution rate of 84% in the treatment of ASs after OLT. Endoscopic treatment of ASs after LDLT is more difficult because of the small size of the ASs, their multiple number and peripheral location. Balloon dilation followed by multiple plastic stent insertion had a mean resolution rate of 53%. Percutaneous transhepatic biliary drainage was required in 16% to 44% of the patients. Refractory cases with complete biliary obstruction and severe stenosis, in whom the stricture could not be traversed with a guidewire, can be treated by magnetic compression anastomosis as a rescue therapy, if the anatomy of the bile ducts is suitable.
In this review, we will focus on the endoscopic treatment of ASs, with special emphasis to refractory cases.

1. Introduction

Biliary complications occur in 6% to 40% of patients after liver transplantation (LT) and cause a significant morbidity [1–11]. Biliary strictures are one of the most common biliary complications after orthotopic liver transplantation (OLT), constituting approximately 40–60% of all [5–7,12]. Although surgical treatment with conversion to a Roux-en-Y choledochojejunostomy was the standard care of treatment for biliary strictures in the past, non-operative treatments, primarily endoscopic, have become the standard practice in the last two decades, leaving the surgical intervention for refractory cases or severe complications. However, the optimal endoscopic treatment of biliary strictures is not well defined.

In this review, we will summarize the risk factors, pathogenesis and diagnosis of biliary strictures after LT and focus on the endoscopic treatment of anastomotic strictures (ASs), with special emphasis to refractory cases.

2. Incidence

Anastomotic strictures develop with an incidence of 6–12% and 8–31% after deceased donor (DDLT) and living donor related LT (LDLT), respectively [2,11,39–44]. Biliary strictures are more common after LDLT because of technical challenges due to small duct size, multiple reconstructions, and devascularization of bile ducts during the hilar dissection [2,23,24,45,46].

3. Risk Factors

The risk factors for biliary strictures can be classified into 4 groups:

1) Donor related risk factors: older donor age, pre-existing immunologic diseases such as primary sclerosing cholangitis, and ABO blood-type incompatibility
2) Graft related risk factors: prolonged cold and warm ischemia time, extended donor criteria grafts, and donation after cardiac death (DCD) [13–21]
3) Surgical risk factors: the use of inappropriate surgical techniques such as inappropriate sutures, an excessively long bile duct, tight anastomosis, excessive dissection of periductal tissue during procurement, excessive use of electrocauterization for bleeding control, bile leak, small caliber of the bile ducts, and disparity between the size of the recipient and donor bile ducts [16,22–28]
4) Post-surgical risk factors: the development of hepatic artery thrombosis (HAT), CMV infection, and acute–chronic rejection episodes [1,8,22,29–31]

4. Diagnosis

4.1. Clinical presentation

The clinical presentation of patients varies considerably. They can present with abdominal pain, anorexia, pruritus, jaundice, and fever. Abdominal pain may be absent because of immunosuppression and hepatic denervation [16,35,47]. Some of the patients are asymptomatic

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and biliary stricture is considered because of persistent elevations in serum cholestatic liver tests.

4.2. Diagnostic work-up

The initial evaluation is to differentiate obstructive jaundice from the other non-obstructive causes of cholestasis such as acute or chronic rejection, recurrence of primary disease, and drug-induced cholestasis. Transabdominal ultrasonography is the first step in the diagnostic work-up with simultaneous Doppler evaluation of the hepatic vessels for the exclusion of hepatic artery thrombosis, stenosis and/or portal or hepatic vein occlusion. Unfortunately, transabdominal ultrasonography has a low sensitivity (38–66%) and could not detect biliary obstructions in most of the time [39,48]. The absence of biliary dilation on ultrasonography should not preclude further evaluation if there is a high clinical suspicion [49,50]. Patients with a normal ultrasonography and a low clinical suspicion of obstructive jaundice should undergo liver biopsy in order to exclude acute–chronic rejection or recurrence of primary disease.

The second step in the evaluation of patients with a high clinical suspicion of obstructive jaundice is to obtain a cholangiography. Magnetic resonance cholangiopancreatography (MRCP) has gained acceptance as an initial diagnostic tool due to its non-invasive nature and high sensitivity (93–97%) and specificity (92–98%) [8,51,52]. It has the advantage of demonstrating the whole biliary tree including the upstream bile ducts in cases of complete obstruction and also suggests a road map for therapeutic ERCP.

The final step in the diagnosis and treatment of biliary strictures is ERCP and/or percutaneous transhepatic cholangiography (PTC) [53]. ERCP is the most common initial choice of modality in patients with duct-to-duct anastomosis. PTC is reserved to patients who fail an ERCP attempt at several steps or inadequate drainage of some of the hepatic sectors and to those with a Roux-en-Y hepaticojejunostomy or choledochojejunostomy.

5. Classification

Biliary strictures can be classified as ASs or non-anastomotic strictures (NAS) according to their location.

5.1. Anastomotic strictures

Most of the ASs occur within the first year after OLT [3,32,33]. They are isolated, short, dominant narrowings within the 5 mm of the biliary anastomosis (Fig. 1). Early ASs, which occur within the first month after LT are mostly due to surgical technical problems whereas delayed ones are due to a combination of surgical technique and fibro-proliferative response to local ischemia. Anastomotic strictures can also occur within the first months after transplantation in recipients of livers from donation after cardio-circulatory determination of death (DCDD), in recipients of livers with prolonged warm ischemia time, and in patients who developed early arterial thrombosis [25,34,35].

5.2. Non-anastomotic strictures

NASs occur in the intrahepatic or extrahepatic bile ducts more than 5 mm proximal to the biliary anastomosis (Fig. 2). These strictures are most often multiple, complex, and longer than ASs and may be associated with rapidly re-accumulating biliary sludge or casts. They mostly develop as a consequence of ischemic injury to the bile ducts. Immunologic factors such as chronic ductopenic rejection, ABO blood-type mismatch, CMV infection, pre-existing primary sclerosing cholangitis, autoimmune hepatitis, and bile salt toxicity could also play a role in the development of NASs [8,30,31,36]. Non-anastomotic stricture recipients of DCDD can develop non-anastomotic strictures as early as three weeks after transplantation, especially ischemia-mediated type, occur before ASs with a mean time of 3 to 6 months after LT [1,37]. They are more difficult to treat and end up with less favorable outcomes including re-transplantation and death in up to 50% of patients following the development of graft failure [1,16,38].

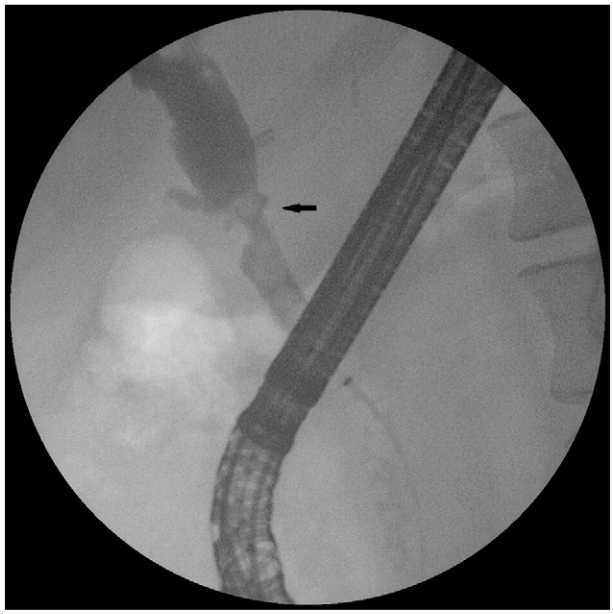

Fig. 1. Anastomosis stricture (arrow) after orthotopic liver transplantation with upstream biliary dilation and choledocholithiasis.

6. Endoscopic treatment of anastomotic biliary strictures after orthotopic liver transplantation

Over the past two decades, endoscopic management has evolved and become the first choice of treatment for ASs. There are several options in the endoscopic management of ASs: balloon dilation (BD), balloon dilation and multiple plastic stent insertion, and metal stent insertion. Sometimes a guide wire cannot be inserted endoscopically through the anastomosis because of an angulated or disconnected stricture. In these patients, PTC may be used initially to traverse the

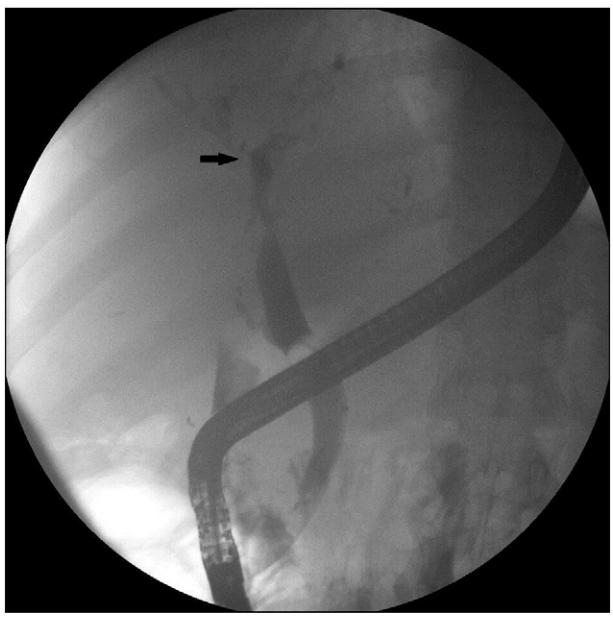

Fig. 2. Non-anastomotic stricture (arrow) after orthotopic liver transplantation extending more than 5 mm proximal to the anastomosis with intrahepatic filling defects due to sludge.