Non-anastomotic biliary strictures after liver transplantation: Focus on percutaneous treatment and extent of disease

ATTILA DOROS*, PÁL ÁKOS DEÁK, ERIKA HARTMANN, ANDREA NÉMETH, ZSUZSA GERLEI, JÁNOS FAZAKAS, DÉNES GÖRÖG, BALÁZS NEMES, IMRE FEHÉRVÁRI, LÁSZLÓ KÓBORI

Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary

*Corresponding author: Attila Doros, MD, PhD; Department of Transplantation and Surgery, Semmelweis University, Baross u. 23, H-1082 Budapest, Hungary; Phone: +36-1-267-6000; Fax: +36-1-317-0964; E-mail: dorattila@yahoo.com

(Received: April 19, 2011; Accepted after revision: December 5, 2011)

Abstract: *Introduction:* Biliary strictures remain a key problem after liver transplantation. Anastomotic strictures are treated by surgery or interventional therapy. Intrahepatic stenosis requires retransplantation. For bridging, percutaneous and endoscopic interventions are used. The extent of the strictures may have an important role in therapy planning. *Methods:* Strictures were divided into four zones (1: extrahepatic, not included in this study; 2: hilar; 3: central; 4: peripheral). Twenty patients were treated with balloon dilatation/stent implantation/retransplantation/supportive care (Zone 1: 0/0/0/0; Zone 2: 8/7/2/0; Zone 3: 7/5/2/1; Zone 4: 1/1/3/1). *Results:* Mean follow-up time was 48 months. In Zone 2, one patient died as a result of recurrent hepatocellular carcinoma (HCC), and seven patients are alive, five after stent placements and two after retransplantation. Four patients are alive in Zone 3: all had stent placements and one later retransplantation. One patient died after retransplantation, two on the waiting list, and one due to chronic liver failure. One patient is alive in Zone 4 after early retransplantation, and three died. *Conclusion:* Percutaneous therapy is safe and effective in intrahepatic biliary stenosis after liver transplantation. It can provide the cure or bridge retransplantation. Based on zonal classification, we recommend the following treatments: Zone 4: early retransplantation; Zone 2: minimally invasive therapy; Zone 3: individual decisions.

Keywords: liver transplantation, biliary complication, percutaneous treatment, interventional radiology

Introduction

In spite of technical refinements, biliary strictures remain a key problem in liver transplantation [1]. Two main types are recognized: anastomotic and non-anastomotic (also called intrahepatic). In anastomotic strictures, good results are achieved with surgery or minimally invasive therapy [2, 3]. Intrahepatic stenosis usually requires retransplantation; however, survival chances are less favorable [4]. For palliation and bridging to retransplantation, percutaneous and endoscopic interventions are used [5]. The treatment options are independent of the variable causes, although best results are achieved when the hepatic artery stays patent [6, 7]. The extent of the strictures may have an important role in therapy planning, and when more peripheral bile ducts are involved, the less successful palliative therapy can be offered. The outcomes of the interventions for intrahepatic biliary strictures were retrospectively analyzed focusing on the extent of the disease. We have raised the question of whether we will be able to offer the patients cure, long-term palliation, or successful bridging. For this, we have tried to separate the patients by applying a zonal classification of the strictures based on the work of Buis et al. [8, 9]. According to their work, Zone 1 consists of all strictures in the extrahepatic region, including the anastomotic region. Zone 2 strictures involve hepatic bifurcation or trifurcation: the lobar ducts. Zone 3 strictures are more severe; they are lesions of the segmental ducts. Zone 4 strictures are even more peripheral.

Methods

Twenty patients with intrahepatic bile strictures were included in this study. Eight patients had Zone 2, eight patients had Zone 3, and four patients had Zone 4 lesions. Altogether, 34 percutaneous cholangiographies (PTC) were performed with the help of ultrasound and fluoroscopy guidance. In 33 cases, PTC was converted to external or external–internal drainage. In 16 patients, 58 balloon dilatations were attempted with 5–8 mm balloon catheters. Twenty self-expandable metallic stents were implanted percutaneously into 13 patients after

clinically unsuccessful balloon dilatation. Nitinol stents (diameter: 6–10 mm) were used in 17 and Wallstents (diameter: 9–12 mm) in 3; the length of the stents were 30–40 mm. Seven patients had to undergo retransplantation. Only one major complication was diagnosed after percutaneous therapy: a bleeding from the access tract, which was embolized with coils.

The choice of treatments was decided individually by the liver transplant team (transplant surgeon, anesthesiologist/ICU, hepatologist/endoscopy specialist, interventional radiologist).

The demographic data and treatment results are presented in *Table I.*

Results

As Zone 1 resembles extrahepatic locations, it was not included in this study. In Zone 2 *(Fig. 1a, b)*, eight patients had balloon dilatations followed by stents in seven cases and retransplantation in two. In Zone 2, all but one patient are alive, five after stent placements and two after retransplantation. One patient died because of the complications of recurrent metastatic hepatocellular carcinoma (HCC) with patent bile ducts. In Zone 3 *(Fig. 2a–d)*, seven of the eight patients had dilatation followed by stent placement in five cases. Retransplantation was performed in one case after metallic stent placement and in one case after balloon dilatation. Four patients are alive in Zone 3; all had stent placements and one was retransplanted with stents later. One patient died after stent placement as a result of chronic liver failure unrelated to the biliary complication. One patient died after repeated balloon dilatations, while waiting for retransplantation. The cause of death of the third patient was secondary biliary cirrhosis. He received only supportive therapy and was waiting for retransplantation. The last patient in this group had several balloon dilatations and was on the waiting list for retransplantation, too. In Zone 4 *(Fig. 3)*, one patient had symptomatic treatment only, being on

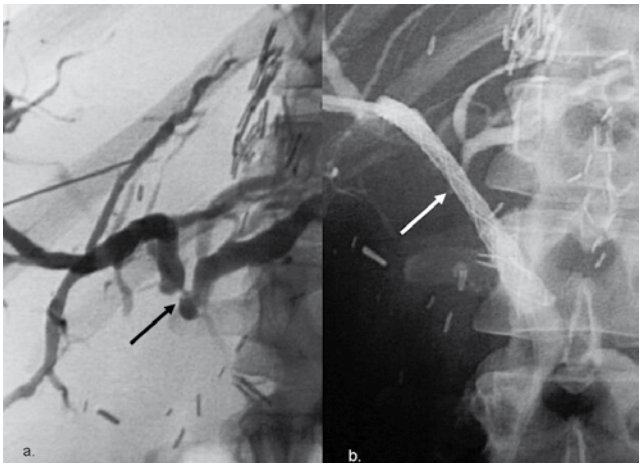

Fig. 1. (a, b) Percutaneous cholangiography showing Zone 2 (hilar) stenosis later treated with balloon dilatation and stent placement (black arrow shows the stricture, and white arrow shows the stent)

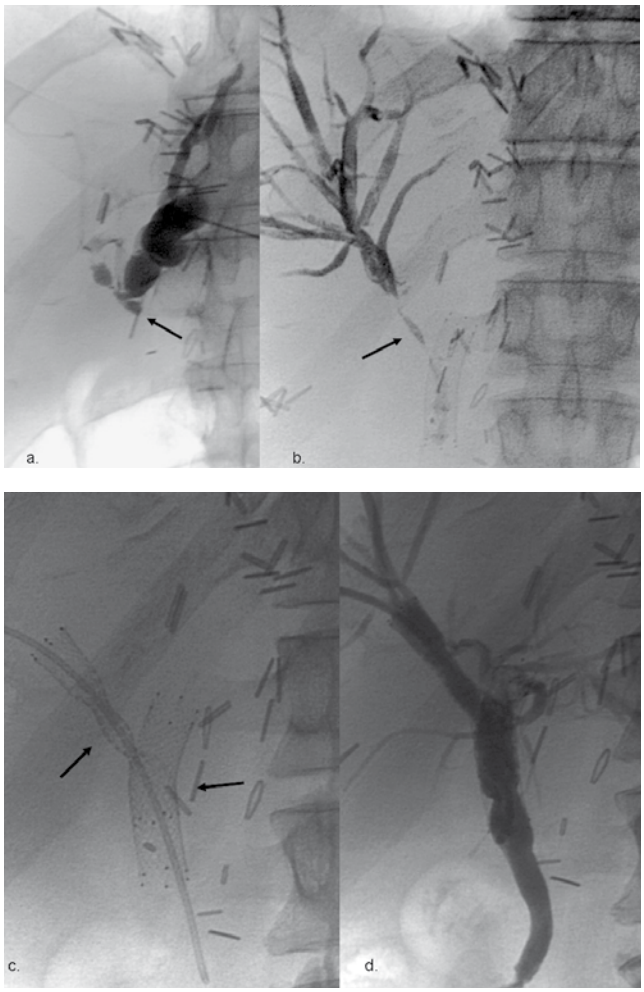

Fig. 2. (a–d) Zone 3 lesions treated with external drains followed by balloon dilatations and stents (arrows show left and right biliary strictures, then the implanted stents)

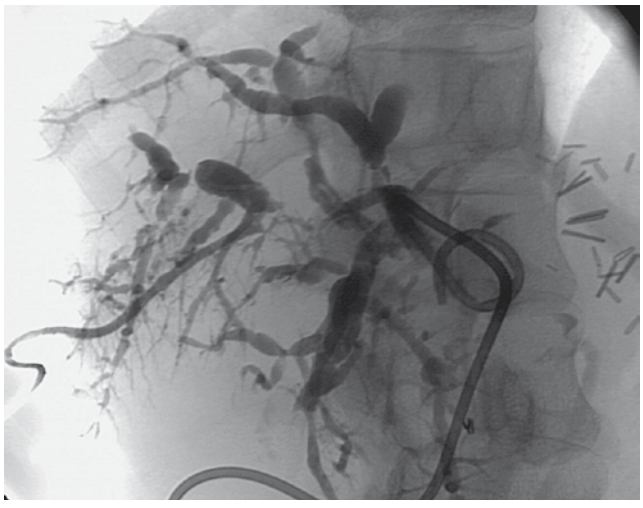

Fig. 3. Zone 4 strictures palliated with double pigtail drainage catheters

Table I Demographic data and treatment results

Gender	Age (years)	Indication of LX	Dilatations	Stents	ReTx, biliary related	Exit, biliary related	Exit, ReTx related	Exit
Female	30	Wilson	1	1	0	0	0	1
Female	41	Acute	3	2	1	0	0	0
Male	55	Adenomatosis	0	0	1	0	1	1
Female	32	Acute	5	1	1	0	1	1
Female	60	Cryptogen	4	1	0	0	0	0
Male	62	Alcoholic	4	2	0	0	0	0
Female	31	Acute	0	0	1	0	0	0
Female	23	Autoimmune	2	1	0	0	0	0
Male	46	PBC	1	1	0	0	0	0
Female	31	HCC/CHCC	3	3	0	0	0	0
Female	39	Autoimmune	6	0	0	1	0	1
Female	11	PSC	3	0	1	0	0	0
Male	53	HCV	4	2	0	0	0	0
Male	59	Alcoholic	3	1	0	0	0	0
Male	50	HCV	0	0	0	1	0	1
Female	23	Autoimmune	6	0	1	0	1	1
Male	31	Acute	3	2	0	0	0	0
Male	50	HCV/HCC	5	2	0	0	0	1
Female	32	Autoimmune	0	0	0	1	0	1
Male	46	Alcoholic	5	1	1	0	0	0
	(mean) *40.25*		*58*	*20*	*7*	*3*	*3*	*8*

the waiting list, and three patients had retransplantation. One patient is alive in Zone 4 after an early retransplantation, and three patients died regardless of the treatment. The average follow-up time was 48 (15–163) months.

Discussion

Intrahepatic or non-anastomotic biliary strictures are one of the serious complications after liver transplantation. The ultimate therapeutic choice is liver retransplantation [4, 10]. The palliative treatment of symptoms may be conservative, consisting management of itching, fluid intake, or minimally invasive procedures. Surgical resection in the form of bilio-enteric anastomosis is possible in selected cases, but like endoscopic stenting it is mostly unsuccessful [11, 12]. Percutaneous interventions, external or external–internal drainage, balloon dilatation, and stent implantation can usually ease the symptoms and stabilize the patient's condition [13]. The success of treatment may depend on the severity of disease. We feel that – as in many medical situations – in cases of non-anastomotic post-transplantation biliary strictures, the real challenge is to decide in each case the optimal treatment and the correct timing. Our retrospective evaluation of our experience in treating intrahepatic biliary strictures concerns outcome depending on the localization and severity of the disease. For zonal classification based on the percutaneous cholangiography findings [9], however, high-quality MRCP (Magnetic Resonance Cholangiopancreatograpy) images might provide the necessary anatomical information. Zone 1 strictures were excluded from this analysis, being extrahepatic. Patients with Zone 2 and 3 lesions were successfully treated percutaneously followed by retransplantation in several cases, but patients in Zone 4 faced worse outcome with chances of survival only after early retransplantation. Many of these patients were treated in the early period of the Hungarian Liver Transplantation when retransplantation was rarely performed because of the lack of donors. Our experience from the later periods and literature data suggest that early retransplantation provides better results than those presented in this study.

We can assume that percutaneous interventions can provide a viable option for bridging to retransplantation, or in many cases even to cure the disease.

The available limited data permitted drawing the conclusion that percutaneous therapy is safe and effective in intrahepatic biliary stenosis after liver transplantation.

Although only a few patients were treated, we emphasize that zonal classification of strictures is advisable: we recommend early retransplantation in Zone 4 strictures, minimally invasive therapy in Zone 2, and individual decisions in Zone 3 lesions.

References

1. Abdullah K et al.: Incidence and management of biliary complications after orthotopic liver transplantation: ten years' experience at King Fahad National Guard Hospital. Transplant Proc 37, 3179–3181 (2005)
2. Polese L et al.: Endoscopic treatment of bile duct complications after orthotopic liver transplantation. Transplant Proc 39, 1942–1944 (2007)
3. Holt AP et al.: A prospective study of standardized nonsurgical therapy in the management of biliary anastomotic strictures complicating liver transplantation. Transplantation 84, 857–863 (2007)
4. Bellido CB et al.: Indications for and survival after liver retransplantation. Transplant Proc 42, 637–640 (2010)
5. Verdonk RC et al.: Nonanastomotic biliary strictures after liver transplantation, part 2: Management, outcome, and risk factors for disease progression. Liver Transpl 13, 725–732 (2007)
6. Glockner JF et al.: Vascular or ischemic complications after liver transplantation. AJR Am J Roentgenol 173, 1055–1059 (1999)
7. Margarit C et al.: Biliary complications secondary to late hepatic artery thrombosis in adult liver transplant patients. Transpl Int 11(Suppl 1), S251–S254 (1998)
8. Buis CI et al.: Causes and consequences of ischemic-type biliary lesions after liver transplantation. J Hepatobiliary Pancreat Surg 13, 517–524 (2006)
9. Buis CI et al.: Nonanastomotic biliary strictures after liver transplantation, part 1: Radiological features and risk factors for early vs. late presentation. Liver Transpl 13, 708–718 (2007)
10. Marudanayagam R et al.: Liver retransplantation in adults: a single-centre, 25-year experience. HPB (Oxford) 12, 217–224 (2010)
11. Eurich D et al.: Successful endoscopic and surgical management of non-anastomotic biliary strictures after liver transplantation – case report. Ann Transplant 14, 47–51 (2009)
12. Filipponi F et al.: Extended right hepatectomy as graft-saving option in non-anastomotic biliary strictures after liver transplantation. Hepatogastroenterology 49, 1679–1681 (2002)
13. Ostroff JW: Management of biliary complications in the liver transplant patient. Gastroenterol Hepatol (N Y) 6, 264–272 (2010)