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Mini Review

Biliary complications after a right-lobe living donor liver transplantation

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Right-lobe living donor liver transplantation (RL-LDLT) has become an acceptable procedure for adult patients with end-stage liver disease in this decade. However, biliary complications in RL-LDLT remain a serious problem: the incidence of anastomotic biliary leakage and stricture after RL-LDLT is reported to be 4.7%–18.2% and 8.3%–31.7%, respectively. The incidence varies according to the type of biliary reconstructions between Roux-en-Y hepaticojejunostomy and duct-to-duct biliary reconstruction. The anatomical biliary diversity of a right-lobe graft makes it difficult to reconstruct the biliary system. Indeed, most biliary strictures in patients with duct-to-duct reconstruction develop in multibranched fashion. In this regard, endoscopic biliary stenting appears to be efficacious for treating multibranched biliary strictures because multiple stenting permits the drainage of each segmental branch of the stricture. In this review, we describe various aspects of biliary complications occurring in RL-LDLT and their treatment.

Key words: living donor liver transplantation, biliary complication, endoscopic treatment.

Introduction

A living donor liver transplantation (LDLT) was first reported in 1988 by Raia in Brazil,[1] and in 1989 the first LDLT was performed by Nagasue in Japan.[2] At that time pediatric LDLTs prevailed throughout Asian countries because deceased organ donation had not become well established, a result of religious beliefs. Following the initial adult-to-adult right-lobe LDLT (RL-LDLT) in 1994,[3] not only the success of RL-LDLTs in Asian countries, including Japan, but also worldwide shortages of deceased donor livers have promoted the RL-LDLT in the United States and European countries.[4–8]

Among various complications associated with the RL-LDLT, biliary complication is very common. As a result of various refinements in surgical techniques, organ preservation, and immunosuppressive management, biliary complications have been reported to occur at a relatively constant rate in recent years, being approximately less than 15% of those reported in left lobe LDLT with Roux-en-Y hepaticojejunostomy (RYHJ),[9,10] as well as in deceased donor liver transplantation (DDLT).[11–14] However, the incidence of biliary complications in RL-LDLT still remains high; the anastomotic biliary leakage and stricture after RL-LDLT are reported to be 4.7%–18.2% and 8.3%–31.7%, respectively.[15–17] The incidence of biliary complications in RL-LDLT varies according to the type of biliary reconstruction (Table 1). Current controversy in RL-LDLT has been focusing on the selection of biliary reconstruction, RYHJ or duct-to-duct choledochocholedochostomy, because the incidence of biliary complication in each procedure differs in different centers, as described in Table 1.

In this review, we describe various aspects of biliary complications occurring in RL-LDLT and their endoscopic treatment based on the anatomical diversity of the biliary system.

Anatomical biliary variations of the right lobe and methods for biliary reconstruction

The anatomical variations of the biliary tree are among the most important and fundamental things a surgeon must know when performing LDLT. In particular, the right hepatic duct, which is present in

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Table 1. Biliary complications after living donor liver transplantaiton.

Reference	Year	Side	Biliary reconstruction	No. of LTs	Anastomotic biliary leakage	Anastomotic biliary stricture
Egawa et al.[9]	2001	L	RY	400	45 (11.5%)	35 (9.0%)
Hashikura et al.[19]	2001	L	RY	110	3 (2.7%)	8 (7.3%)
Liu et al.[15]	2004	R	DD	41	3 (7.3%)	10 (24.3%)
Gondolesi et al.[16]	2004	R	DD	41	3 (7.3%)	13 (31.7%)
		R	RY	55	10 (18.2%)	9 (16.3%)
Kasahara et al.[17]	2005	R	DD	192	9 (4.7%)	51 (26.6%)
		R	RY	121	15 (12.4%)	10 (8.3%)

LT, liver transplantation; RY, Roux-en-Y hepaticojejunostomy; DD, duct-to-duct choledochocholedochostomy; L, left; R, right

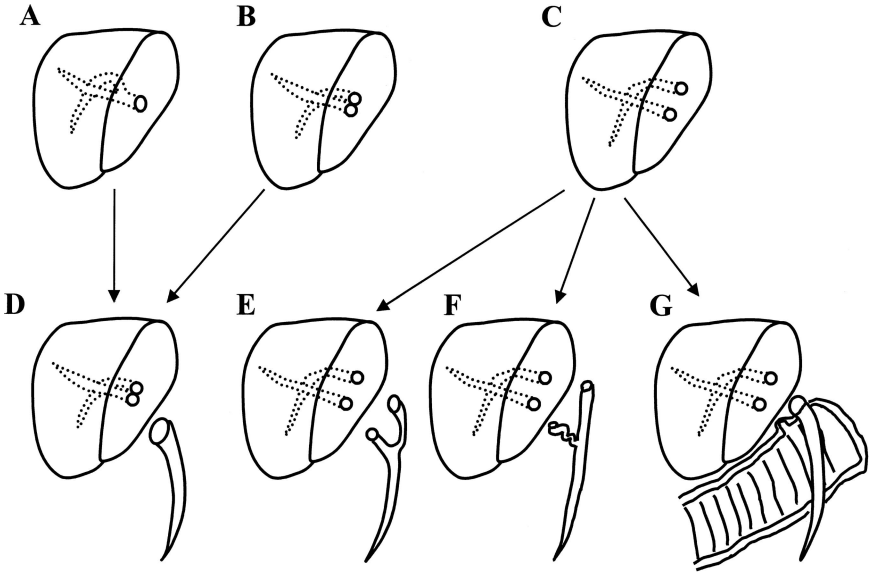

Fig. 1. Anatomical variations in the biliary system of the right lobe graft (**A–C**) and the corresponding biliary reconstructions (**D–G**) in right-lobe living donor liver transplantation (RL-LDLT). **A** A single biliary orifice. **B** Double biliary orifices. **C** Separate biliary orifices. **D** A single duct-to-duct biliary reconstruction. **E** Double duct-to-duct biliary reconstructions using the right and left hepatic ducts. **F** Double duct-to-duct biliary reconstructions using the cystic duct and the common hepatic duct. **G** Mixed type using both duct-to-duct biliary reconstruction and Roux-en-Y hepaticojejunostomy

55.8%–73.6% of the liver, is more variable than the left hepatic duct.[18,19] Moreover, the right hepatic duct of the donor is resected several millimeters proximal from the confluence. Consequently, the right lobe grafts have multiple biliary orifices at a rate of 39.1%–60.4%.[16,17,20]

When the two or three biliary orifices are closely located, a single duct-to-duct biliary reconstruction could be performed by the ductoplasty (Fig. 1A, B, D).[16,20,21] In contrast, when the two or three biliary orifices are distantly located, double duct-to-duct biliary reconstructions by anastomosing each orifice to the right and left hepatic ducts separately or to the common hepatic duct and the cystic duct[21,22] could be performed (Fig. 1C, E, F). If the duct-to-duct biliary reconstructions described above could not be performed, either a single duct-to-duct biliary reconstruction plus RYHJ[16,17] (Fig. 1G) or RYHJ alone would be performed.

In RL-LDLT, duct-to-duct biliary reconstruction, which is the first choice in DDLT, has the following advantages over RYHJ: (i) preserved function of sphincter of Oddi as a defense against enteric reflux and ascending cholangitis; (ii) no need for intestinal manipulation, thus preventing possible intraoperative contamination; (iii) technically faster and easier than RYHJ; (iv) the physiological bilio-enteric continuity enabling endoscopical access after RL-LDLT,[17,21,23] (v) fewer incidents of surgical revision because of biliary stricture;[17] (vi) more treatment options for biliary complications, including percutaneous approach, endoscopic approach, surgical revision, and surgical conversion to RYHU.

Biliary leakage

Incidence and etiology

Biliary leakage usually develops within a month after RL-LDLT. The respective incidence of anastomotic biliary leakage in RL-LDLT with RYHJ and that with duct-to-duct choledochocholedochostomy are 12.4%–18.2%[16,17] and 4.7%–7.3%.[15–17] Remarkably, refractory biliary leakage is associated with significant mortality in

RL-LDLT with RYHJ[16,17]: 12%–19.1% of the patients died from sepsis.

Anastomotic biliary leakage is caused primarily by an ischemic change of biliary stump in RL-LDLT.[11] Double or triple hepaticojejunostomies are an obvious risk factor for biliary leakage in patients with RYHJ.[17,24,25] In DDLT, the T-tube-related biliary leakage occurs in up to 33% of cases.[11] The largest prospective randomized study comparing 90 recipients of DDLT with or without T-tubes demonstrated significantly more biliary complications in the T-tube group (33%) than in the recipients without T-tubes (15.5%).[26] In RL-LDLT with duct-to-duct reconstruction, however, the incidence of biliary leakage is less common regardless of whether a drainage catheter or a T-tube is used: 4.7%–7.3%.[15–17] In one report, biliary leakage from the cut surface developed in 8 of 96 (8.3%) patients.[16] Cut-surface biliary leakage may be caused by increased pressure of the intrahepatic bile duct.[11]

Treatment

Biliary leakage is first treated with a percutaneous aspiration puncture or drainage. However, a surgical revision should be considered if the anastomosis is seriously disrupted or if the biliary extravasation is very large (Fig. 2A).[11] In RL-LDLT patients with duct-to-duct biliary reconstruction, endoscopic retrograde cholangiography (ERC) could be secondly considered. When ERC can detect the exact portion of the biliary leakage, endoscopic nasobiliary drainage (ENBD) or endoscopic biliary drainage (EBD) could be placed proximal to the biliary leakage (Fig. 2B).[17,27,28] In one report, 8 of 8 (100%) biliary leakages could be successfully treated with EBD.[28] In another one, however, 5 of 10 (50%) patients were successfully treated with ENBD, 4 (40%) required surgical revision, and 1 died from sepsis.[17] If an endoscopic reduction of intraductal pressure by ENBD, EBD, or endoscopic spincterotomy (ES) fails, a surgical option should be considered.[11]

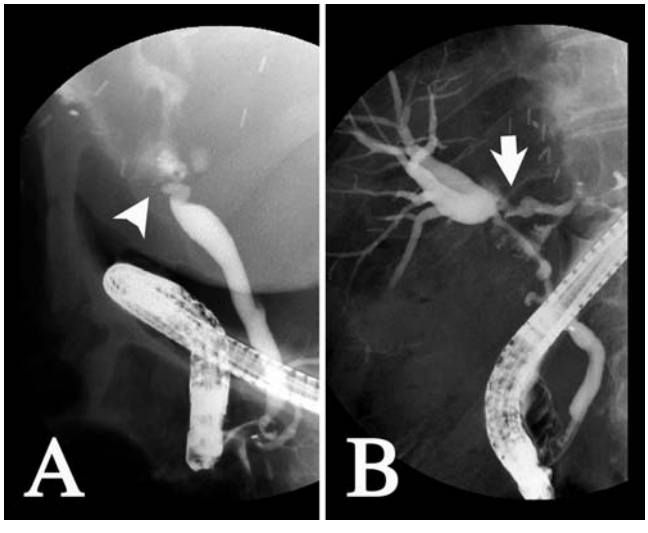

Fig. 2. Retrograde cholangiograms demonstrating biliary leakage in patients after RL-LDLT with duct-to-duct biliary reconstruction. **A** Major biliary leakage (*arrowhead*), by which the proximal biliary system could not be found, was confirmed at the anastomotic portion. **B** The minor leakage (*arrow*) resolved within 20 days after an endoscopic nasobiliary drainage (ENBD) tube had been placed

Biliary stricture

Incidence and etiology

Biliary stricture develops at an average period of 5.8 to 8 months after RL-LDLT (range, 1 to 36 months).[15–17] The respective incidence of anastomotic biliary stricture in RL-LDLT with RYHJ and that with duct-to-duct choledochocholedochostomy are 8.3%–16.3%[16,17] and 24.3%–31.7%.[15,16,17]

Multiple etiologic factors may influence the anastomotic biliary stricture. The most critical factor appears to be the ischemic change of the biliary stumps in both the donor's right lobe graft and the recipient's biliary duct. The second is biliary leakage because 40% (4/10) and 11.8% (6/51) anastomotic biliary strictures developed secondary to biliary leakage of the RL-LDLT patients with RYHJ and with duct-to-duct biliary reconstruction, respectively.[17] Other etiologic factors for biliary stricture after RL-LDLT include hepatic artery complication and cytomegalovirus infection. In contrast, blood type incompatibility is not a significant risk factor for biliary stricture in RL-LDLT.[17]

A noteworthy characteristic of anastomotic biliary strictures in RL-LDLT with duct-to-duct biliary reconstruction is the fashion of the biliary stricture (Fig. 3).[23] Anastomotic biliary strictures of DDLT develop in a single unbranched fashion,[11,29,30] but those of RL-LDLT occur in a multibranched fashion (18/19; 94.7%)[23] because of the high rate of multiple orifices in the right lobe graft (39.1%–60.4%)[16,17,20] and the resulting complicated methods for biliary reconstructions. This difference sometimes puzzles endoscopists when deciding the therapeutic strategy to use in repairing post-transplantation strictures.

Treatment

In RL-LDLT patients with RYHJ, anastomotic biliary stricture is initially treated with percutaneous transhepatic balloon dilation (PTBD) and/or stenting. However, the success rate of PTBD is lower in the RL-LDLT group (33.3%–50%) compared with the DDLT

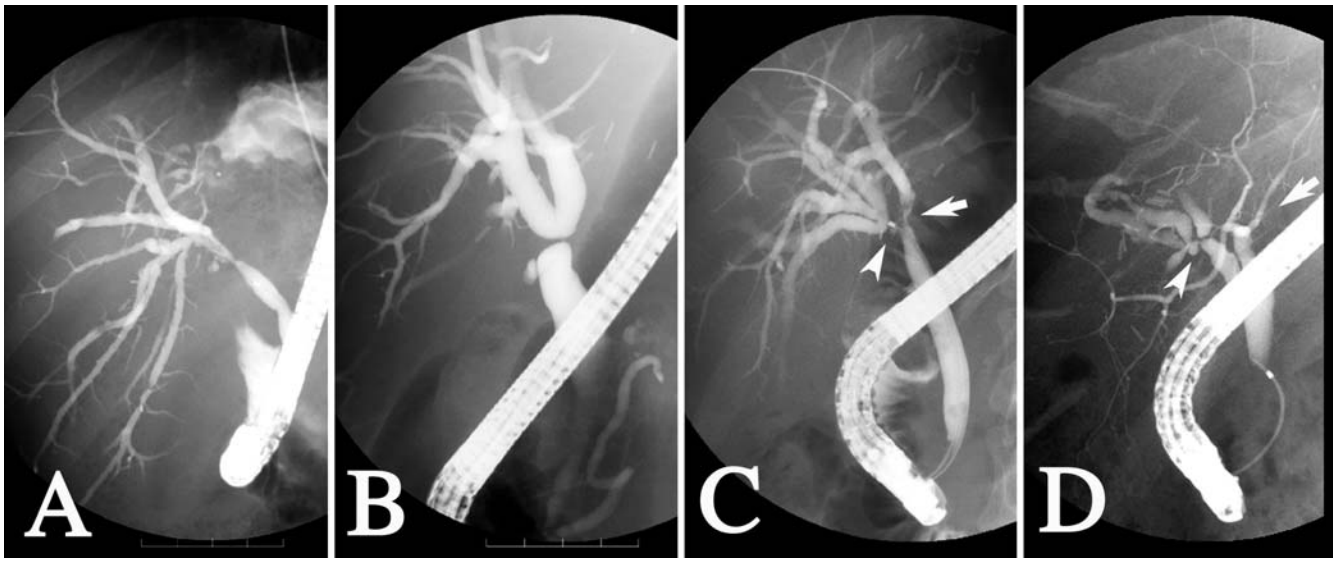

Fig. 3. Types of posttransplantation biliary stricture after RL-LDLT with duct-to-duct biliary reconstruction.[23] **A** An unbranched stricture; **B** a fork-shaped stricture; **C** a trident-shaped stricture; **D** a multibranched stricture. In the trident-shaped and multibranched strictures, anastomoses of the posterior segmental branch and the left hepatic duct are intact (*arrow* in **C** and **D**). Trident-shaped and complicated anastomotic biliary strictures develop at anastomoses of the anterior segmental branch and the right hepatic duct (*arrowhead* in **C** and **D**, respectively)

group (61.0%).[16,17,31] Consequently, 44.4%–50.0% of the RL-LDLT group required surgical revision. In one report, a recurrent stricture after surgical revision to RYHJ was successfully treated with magnetic compression anastomosis.[17,32]

In RL-LDLT patients with duct-to-duct biliary reconstruction, most anastomotic biliary strictures develop in fork-shaped or trident-shaped fashion even if the biliary system had been reconstructed in a single duct-to-duct fashion.[23] In this regard, endoscopic biliary stenting appears to be efficacious for treating multibranched biliary strictures because multiple stenting permits the drainage of each segmental branch of the stricture. Notably, the success rate of the endoscopic treatment in the RL-LDLT group (74.5%–75.0%) is comparable to that in the DDLT group (68%–90.0%).[17,28–30,33] Because of the relatively low success rate of endoscopic or percutaneous balloon dilation in the DDLT group (40%–57%),[31,34,37] endoscopic stenting should be attempted prior to more invasive interventions.

Another option is the application of expandable metallic stenting. However, the use of a metallic stent for benign biliary stricture is controversial because of the high rate of stent occulusion and the obvious difficulties in cases that require surgical conversion to RYHJ.[11,34,38,39]

Conclusion

RL-LDLT can provide a realistic hope of new life for patients with end-stage liver disease. At present, however, a considerable number of patients with duct-to-duct biliary reconstruction still develop biliary complications. In patients with duct-to-duct reconstruction, the incidence of biliary leakage is lower, but that of biliary stricture is higher than those in patients with RYHJ.[16,17]

The endoscopic approach has played an important role in the treatment of biliary strictures in RL-LDLT with duct-to-duct biliary reconstruction. For example, endoscopic stenting has reduced the number of cases with biliary stricture that needed surgical procedures in the duct-to-duct group (17.6%) compared with the RYHJ group (50%). Long-term follow-up and more precise analyses of patients with biliary complications in RL-LDLT will facilitate the improvement of endoscopic treatment.

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