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Unilateral Versus Bilateral Biliary Drainage for Post-Transplant Anastomotic Stricture

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Living donor liver transplantation is the most common type of liver transplantation in Asia. Post-transplant biliary stricture is frequent in living donor liver transplantation, and endoscopic management is considered to be the treatment of choice. However, endoscopic management is still challenging in patients who undergo right lobe living donor liver transplantation because of the anatomical alteration. In this article, we reviewed the recently updated results for proper endoscopic biliary drainage in post-living donor liver transplantation anatomical biliary stricture and compared unilateral and bilateral drainage. **Clin Endosc 2020;53:255-260**

Key Words: Biliary stent; Biliary stricture; Endoscopic retrograde cholangiopancreatography; Living donor liver transplantations

INTRODUCTION

Living donor liver transplantation (LDLT) is the most common type of liver transplantation (LT) in Asia.[1] Duct-to-duct anastomosis is currently the most frequently used technique for the reconstruction of bile ducts during LDLT. This is because it is physiologic and enables the use of an endoscopic approach if biliary complications occur after surgery.[2] Biliary stricture occurs in approximately 13%–14% of all patients undergoing LT, and more frequently in LDLT than in deceased donor LT (DDLT).[3-5] Anastomotic biliary strictures (ABSs) account for approximately 80% of all post-transplant biliary strictures, and are usually single, short (up to 5 mm), and localized to the anastomosis site.[6]

Endoscopic management is currently considered the treatment of choice for ABS. However, endoscopic management is still challenging among patients who undergo right lobe LDLT because of the anatomical alterations. In right lobe LDLT patients, the right anterior and right posterior segmental ducts of the donor are connected to the recipient's bile duct (Fig. 1). Even duodenal intubation with an approach to the ampulla is sometimes difficult due to the absence of the left lobe of the liver in right lobe LDLT patients. The shorter bile ducts and the narrower confluence in the right lobe with two bile duct anastomotic sites that connect the right anterior and right posterior segmental duct also make endoscopic procedures difficult.[7,8] It is, therefore, important to choose the endoscopic drainage technique with the optimal effect and the lowest risk of procedure-related adverse events. In this article, we reviewed recent studies on endoscopic biliary drainage in post-LDLT ABS. We also compared unilateral and bilateral drainage in post-LDLT ABS.

ANASTOMOTIC BILIARY STRICTURE AFTER LDLT

ABS is mainly caused by ischemic damage, which is known to cause more damage to biliary epithelial cells than to hepatocytes or surrounding vascular endothelial cells.[9] Reduced blood supply to the anastomosis and multiple small ducts in

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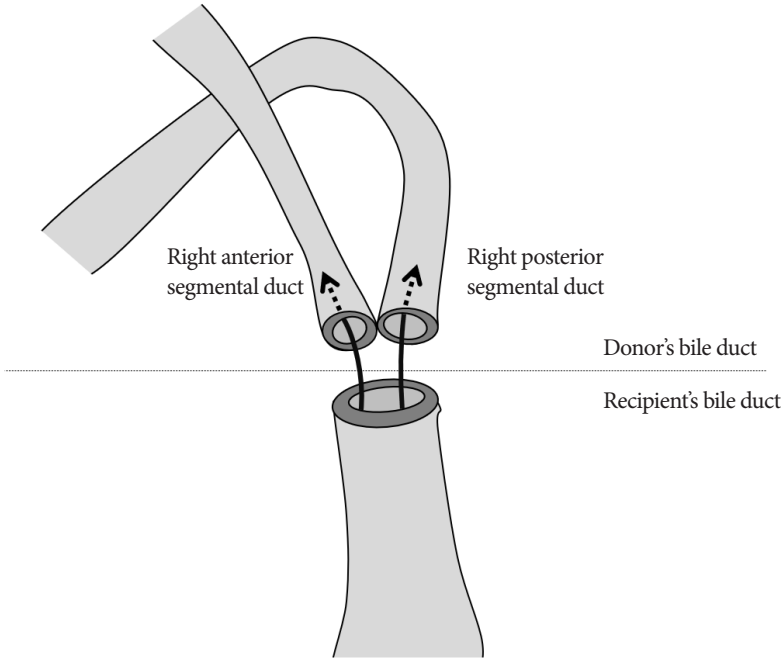

Fig. 1. Schematic diagram of biliary reconstruction during right lobe living donor liver transplantation.

the graft can be caused by differences in diameter between the donor and recipient bile ducts.[10] In addition, acute cellular rejection, recurrent biliary infection, and postoperative use of a biliary drainage catheter may contribute to the development of ABS.[10-12] The skill and experience of the surgeon performing the LDLT is also considered a factor in the formation of ABS.[13] In LDLT patients, strictures are often very tight and twisted due to the presence of dense fibrotic tissue and transplanted liver hypertrophy, making this procedure more challenging.[8] Several risk factors for postoperative biliary stricture, such as multiple bile duct grafts, bile leakage, and hepatic artery stenosis, have been reported in the literature.[14]

It is necessary to treat ABS after LT repeatedly for a long time, and inappropriate treatment may have a detrimental effect on the graft and patient survival. When ABS is adequately managed, it does not affect the overall survival of LDLT patients.[14-17]

NON-SURGICAL BILIARY DRAINAGE FOR ANASTOMOTIC BILIARY STRICTURE AFTER LDLT

Biliary stricture that occurs after LDLT should be optimally managed using all available methods. Recently, surgical treatment has been used mainly in refractory cases that cannot be managed using other methods. Non-surgical treatment methods for post-LT biliary stricture include endoscopic and percutaneous approaches. The former is the primary modality of choice in most institutions.

Generally, in endoscopic approaches, biliary stents are placed along the preceding guidewire through the ABS, and the details of each procedure are decided by the operator after considering various clinical and technical aspects. These approaches generally involve the temporary placement of single or multiple plastic stents (PSs) after balloon dilation.[18] The clinical outcomes of endoscopic approaches in post-LDLT ABS with duct-to-duct anastomosis reported by previous studies are summarized in Table 1.[14,16,19-30] The reported rate of initial successful management with endoscopic approaches ranges from 46.7% to 88.6%. The reported resolution rate of non-surgical management ranges between 36.9% and 100%. A median of 1.4–6.3 endoscopic sessions and percutaneous back-ups are performed during the follow-up period.[14,16,19-30] ABSs that develop after LDLT can be technically challenging to manage using endoscopic approaches because of the small diameter of donor intrahepatic ducts. The strictures that develop at each of the two biliary anastomosis sites also hamper endoscopic approaches. As a result, even after prolonged intervention, the rate of successful treatment of ABSs after LDLT is relatively low. Single operator peroral cholangioscopy has recently enabled the passage of a guidewire through the

Table 1. Literature Review of Clinical Outcomes through Endoscopic Approach to Anastomotic Biliary Stricture after Living Donor Liver Transplantation with Duct to Duct Anastomosis

Study	No. of enrolled patients (No. of patients who had multiple anastomotic stricture)	Follow-up period (mo)	Initial success rate of endoscopic approach (%)	Sessions of endoscopy during follow-up (median)	Stricture resolution rate with non-surgical approach (%)	Needs of percutaneous approach (%)	Sessions of percutaneous drainage during follow-up (median)	Surgery (%)	Recurrence rate (%)
You et al. (2019)[19]	110 (110)	56.2	60.0 (66/110)	4	61.8 (68/110)	N/A	8.7	0	N/A
Jang et al. (2017)[20]	35 (N/A)	18.7	82.9 (29/35)	N/A	100 (35/35)	N/A	N/A	0	20.7 (6/29)
Hsieh et al. (2013)[22]	38 (10)	74.2	84.2 (32/38)	4	100 (35/35)	15.8 (6/38)	N/A	0	21 (8/38)
Na et al. (2014)[16]	65 (N/A)	45.7	81.5 (53/65)	3.2	89.2 (58/65)	13.8 (9/65)	N/A	4.6 (3/65)	N/A
Kurita et al. (2013)[21]	88 (N/A)	53	88.6 (78/88)	1.4	N/A	N/A	N/A	N/A	N/A
Lee et al. (2011)[23]	137 (36)	N/A	46.7 (64/137)	4.8	100 (137/137)	53.3 (73/137)	N/A	0	N/A
Kim et al. (2011)[24]	147 (N/A)	43	55.8 (82/147)	6.3	36.9 (52/141)	44.2 (65/147)	N/A	N/A	11.5 (6/52)
Chang et al. (2010)[25]	121 (9)	33	63.7 (72/113)	3.2	N/A	28.3 (32/113)	N/A	4.1 (5/121)	N/A
Kato et al. (2009)[27]	41 (14)	29.1	75.6 (31/41)	5	51.2 (21/41)	24.4 (10/41)	N/A	4.9 (2/41)	25 (7/28)
Seo et al. (2009)[14]	29 (N/A)	31	62.1 (18/29)	2.3	96.6 (28/29)	51.7 (15/29)	N/A	3.4 (1/29)	30 (6/20)
Kim et al. (2009)[26]	60 (6)	6	63.3 (38/60)	2	96.7 (58/60)	68.2 (15/22)	N/A	N/A	13.2 (5/38)
Yazumi et al. (2006)[28]	75 (19)	N/A	64.0 (48/75)	N/A	76 (57/75)	36 (27/75)	N/A	16 (12/75)	10.7 (3/28)
Tsujino et al. (2006)[29]	17 (8)	10	70.6 (12/17)	3	82.4 (14/17)	5.9 (1/17)	N/A	23.5 (4/17)	44.4 (4/9)
Hisatsune et al. (2003)[30]	22 (N/A)	N/A	63.6 (14/22)	N/A	N/A	18.2 (4/22)	N/A	27.3 (6/22)	N/A

N/A, not applicable.

stricture under direct visualization in cases where the use of conventional endoscopic approaches is difficult.[31,32]

Percutaneous approaches are often used for rescue therapy in cases where an endoscopic approach was unsuccessful. A percutaneous approach is required in 5.9% to 73.7% of cases during endoscopic management.[14,16,22-30] A percutaneous procedure is used for the estimation of stricture resolution and for stent replacement periodically or simultaneously during an endoscopic session in which the rendezvous method is used. In addition, magnetic compression anastomosis was reported to be successful in patients with refractory ABS after LDLT.[33]

As the management of post-LDLT ABS requires a considerable number of repetitive treatments, the failure of any approach does not mean that it will never be used again. Since the available methods are complementary to each other, it is essential to use the appropriate combination of methods to achieve stricture resolution.

OPTIMAL ENDOSCOPIC DRAINAGE STRATEGIES FOR ANASTOMOTIC BILIARY STRICTURE AFTER LDLT

Endoscopic stenting strategies: unilateral versus bilateral drainage in patients with right lobe living donor liver transplantation

Despite its importance, studies that investigate the optimal drainage volume during the treatment of post-LDLT ABS are scarce. For this reason, we estimated the appropriate drainage volume indirectly by examining the results of a malignant hilar obstruction (MHO). ABS after LDLT with duct-to-duct anastomosis seems to be structurally similar to advanced types of MHO (Bismuth type III or IV). Theoretically, the right lobe of the liver accounts for 55%–60%, the left lobe accounts for 30%–35%, and the caudate lobe accounts for 10% of the liver volume.[11] In the past, approximately 25% unilateral drainage was considered sufficient for palliative biliary decompression in MHO.[33-35] However, the importance of draining more than 50% of the viable liver volume was demonstrated.[36-38] For bil-

iary stricture in LDLT patients, unilateral drainage may not be sufficient, given the smaller absolute liver volume and the effects of possible underlying diseases.

Although a tight ABS after LDLT with small anastomotic bile duct diameters and acute angulation of the biliary tract may not physically allow the placement of multiple stents, some studies have suggested that an aggressive endoscopic approach with placement of the highest number of stents possible might produce better clinical outcomes.[16,22,39] Hsieh et al., reported an initial endoscopic technical success rate of 84% and successful resolution of ABS in all patients, with a median of three stents per procedure and a median follow-up period of 74.2 months.[22] In this study, after the initial insertion of the PSs across the stricture, the maximum number of additional stents was placed after proper balloon dilatation. Using a similar method to insert as many stents as possible with the maximal diameter of the stents, Na et al. reported an 81.5% initial endoscopic technical success rate and an 89.2% stricture resolution rate with repeated endoscopic sessions during a median follow-up period of 45.7 months.[16] Although these non-comparative retrospective studies on maximal stenting strategies reported particularly high success rates in relatively large numbers of patients with long-term follow-up periods, the numbers of endoscopy sessions required until stricture resolution were not significantly different from those reported by studies that involved other strategies. Therefore, a conservative interpretation of the superiority of the maximal stenting strategy is necessary.

In cases where multiple stents can be inserted, it is necessary to consider the drainage volume of the transplanted liver. Bilateral drainage may be more efficient than unilateral drainage as the index procedure as it allows sufficient drainage of the transplanted liver. In a recent large single-center retrospective study that involved 110 right lobe LDLT patients with two duct-to-duct anastomosis sites, most patients required bilateral drainage using endoscopic and/or percutaneous methods more than once during the follow-up period.[19] Several clinical outcome measures, including clinical success, complication, and mortality rates were not significantly different between the unilateral and bilateral drainage groups. However, 63.6% (35 of 55) of the patients with unilateral drainage eventually underwent bilateral drainage as well, 64.5% (71 of 110) of the patients underwent bilateral drainage more than once, and 24.5% (27 of 110) had ABS resolution with only unilateral biliary drainage during the follow-up period. Even though bilateral stenting was technically challenging, the authors suggested that maximal drainage should be attempted in patients with post-LDLT ABS. They concluded that the endoscopic and percutaneous approaches are complementary.

Other technical aspects of endoscopic management

The conventional treatment for post-LDLT ABS involves repeated biliary plastic stenting and regular balloon dilatation until the stricture is resolved. PSs have mainly been used in the repetitive endoscopic management of these patients, and repeated hospital admissions for multiple PS insertions by endoscopic retrograde cholangiopancreatography (ERCP) seem to be inevitable.[23,40] Some endoscopists have recommended the use of the "inside-stent" method, as it has shown positive results in prolonging stent patency and maintaining the advantages of duct-to-duct biliary anastomosis for post-LDLT ABS by preventing sphincterotomy. However, further prospective randomized studies are needed to prove its superiority to conventional methods.[21,28-30] Several recent studies on covered self-expandable metal stents (SEMS) for benign biliary strictures, including randomized controlled studies on ABS after DDLT, have reported good stricture resolution rates with fewer ERCP sessions.[40-43] In post-LDLT ABS, although some studies have reported promising results, limited experience and possible stent migration are still regarded as disadvantages of using SEMS in these cases.[20,44-46]

Stent maintenance period and endoscopic treatment intervals

PSs are usually exchanged every three months to prevent stent dysfunction based on the protocol for benign biliary stricture in non-LT cases. Studies have reported that a mean interval of two to six months is needed between ERCP sessions and that one year might be needed to achieve ABS resolution.[18,22,24,28,47,48] Although some effort has been made to reduce the stent placement period through the employment of shorter stent change intervals and the use of maximal stent diameters, little evidence has been provided to support the recognition of these methods as standard methods.[39,49] A sufficient period for stent placement may be necessary, as stricture recurrences seem to be frequent in patients with short stenting durations.[14] Among LDLT patients undergoing balloon dilation and/or conventional PS placement, the reported rates of stricture recurrence range from 10.7% to 44.4% during a median follow-up period of 6 to 74.2 months.[14,20,22,24,26-29] According to previous studies, the majority of stricture recurrences occurred within one year after stent removal. As most recurrent strictures are successfully managed via repeated endoscopic procedures, only a minority of patients require percutaneous transhepatic biliary drainage or surgery. A schematic diagram that summarizes the most optimal drainage strategy is shown in Fig. 2.

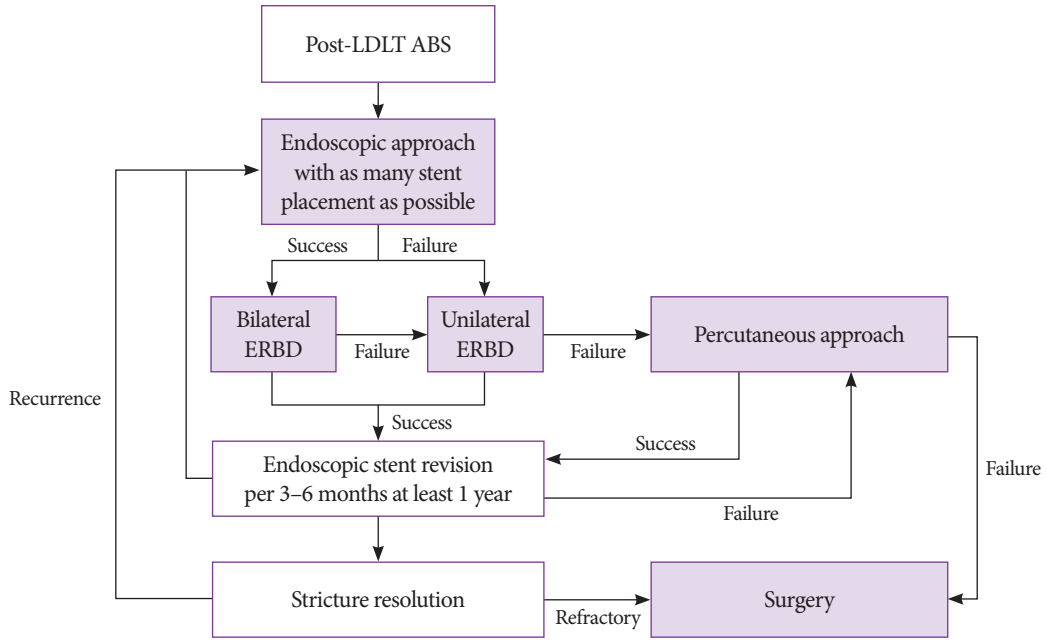

Fig. 2. A schematic diagram of the proper drainage strategy for anastomotic biliary stricture (ABS) after living donor liver transplantation. ERBD, endobiliary retrograde biliary drainage; LDLT, living donor liver transplantation.

CONCLUSIONS

Post-LT ABS still occurs in many patients, and most frequently in patients undergoing LDLT. The endoscopic approach for post-LDLT ABS is considered the first-line method and generally involves the insertion and regular replacement of multiple PSs after balloon dilation. To determine the optimal protocol for the endoscopic treatment of LDLT patients, various aspects, such as proper drainage volume of the transplanted liver, technical skills in performing the endoscopic procedures, and stent characteristics, should be considered. Studies indicate that the strategy of inserting as many stents as possible during the index endoscopic procedure and, if possible, performing bilateral drainage may be advantageous. The percutaneous approach can be used as a complementary or back-up therapy to increase the success rate of the endoscopic approach, whereas surgery can be reserved for refractory cases.

Conflicts of Interest

The authors have no financial conflicts of interest.

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