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ORIGINAL ARTICLE

Double-balloon enteroscopy for bilioenteric anastomotic stricture after pediatric living donor liver transplantation

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Summary

Bilioenteric anastomotic stricture after liver transplantation is still frequent and early detection and treatment is important. We established the management using double-balloon enteroscopy (DBE) and evaluated the intractability for bilioenteric anastomotic stricture after pediatric living donor liver transplantation (LDLT). We underwent DBE at Jichi Medical University from May 2003 to July 2009 for 25 patients who developed bilioenteric anastomotic stricture after pediatric LDLT. The patients were divided into two types according to the degree of dilatation of the anastomotic sites before and after interventional radiology (IVR) using DBE. Type I is an anastomotic site macroscopically dilated to five times or more, and Type II is an anastomotic site dilated to less than five times. The rate of DBE reaching the bilioenteric anastomotic sites was 68.0% (17/25), and the success rate of IVR was 88.2% (15/17). There were three cases of Type I and 12 cases of Type II. Type II had a significantly longer cold ischemic time and higher recurrence rate than Type I ($P = 0.005$ and $P = 0.006$). In conclusion, DBE is a less invasive and safe treatment method that is capable of reaching the bilioenteric anastomotic site after pediatric LDLT and enables IVR to be performed on strictures, and its treatment outcomes are improving. Type II and long cold ischemic time are risk factors for intractable bilioenteric anastomotic stricture.

Introduction

Biliary complications after liver transplantation are still frequent regardless of improvements and innovations in surgical techniques [1], and occasionally lead to graft failure or become fatal. Therefore, early detection and treatment are important [1,2]. Although the pathophysiology of biliary anastomotic stricture suggests that only dilating or stenting the ischemic duct might only constitute temporary measures in a significant proportion of children, whereas surgical reanastomosis on well vascularized tissue offers by far the best option in terms of permanency of the results. Initially, surgical reanastomosis for biliary anastomotic strictures was the first choice, but currently, with advances in interventional radiology (IVR) treatment, IVR treatment is the first choice.

In the case of the choledochocholedochostomic anastomotic strictures, IVR by endoscopic retrograde cholangiopancreatography is the first choice [3,4]. On the other hand, in the case of bilioenteric anastomotic strictures, as it is impossible to reach the anastomotic site, IVR by percutaneous transhepatic cholangiography (PTC) was the first choice [5,6]. Since double-balloon enteroscopy (DBE) which can observe the entire small intestine has become developed [7], it is now possible to reach bilioenteric anastomotic sites, and the effectiveness of IVR using DBE (DBE-IVR) has been reported [8–12]. Moreover, there have been reports of successful cases of DBE not only in adults, but also in children [13], and our facility has also reported DBE-IVR cases for bilioenteric anastomotic stricture after pediatric living donor liver transplantation (LDLT) [14,15].

In our facility, the first choice of IVR treatment for bilioenteric anastomotic stricture after pediatric LDLT is DBE-IVR. We hereby retrospectively report that we established the management using DBE for bilioenteric anastomotic stricture after pediatric LDLT by revealing the outcomes of DBE-IVR in our facility. Moreover, we retrospectively classified anastomotic strictures according to macroscopic findings of bilioenteric anastomotic sites before and after DBE-IVR, and evaluated the intractability for bilioenteric anastomotic stricture after pediatric LDLT.

Patients and methods

Our outpatients are 209 pediatric patients of whom 145 patients underwent LDLT in our facility from May 2001 to April 2009, and 64 patients underwent LDLT in other facilities after June 1991. Of the total 209 pediatric patients, 33 patients (33/209, 15.8%) developed bilioenteric anastomotic strictures.

The indication of IVR for bilioenteric anastomotic stricture is regarded as intrahepatic bile duct dilatation of more than 3 mm and/or liver dysfunction in our facility.

We underwent DBE (EC-450 BIS; Fujinon, Saitama, Japan) at Jichi Medical University from May 2003 to July 2009 for 25 patient (54 times in total) who developed bilioenteric anastomotic stricture after pediatric LDLT. There were 13 male and 12 female patients. The primary diseases included 21 patients of biliary atresia, 1 patient of Wilson disease, 1 patient of fulminant hepatic failure, 1 patient of cystic fibrosis, and 1 patient of ornithine transcarbamylase deficiency. At the time of DBE, their age was 4.3–18.3 years (median: 12.5 years), and their weight was 14.0–76.0 kg (median: 37.6 kg). The period of observation after DBE was 5–79 months.

The patients were divided into two types according to the degree of dilatation of the anastomotic sites before and after IVR using DBE. We defined that Type I (membranous type; Fig. 1) is an anastomotic site macroscopically dilated to five times or more, and Type II (fibrous scar type; Fig. 2) is an anastomotic site dilated to less than five times.

For Type I and Type II, perioperative factors were retrospectively examined and risk factors for intractable anastomotic strictures were also examined using Student's *t*-test and Fisher's exact probability test as computed by SPSS (SPSS II, Chicago, IL, USA). All *P*-values of <0.05 were considered to be statistically significant.

Results

The reaching rate of DBE for the bilioenteric anastomotic sites was 68.0% (17/25), which was 79.6% (43/54) of the total number of times. However, the reaching rate of DBE for the bilioenteric anastomotic sites was 64.0% (16/25) before 2008 and 93.1% (27/29) after 2008. The success rate improved after 2008. Moreover, the success rate of IVR was 88.2% (15/17), which was 83.7% (36/43) of the total number of times. In addition, no complications caused by DBE and DBE-IVR were observed in any of the cases.

Of the total 15 patients in whom DBE-IVR could be performed, nine patients were treated with DBE-IVR alone, and the other six patients were treated with IVR in conjunction with PTC (Fig. 3). Of the total nine patients treated with DBE-IVR alone, four patients (44.4%) experienced a recurrence and underwent repeated DBE-IVR, and an internal stent was placed in all of these patients (Fig. 4a).

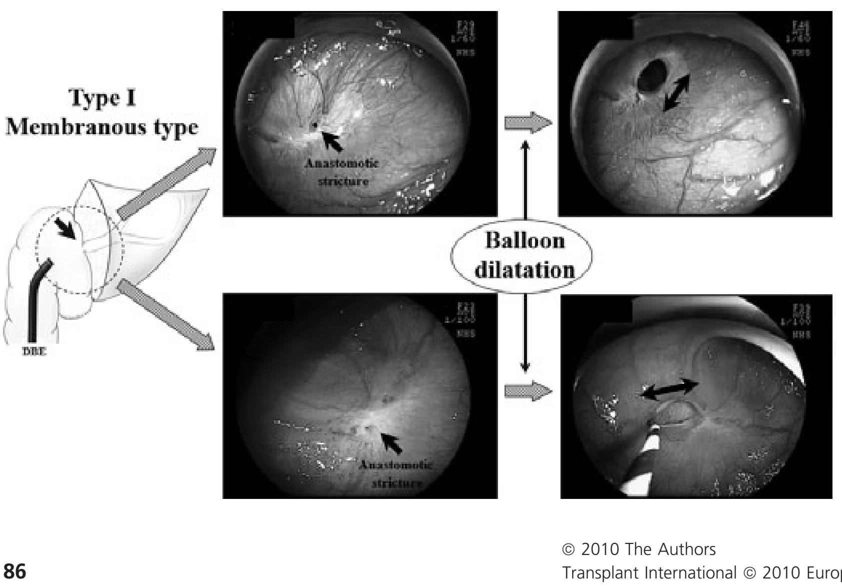

Figure 1 Macroscopic findings by double-balloon enteroscopy (DBE) before and after balloon dilatation for bilioenteric anastomotic stricture. Type I (membranous type) is an anastomotic site macroscopically dilated to five times or more.

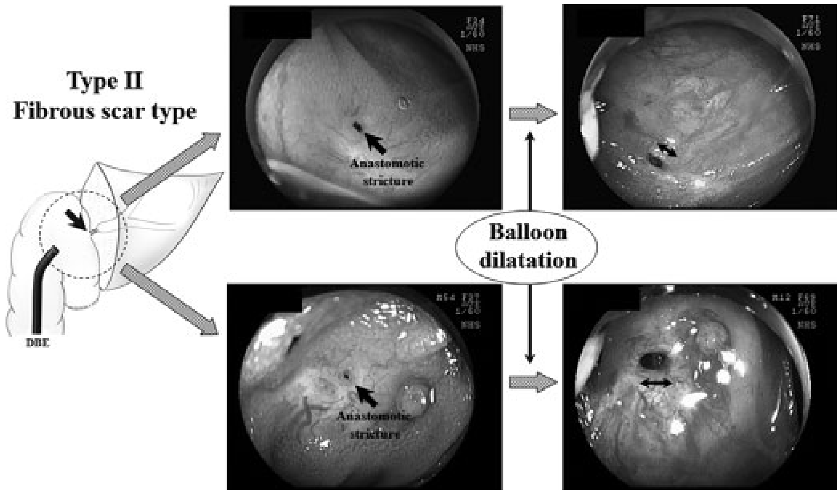

Figure 2 Macroscopic findings by double-balloon enteroscopy (DBE) before and after balloon dilatation for bilioenteric anastomotic stricture. Type II (fibrous scar type) is an anastomotic site macroscopically dilated to less than five times.

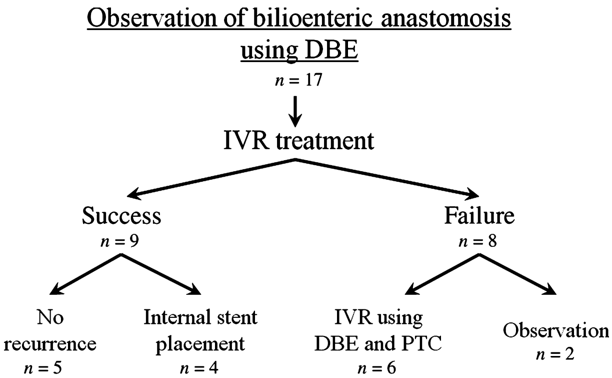

Figure 3 Results of endoscopic therapy using double-balloon enteroscopy (DBE) for bilioenteric anastomotic stricture after pediatric living donor liver transplantation. IVR, interventional radiology; PTC, percutaneous transhepatic cholangiography.

Moreover, of the total 15 patients in whom DBE-IVR could be performed, there were three patients of Type I and 12 patients of Type II (Table 1). Type I patients had a significantly longer period from post-LDLT to DBE than Type II ($P = 0.028$). Moreover, Type II had a significantly longer cold ischemic time than Type I ($P = 0.005$), but there were no significant differences in warm ischemic time, acute cellular rejection, and cytomegalovirus infection between the two types. The complication rate for hepaticolithiasis tended to be high in Type II ($P = 0.070$) and the recurrence rate of bilioenteric anastomotic stricture was significantly higher in Type II ($P = 0.006$).

Discussion

For bilioenteric anastomotic stricture after pediatric LDLT in our facility, the reaching rate of DBE for the anastomotic sites was 68.0%, and the success rate of IVR was 83.7%. Considering the reaching rate after 2008 (93.1%) and the pediatric patients, this is a satisfactory result. The success rate was improved from 64.0% to 93.1% after 2008. Moreover, as DBE-IVR can be repeated in a less invasive and safe manner and there is no reduction in quality of life by tube management for percutaneous transhepatic cholangio drainage (PTCD), DBE can be said to be one effective therapeutic option. However, it may be considered to be disadvantageous that DBE is not sufficiently spreadable, technical skills and experiences are required, and there are limitations in the suitability for some children. In our facility, after considering the advantages and disadvantages of DBE, we established a therapeutic strategy for bilioenteric anastomotic stricture after pediatric LDLT (Fig. 5). Although the indication of DBE is determined with 15.0 kg of body weight as one criterion, patients with body weight of less than 15.0 kg are not all necessarily indication, and may be considered as an indication of DBE if PTCD is difficult. If there is no indication of DBE or DBE fails, PTCD is performed. Furthermore, if PTCD also fails or present intractable anastomotic stricture is found, surgical reanastomosis is considered.

In successful DBE patients, if bilioenteric anastomotic strictures occur repetitively, internal stent placement is performed for the purpose of preventing restricture (Figs 4a and 6), and multiple internal stents placement is performed for the purpose of bile drainage effects (Fig. 4 b). However, internal stent placement causes stent occlusion (Fig. 7a), leads to calculus formation (Fig. 7b), and also leads to granulation because of mechanical stimulation (Fig. 7c), and therefore, periodic replacement or removal is necessary, requiring repeated DBE. For patients with risk factors for intractable anastomotic strictures,

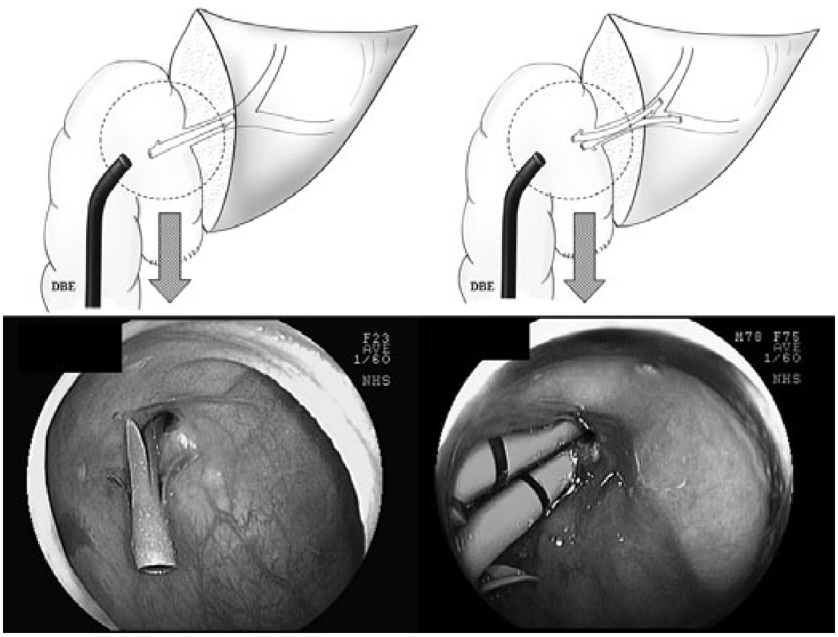

Figure 4 Internal stent placement via bilioenteric anastomosis for intractable bilioenteric anastomotic stricture after interventional radiology using double-balloon enteroscopy (DBE).

Table 1. Each data of bilioenteric anastomotic strictures classified into two types by macroscopic findings after interventional radiology using double-balloon enteroscopy.

	Type I (membranous type)	Type II (fibrous scar type)	*P*-value
Patient	3 (male:l, female:2)	12 (male:6, female:6)	–
Age at DBE (years old)	8.3 ± 2.5	11.6 ± 3.8	0.064
Duration from LDLT to DBE (years)	6.0 ± 1.3	3.1 ± 3.8	0.028
Body weight at DBE (kg)	26.9 ± 10.9	37.4 ± 17.1	0.128
Cold ischemic time	1 h 06 m ± 0 h 31 m	2 h 56 m ± l h 30 m*	0.005
Warm ischemic time	l h l8 m ± 0 h 05 m	l h l0 m ± 0 h 23 m*	0.183
Acute cellular rejection before DBE	1 patient	3 patients*	0.480
Cytomegalovirus infection before DBE	0 patient	4 patients*	0.157
Hepaticolithiasis at DBE	0 patient	7 patients	0.070
Recurrent bilioenteric anastomotic stricture	0 patient	10 patients	0.006

DBE, double-balloon enteroscopy; LDLT, living donor liver transplantation.
*Except for three cases who underwent LDLT in other facilities.

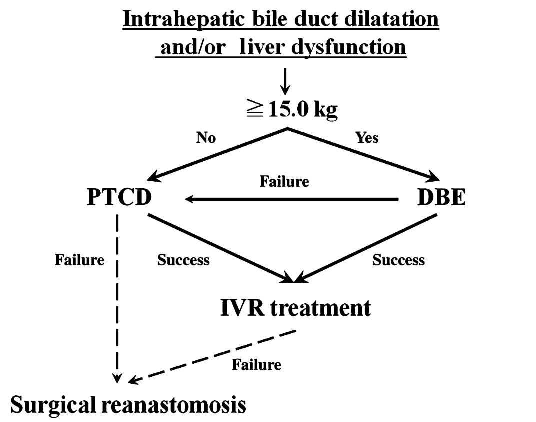

Figure 5 Therapeutic strategy for bilioenteric anastomotic stricture after pediatric living donor liver transplantation. PTCD, percutaneous transhepatic cholangio drainage; DBE, double-balloon enteroscopy; IVR, interventional radiology.

internal stent placement should be considered from the initial treatment.

Retrospectively, it is believed that there are two types of macroscopic findings of anastomotic stricture after DBE-IVR: namely, the membranous type (Type I) in which dilatation of the anastomotic site is easy by IVR therapy and membrane-like findings are observed (Fig. 1), and the fibrous scar type (Type II) in which dilatation of the anastomotic site is difficult and fibrous stricture-like findings are observed (Fig. 2). Specifically, we defined that Type I is an anastomotic site macroscopically dilated to five times or more, and Type II is an anastomotic site dilated to less than five times. However, this classification is merely based on macroscopic findings under DBE and no histopathological evaluations by biopsy of anastomotic

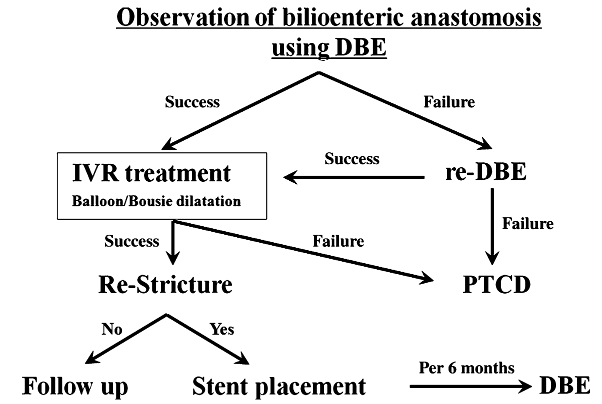

Figure 6 Therapeutic strategy of endoscopic therapy using double-balloon enteroscopy (DBE) for intractable bilioenteric anastomotic stricture after pediatric living donor liver transplantation. IVR, interventional radiology; PTCD, percutaneous transhepatic cholangio drainage.

sites using DBE are made, and therefore this issue should be addressed in the future.

Type I had a significantly longer period from post-LDLT to DBE than Type II ($P = 0.028$), and this supports the recommendations that as Type II is clinically monitored over time for intrahepatic bile duct dilatation and persistent mild liver dysfunction, it is an indication for early treatment, and Type I normally presents only mild intrahepatic bile duct dilatation or normal liver function, but liver dysfunction is often spastically occurred because of events such as infection, and therefore it is only monitored for a long time. Type II which is an indication of early treatment has a significantly high recurrence rate of bilioenteric anastomotic stricture ($P = 0.006$), and this can be said to have a clinically poor prognosis. Moreover, in Type II, cold ischemic time was significantly longer ($P = 0.005$). Therefore, in the current study, it is believed that anastomotic findings of Type II and longer cold ischemic time were risk factors for intractable bilioenteric anastomotic stricture, and macroscopic classification of bilioenteric anastomotic sites after DBE-IVR appeared to be a useful classification that could predict the clinical prognosis of bilioenteric anastomotic stricture. Moreover, in Type II, as the complication rate for hepaticolithiasis tended to be high ($P = 0.070$), there is a possibility that hepaticolithiasis are a risk factor for intractable bilioenteric anastomotic stricture. However, as the number of cases was small, further cases should be collected and further examination will be necessary in the future.

Double-balloon enteroscopy is a less invasive and safe treatment method that is capable of reaching the bilioenteric anastomotic site after pediatric LDLT and enables IVR to perform for strictures, and its treatment outcomes are improving. Moreover, as DBE can be performed on patients with mild intrahepatic bile duct dilatation as well, early detection and treatment of bilioenteric anastomotic stricture is also possible.

Authorship

YS and KM: study organization and paper writing. TY, WH, NO, TW, MU, SE, TU, SH, TF, YS and MH: study performing. HY, YY and HK: supervisors.

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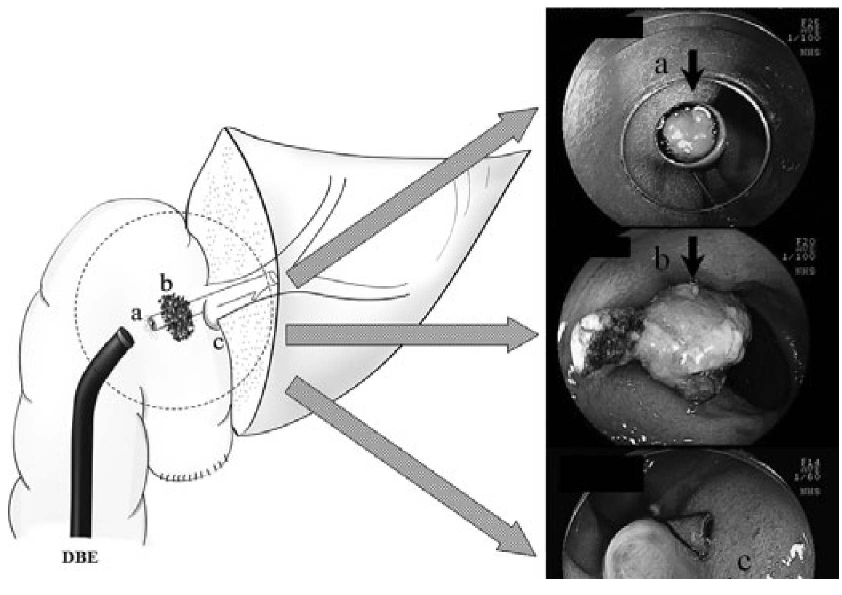

Figure 7 Complications of internal stent placement using double-balloon enteroscopy (DBE) via bilioenteric anastomosis: (a) occlusion, (b) calculus formation, and (c) granulation.

References

1. Todo S, Frukawa H, Kamiyama T. How to prevent and manage biliary complications in living donor liver transplantation? *J Hepatol* 2005; **43**: 22.
2. Colonna JO, Shaked A, Gomes AS, *et al.* Biliary strictures complicating liver transplantation. Incidence, pathogenesis, management and outcome. *Ann Surg* 1992; **216**: 344.
3. Rerknimitr R, Sherman S, Fogel EL, *et al.* Biliary tract complications after orthotopic liver transplantation with choledochocholedochostomy anastomosis: endoscopic findings and results of therapy. *Gastrointest Endosc* 2002; **55**: 224.
4. Williams ED, Draganov PV. Endoscopic management of biliary strictures after liver transplantation. *World J Surg* 2009; **15**: 3725.
5. Mita A, Hashikura Y, Masuda Y, *et al.* Nonsurgical policy for treatment of bilioenteric anastomotic stricture after living donor liver transplantation. *Transpl Int* 2008; **21**: 320.
6. Davidson BR, Rai R, Nandy A, *et al.* Results of choledochojejunostomy in the treatment of biliary complications after liver transplantation in the era of nonsurgical therapy. *Liver Transpl* 2000; **6**: 201.
7. Yamamoto H, Sekine Y, Sato Y, *et al.* Total enteroscopy with a nonsurgical steerable double-balloon method. *Gastrointest Endosc* 2001; **53**: 216.
8. Kuno A, Yamamoto H, Kita H, *et al.* Double-balloon enteroscopy through a Roux-en-Y anastomosis for EMR of an early carcinoma in the afferent duodenal limb. *Gastrointest Endosc* 2004; **60**: 1032.
9. Ryozawa S, Iwamoto S, Iwano H, *et al.* ERCP using double-balloon endoscopes in patients with Roux-en-Y anastomosis. *J Hepatobiliary Pancreat Surg* 2009; **16**: 613.
10. Monkemuller K, Fry LC, Bellutti M, *et al.* ERCP with double balloon enteroscope in patients with Roux-en-Y anastomosis. *Surg Endosc* 2009; **23**: 1961.
11. Chahal P, Baron TH, Poterucha JJ, *et al.* Endoscopic retrograde cholangiography in post-orthotopic liver transplantation with Roux-en-Y biliary reconstruction. *Liver Transpl* 2007; **13**: 1168.
12. Koornstra JJ. Double balloon enteroscopy for endoscopic retrograde cholangiopancreaticography after Roux-en-Y reconstruction: case series and review of the literature. *Neth J Med* 2008; **66**: 275.
13. Nishimura N, Yamamoto H, Yano T, *et al.* Safety and efficacy of double-balloon enteroscopy in pediatric patients. *Gastrointest Endosc* 2010; **71**: 287.
14. Haruta H, Mizuta K, Yamamoto H, *et al.* A case of successful enteroscopic balloon dilatation for late anastomotic stricture of choledochojejunostomy after living donor liver transplantation. *Liver Transpl* 2005; **11**: 1608.
15. Kawano Y, Mizuta K, Hishikawa S, *et al.* Rendezvous penetration method using double-balloon endoscopy for complete anastomosis obstruction of hepaticojejunostomy after pediatric living donor liver transplantation. *Liver Transpl* 2008; **14**: 385.