

# Outcomes of management for biliary stricture after living donor liver transplantation with hepaticojejunostomy using short-type double-balloon enteroscopy

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## Abstract

**Background and aims** To evaluate the outcomes of management for biliary stricture (BS) after living donor liver transplantation (LDLT) using short-type double-balloon enteroscopy.

**Methods** This study retrospectively evaluated 20 patients who underwent endoscopic retrograde cholangiography using short-type double-balloon enteroscopy (sDB-ERC) upon suspicion of BS after LDLT with hepaticojejunal (HJ) reconstruction at Okayama University Hospital.

**Results** Scope insertion to the HJ site and sDB-ERC succeeded in 85 % (17/20) and 82.4 % (14/17) of patients, respectively. Of 14 patients who required treatment for BS, 11 were successfully treated using sDB-ERC, and 3 were successfully treated using sDB-ERC and rendezvous procedures. Adverse events occurred in 2.9 % of all sessions (2/68). After resolution of BS, 7 patients (50 %) experienced a recurrence. Of these, 6 (85.7 %) were treated with only balloon dilation, and 1 (14.3 %) was treated with both balloon dilation and stent deployment ( $P = 0.029$ ).

**Conclusions** sDB-ERC is a useful procedure for diagnosis and treatment for BS after LDLT with HJ reconstruction. Balloon dilation combined with stent deployment might be recommended for definite resolution of BS.

**Keywords** Living donor liver transplantation (LDLT) · Double-balloon enteroscopy (DBE) · DB-ERC · Biliary stricture (BS)

Biliary stricture (BS) is one of the most problematic adverse events following living donor liver transplantation (LDLT) [1, 2]. In the case of BS with duct-to-duct anastomosis, which occurs in 24.3–31.7 % of cases, endoscopic treatment using endoscopic retrograde cholangiography (ERC) is the first-choice treatment; other options include endoscopic treatment, percutaneous transhepatic biliary drainage (PTBD), and re-surgery [3–8].

On the other hand, in most cases of BS with hepaticojejunal (HJ) reconstruction, which occurs in 7.3–16.3 % of cases, PTBD has been selected as the first-line treatment because endoscopy is difficult using a conventional endoscope [9]. Since the development of double-balloon enteroscopy (DBE), ERC using DBE has facilitated treatment for patients with HJ [10, 11]. In our institution, ERC using a short-type DBE (sDB-ERC) has been performed as a first-line procedure for BS with HJ since 2008. In this study, we retrospectively evaluated the outcomes of sDB-ERC for patients who underwent HJ reconstruction after LDLT.

## Methods

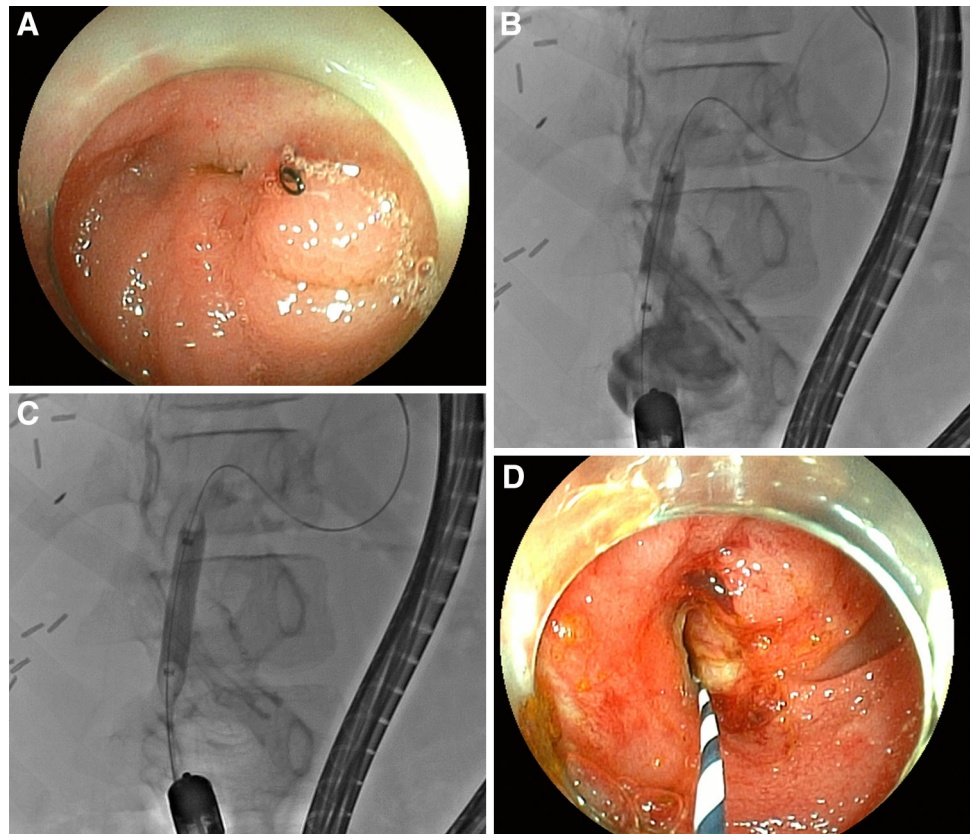
### Patients

Between April 2001 and April 2014, 132 patients underwent LDLT with HJ reconstruction at Okayama University Hospital. Of these, 20 (15.2 %) were suspected of having BS and underwent sDB-ERC. The indication for sDB-ERC was based on clinical symptoms, including at least one of

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**Fig. 1** Balloon dilation for biliary stricture using short-type double-balloon enteroscopy. **A** Endoscopic imaging showing hepaticojejunal anastomotic stricture. **B** Fluoroscopic imaging showed a residual balloon waist at the choledochojejunal anastomotic site. **C** Fluoroscopic imaging showing complete inflated balloon dilation of the choledochojejunal anastomotic site. **D** Endoscopic imaging showing sufficient opening of the anastomosis



the following: (1) fever, jaundice, and abdominal pain; (2) increasing elevation of hepatobiliary enzymes; (3) bile leakage; and (4) detection of dilation of the intrahepatic bile duct based on radiological studies, such as computed tomography and magnetic resonance cholangiopancreatography. Written informed consent was obtained from all patients.

#### sDB-ERC procedure

The patients were placed in a prone or semiprone position. sDB-ERC was performed under conscious sedation using intravenous diazepam (5–10 mg) and pethidine hydrochloride (35–140 mg).

A short-type DBE (EC-450BI5 or EI-530B; Fujifilm, Saitama, Japan), with a 1520-mm working length and a 2.8-mm working channel, was used. For reaching the HJ anastomosis, a standard push-and-pull technique was used throughout the scope insertion with CO<sub>2</sub> insufflation.

In most cases with ERC, a 4-Fr tapered catheter and 0.035-in. guide wire were used. In cases with BS, dilation using a 6- or 8-mm balloon catheter (Quantum TTC, Cook Medical, Winston-Salem, NC, USA) was performed. The diameter of the balloon catheter was decided based on the diameter of the dilated bile duct. The balloon was inflated

at the BS for 30–60 s until complete swelling to a maximum of 6 atm. (Fig. 1A–D).

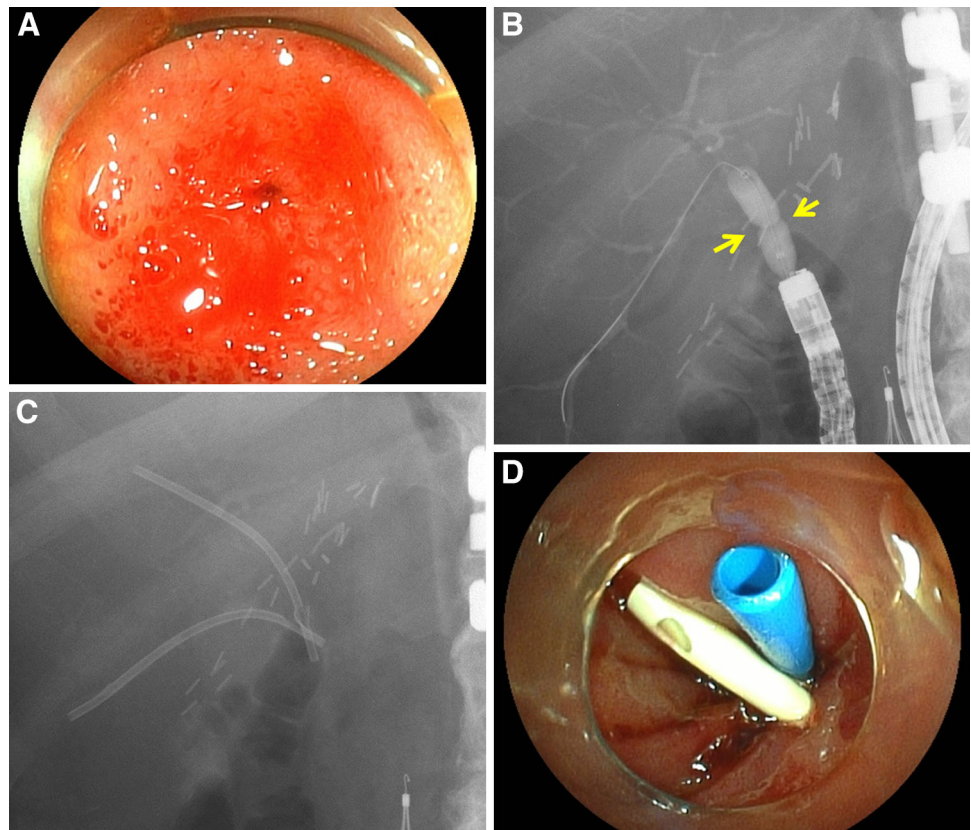
If residual balloon waste was observed after inflation, endoscopic biliary stenting (EBS) was also performed (Fig. 2A–D). As stents for EBS, single or multiple 5- to 7-Fr plastic tubes were used. Thereafter, balloon dilation and stent replacement were performed every 2–4 months until the stricture was resolved. If the improvement of BS was gained under endoscopic vision directly and contrast material flowed out into the jejunum within 30–60 s, the BS was considered resolved, and the stents were subsequently removed.

In cases where sDB-ERC failed, PTBD was performed under ultrasound guidance, following percutaneous balloon dilation. In cases where the anastomosis could be reached with DBE, a rendezvous procedure was also employed [12]. In addition, if a concomitant bile duct stone was revealed, extraction using a retrieval balloon catheter and basket catheter was performed.

#### Follow-up

After resolution of BS, follow-up was carried out at 1- to 3-month intervals. If the recurrence of BS was suspected based on clinical symptoms, abnormal laboratory data, or

**Fig. 2** Balloon dilation and biliary stenting for biliary stricture using short-type double-balloon enteroscopy. **A** Endoscopic imaging showing hepaticojejunal anastomotic stricture. **B** Fluoroscopic imaging showing incomplete inflated balloon dilation of the choledochojejunal anastomotic site. **C** Fluoroscopic imaging showing deployment of two 7-Fr plastic stents. **D** Endoscopic imaging showing insufficient opening of the anastomosis



**Table 1** Patient characteristics

Patient number	Sex	Age (years)	Indication for LDLT	Graft	Number of anastomosis (no)	Digestive reconstruction	Bile leakage	Concomitant bile duct stone	Time from operation (mo)
1	Male	33	BA	Left	2	Unclassified	No	No	14.0
2	Male	63	LC(HBV)	Right	1	RY	No	No	8.2
3	Female	56	HCC(HBV)	Right	1	RY	No	Yes	7.5
4	Male	55	HCC(HBV)	Left	1	RY	No	No	6.2
5	Male	49	Budd–Chiari syn	Right	2	RY	Yes	No	9.4
6	Female	61	HCC(HBV)	Left	1	RY	No	No	55.2
7	Female	64	BA	Right	2	RY	No	No	8.2
8	Female	35	LC(HCV)	Right	2	Unclassified	No	Yes	11.0
9	Male	61	HCC(HBV)	Right	4	RY	Yes	No	93.1
10	Female	52	LC(HCV)	Right	1	RY	No	No	3.8
11	Male	50	LC(HCV)	Right	1	RY	No	Yes	4.7
12	Male	5	Alagille syn	Posterior segment	1	RY	No	Yes	36.4
13	Male	53	LC(PSC)	Left	1	RY	No	No	108.8
14	Male	54	BA	Right	2	RY	Yes	No	1.4
15	Male	11	BA	Left	1	RY	No	No	7.8
16	Female	74	LC(PBC)	Right	1	RY	No	No	162.8
17	Female	65	LC(PBC)	Right	2	RY	No	No	11.2
18	Male	52	LC(HCV)	Right	2	RY	Yes	No	1.9
19	Male	65	LC(NBNC)	Right	2	RY	No	No	89.6
20	Male	59	LC(HBV)	Right	1	RY	No	No	79.1

LDLT living donor liver transplantation, BA biliary atresia, LC liver cirrhosis, HCC hepatocellular carcinoma, HBV hepatitis B virus, HCV hepatitis C virus, NBNC non-B and non-C hepatitis virus, PSC primary sclerosing cholangitis, PBC primary biliary cirrhosis, RY Roux-en-Y, mo month, no number

radiological studies, sDB-ERC was performed. After confirmation using sDB-ERC, re-intervention using balloon dilation and/or stent replacement was performed.

### Assessment

Technical success was evaluated based on successful scope insertion to the HJ anastomosis, completion of the cholangiogram, and completion of treatment. Clinical success was evaluated based on improvement of clinical symptoms and laboratory examinations. Adverse events were assessed over about total sessions.

### Statistical analysis

Noncontinuous variables were compared using Fisher's exact test. A *P* value <0.05 was considered significant. Cumulative bile duct patency after balloon dilation or stent removal was estimated using Kaplan–Meier analysis, and the difference was evaluated using a log-rank test. All statistical analyses were performed using JMP 9 (SAS Institute Inc., Cary, NC, USA).

## Results

### Characteristics of patients

Characteristics of the 20 patients are given in Table 1. Thirteen men and seven women with a median age of 55 (5–74) years were included. The most common indication for LDLT was liver cirrhosis (50 %). Reconstruction of the digestive tract was performed using Roux-en-Y in 18 patients (90 %) and an unclassified type due to multiple surgeries in two patients. In regard to postoperative adverse events, bile leakage and concomitant bile duct stones occurred in each of the 4 patients (20 %). The median time of diagnosis for BS after LDLT was 10.2 (1.4–108.8) months.

### Technical and clinical success

Table 2 shows the technical and clinical outcomes of the 20 patients who underwent sDB-ERC. The success rate of scope insertion to the HJ site was 85 % (17/20). The median time to reach the HJ anastomosis was 35

**Table 2** Technical and clinical outcomes of initial management for biliary stricture using a short-type double-balloon enteroscopy

Patient number	Scope insertion	Insertion time (min)	ERC	Type of stricture <sup>a</sup>	Treatment	Total procedure time (min)	Clinical success
1	Success	24	Success	NAS	Balloon	70	Success
2	Failure	–	–	–	–	–	Failure
3	Success	13	Success	AS	Balloon	72	Success
4	Success	50	Failure	NAS	–	137	Failure
5	Success	25	Failure	AS	–	180	Failure
6	Failure	–	–	–	–	–	Failure
7	Success	8	Success	AS	EBS	42	Success
8	Success	5	Success	AS and NAS	EBS	82	Success
9	Failure	–	–	–	–	–	Failure
10	Success	17	Success	Non-stricture	–	60	N.A.
11	Success	17	Success	AS	Balloon	54	Success
12	Success	35	Success	AS	Balloon	85	Success
13	Success	27	Success	Non-stricture	–	46	N.A.
14	Success	43	Failure	AS	EBS	74	Failure
15	Success	35	Success	AS and NAS	Balloon	130	Success
16	Success	39	Success	AS	Balloon	75	Success
17	Success	87	Success	AS	Balloon	103	Success
18	Success	85	Success	AS	EBS	123	Success
19	Success	49	Success	AS	EBS	101	Success
20	Success	42	Success	Non-stricture	–	46	N.A.

ERC endoscopic retrograde cholangiography, EBS endoscopic biliary stenting, PTBD percutaneous transhepatic biliary drainage, min minutes, no number, mo month, BS biliary stricture

<sup>a</sup> Biliary strictures were classified as anastomotic stricture (AS) and non-anastomotic stricture (NAS)

**Table 3** Follow-up after endoscopic management for biliary stricture using a short-type double-balloon enteroscopy

Patient number	Type of stricture	Treatment procedure	Endoscopic treatment group	Total number of ERC (no)	Adverse events	BS resolution	BS recurrence	Time to BS recurrence (mo)	Follow-up (mo)
1	NAS	sDB-ERC	Balloon	1	None	Yes	Yes	2.6	59.3
2	AS	PTBD	–	1	None	Yes	–	–	–
3	AS	sDB-ERC	Balloon	1	None	Yes	Yes	4.4	53.7
4	AS and NAS	sDB-ERC with RV	EBS	21	None	Yes	No	–	30.6
5	AS	sDB-ERC with RV	EBS	6	Bleeding	Yes	No	–	43.4
6	AS	PTBD	–	1	None	Yes	–	–	–
7	AS	sDB-ERC	EBS	3	None	Yes	No	–	40.3
8	AS and NAS	sDB-ERC	EBS	10	None	Yes	Yes	5.3	28.8
9	AS	PTBD	–	1	None	Yes	–	–	–
10	Non-stricture	–	–	1	None	–	–	–	–
11	AS	sDB-ERC	Balloon	1	None	Yes	Yes	4.6	15.3
12	AS	sDB-ERC	Balloon	1	Ischemic liver graft	Yes	Yes	7.3	25.7
13	Non-stricture	–	–	1	None	–	–	–	–
14	AS	sDB-ERC with RV	EBS	6	None	Yes	No	–	9.9
15	AS and NAS	sDB-ERC	Balloon	1	None	Yes	Yes	9.6	17.8
16	AS	sDB-ERC	Balloon	1	None	Yes	Yes	7.4	18.2
17	AS	sDB-ERC	Balloon	1	None	Yes	No	–	14.2
18	AS	sDB-ERC	EBS	4	None	Yes	No	–	9.3
19	AS	sDB-ERC	EBS	5	None	Yes	No	–	6.2
20	Non-stricture	–	–	1	None	–	–	–	–

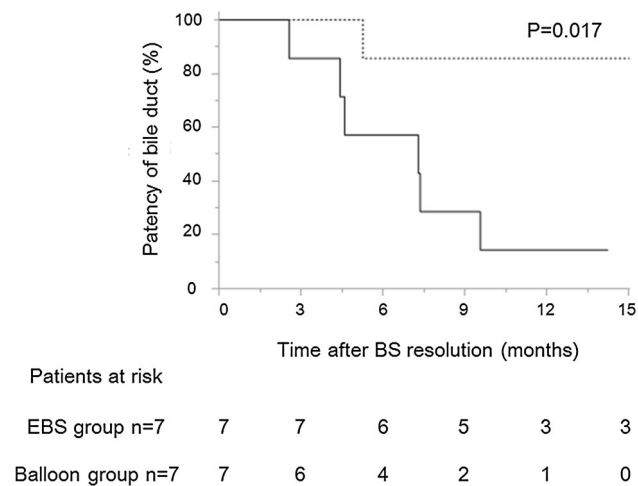
AS anastomotic stricture, NAS non-anastomotic stricture, sDB-ERC endoscopic retrograde cholangiography using short-type double-balloon enteroscopy, PTBD percutaneous transhepatic biliary drainage, RV rendezvous procedure, EBS endoscopic biliary stenting, mo month, no number

(5–87) min. In three patients where sDB-ERC was unsuccessful, severe adhesion of the afferent loop contributed to failed insertion. Of the 17 patients with successful insertion, 14 patients (82.4 %) achieved successful ERC, and 11 patients required and received treatment for BS. In unsuccessful cases, severe biliary stricture that hindered advance of the guidewire contributed to the failed ERC. Consequently, sDB-ERC was successful in 14 of 20 patients (70 %), and the median procedure time from scope insertion to scope withdrawal was 75 (42–180) min. Meanwhile, PTBD was performed for the remaining six patients. After PTBD, three patients also underwent the rendezvous procedure. All patients achieved clinical improvement, including bile leakage and

concomitant bile duct stones, by combining sDB-ERC and PTBD.

### Details of endoscopic treatment

Among the 14 patients who achieved successful biliary drainage with sDB-ERC and rendezvous procedures, seven patients received only balloon dilation (balloon group), and seven underwent both balloon dilation and endoscopic biliary stenting (EBS group) as the initial endoscopic treatment (Table 3). In the EBS group, all patients achieved resolution of the BS, and their stents were removed. The median time from stent deployment to removal was 14.9 (6.4–38.2) months, and the median number of ERCs was 6 (3–21).



**Fig. 3** Bile duct patency after treatment comparing the balloon group (solid line) and endoscopic biliary stenting EBS group (dotted line). The EBS group had significantly longer bile duct patency than the balloon group ( $P = 0.017$ )

### Recurrence of the biliary stricture

The median follow-up period from the initial resolution of the BS to the latest medical care day was 22.0 (6.2–59.3) months. Of the 14 patients who achieved BS resolution, 7 patients (50 %) experienced recurrence of BS and underwent repeat sDB-ERC at a median of 5.3 (2.6–9.6) months after the final endoscopic treatment (Table 3). Among seven patients, 6 (85.7 %) were in the balloon group, and 1 (14.3 %) was in the EBS group ( $P = 0.029$ ). In addition, the EBS group had significantly longer bile duct patency than the balloon group ( $P = 0.017$ ; Fig. 3).

### Adverse events

Adverse events related to sDB-ERC procedures occurred in 2 of 68 total sessions (2.9 %), with liver graft ischemia in 1 [13] and bleeding after balloon dilation of the anastomotic stricture which required angiography with embolization in one. No pancreatitis or perforation occurred.

### Discussion

The current data suggest that sDB-ERC can be successfully performed for diagnosis and treatment of BS in post-LDLT patients with HJ reconstruction. This newer procedure has not yet been established as a standard treatment, and only a few case reports regarding the endoscopic treatment of BS in LDLT patients with HJ reconstruction have been published [10, 11]. Sanada et al. [10] reported that the success rate of insertion into the HJ site was 68 % (17/25), the

success rate of treatment was 88.2 % (15/17) and that there were no adverse events. These results are similar to those of the current study. In contrast, the success rates of the treatment for postoperative BS by PTBD have been reported as 55–95 %, with adverse event rates of 11–35 %, including hepatic artery injury, post-procedure sepsis, and liver abscess [14]. Based on these results, sDB-ERC is less invasive than PTBD, while successful treatment was achieved with both sDB-ERC and PTBD. Therefore, sDB-ERC should be considered as a potential alternative to PTBD.

Similar to the current recurrence rate for BS, Sanada et al. [10] reported a recurrence rate of 44 % (4/9) in patients who underwent HJ reconstruction after balloon dilation. However, interestingly, the recurrence rate and interval in the current study were superior when balloon dilation was combined with stent placement than when balloon dilatation alone was performed. These results suggest that not only balloon dilation, but also stent placement, is necessary for treatment of BS of LDLT with HJ reconstruction, as well as with duct-to-duct reconstruction [15].

The limitation of this study is that it was a retrospective, single-center study involving a small population. Further cases should be collected, and a randomized controlled trial will be needed in the future.

In conclusion, sDB-ERC is a less invasive, safe treatment method and should be considered as first-line treatment prior to percutaneous procedures for BS in patients after LDLT with HJ reconstruction. Repeated balloon dilation combined with stent deployment might be recommended for definite resolution of BS.

### Compliance with ethical standards

**Disclosures** Takeshi Tomoda, Koichiro Tsutsumi, Hironari Kato, Sho Mizukawa, Syuntaro Yabe, Yutaka Akimoto, Hiroyuki Seki, Daisuke Uchida, Kazuyuki Matsumoto, Naoki Yamamoto, Shigeru Horiguchi, and Hiroyuki Okada have no conflicts of interest or financial ties to disclose.

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