

A comparative evaluation of treatment methods for bile duct stones after hepaticojejunostomy between percutaneous transhepatic cholangioscopy and peroral, short double-balloon enteroscopy

Koichiro Tsutsumi, Hironari Kato, Shuntaro Yabe, Sho Mizukawa, Hiroyuki Seki, Yutaka Akimoto, Daisuke Uchida, Kazuyuki Matsumoto, Takeshi Tomoda, Naoki Yamamoto, Shigeru Horiguchi, Hirofumi Kawamoto and Hiroyuki Okada

Abstract

Background: Bile duct stones after hepaticojejunostomy are considered a troublesome adverse event. Although percutaneous transhepatic procedures using a cholangioscopy is performed to treat these bile duct stones, a peroral endoscopic procedure using a short, double-balloon enteroscope (sDBE) is an alternative. This study aimed to compare the immediate and long-term outcomes of both treatments for bile duct stones in patients who underwent prior hepaticojejunostomy.

Methods: Between October 2001 and May 2013, 40 consecutive patients were treated for bile duct stones after hepaticojejunostomy at a tertiary care hospital. Initial success with biliary access, biliary intervention-related technical success, clinical success, adverse events, hospitalization duration, and stone-free survival were retrospectively evaluated.

Results: The initial success rates for biliary access were 100% (8/8) with percutaneous transhepatic cholangioscopy (PTCS) and 91% (29/32) with sDBE. In three patients in whom biliary access during initial sDBE failed, successful access with subsequent PTCS was achieved, and biliary intervention-related technical success and clinical success were eventually achieved in all 40 patients. The rate of adverse events was significantly lower with sDBE than with PTCS (10% versus 45%; $p = 0.025$). The median hospitalization duration for complete stone clearance was significantly shorter with sDBE than with PTCS (10 versus 35 days; $p < 0.001$). During the median 7.2 year or 3.1 year follow up, the probabilities of being stone-free at 1, 2, and 3 years were 100%, 73%, and 64% for PTCS and 85%, 65%, and 59% for sDBE, respectively ($p = 0.919$).

Conclusions: sDBE was useful, with few adverse events and short hospitalization; therefore, experienced endoscopists can consider it as first-line treatment for bile duct stones in patients with prior hepaticojejunostomy.

Keywords: choledochojejunostomy, hepaticojejunostomy, common bile duct gallstones, double-balloon enteroscopy, percutaneous transhepatic cholangioscopic treatment

Introduction

Bile duct stones are a troublesome postoperative adverse event in patients with a hepatobiliary-pancreatic disease undergoing hepaticojejunostomy such as Roux-en-Y hepaticojejunostomy

(RYHJ) and pancreatoduodenectomy. Bile duct stones after hepaticojejunostomy are mostly caused by cholestasis or reflux cholangitis, and many stones consist of calcium bilirubinate [Kondo *et al.* 1995]. These stones cause recurrent

Ther Adv Gastroenterol

2017, Vol. 10(1) 54–67

DOI: 10.1177/
1756283X16674633

© The Author(s), 2016.
Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Correspondence to:
Koichiro Tsutsumi, MD, PhD
Department of
Gastroenterology and
Hepatology, Okayama
University Graduate School
of Medicine, Dentistry, and
Pharmaceutical Sciences,
2-5-1 Shikata-cho, Kita-
ku, Okayama 700-8558,
Japan
[tsutsumi@cc.okayama-u.
ac.jp](mailto:tsutsumi@cc.okayama-u.ac.jp)

Hironari Kato, MD, PhD
Shuntaro Yabe, MD
Sho Mizukawa, MD
Hiroyuki Seki, MD, PhD
Yutaka Akimoto, MD, PhD
Daisuke Uchida, MD, PhD
Kazuyuki Matsumoto, MD, PhD
Takeshi Tomoda, MD, PhD
Naoki Yamamoto, MD, PhD
Shigeru Horiguchi
Hiroyuki Okada, MD, PhD
Department of
Gastroenterology and
Hepatology, Okayama
University Graduate School
of Medicine, Dentistry, and
Pharmaceutical Sciences,
Okayama, Japan
Hirofumi Kawamoto, MD, PhD
Department of General
Internal Medicine 2,
Kawasaki Hospital,
Kawasaki Medical School,
Okayama, Japan

cholangitis, which can lead to a progressive intrahepatic biliary stricture, a bilioenteric anastomotic stricture (BAS), and secondary biliary cirrhosis [Hwang *et al.* 2004]. Conversely, the concomitance of BAS and intrahepatic biliary stricture induces cholestasis and can consequently cause lithogenesis and stone recurrence [Bonnel *et al.* 1991].

Therefore, both complete stone clearance and maintained resolution of these strictures using minimally-invasive treatments are ideal and essential for these patients.

Treatment options for bile duct stones in these patients are percutaneous transhepatic treatment, peroral endoscopic treatment, and surgery. Generally, peroral endoscopic procedures across a bilioenteric anastomosis (BA) are extremely difficult using conventional endoscopes such as push enteroscopes and pediatric colonoscopies, because of the difficulty reaching the BA site, especially in patients with RYHJ. Hence, percutaneous transhepatic procedures using a cholangioscopy are initially performed in most of these patients. However, surgery is invasive and technically challenging, and it causes significant morbidity for these patients.

Developments in deep enteroscopy techniques using a balloon enteroscopy now allow peroral endoscopic procedures in patients with surgically altered anatomies [Aabakken *et al.* 2007; Shimatani *et al.* 2009; Itoi *et al.* 2010a; Tsujino *et al.* 2010; Shah *et al.* 2013; Siddiqui *et al.* 2013]. In particular, the usefulness of short double-balloon enteroscopy (sDBE) has been reported for various biliary interventions such as dilation of biliary strictures, stent placement, and stone extraction [Shimatani *et al.* 2009; Tsujino *et al.* 2010; Siddiqui *et al.* 2013]. This novel procedure has been gradually introduced for the treatment of bile duct stones in patients with hepaticojejunostomy [Tazuma and Nakanuma, 2015]. However, the immediate and long-term outcomes of this procedure as well as the superiority of percutaneous transhepatic cholangioscopy (PTCS) or sDBE for these patients are unknown.

In this retrospective study, we aimed to evaluate and compare the efficacy, safety, and long-term outcomes between PTCS and sDBE for the treatment of bile duct stones in patients with prior hepaticojejunostomy.

Materials and methods

Patient population

For the treatment of bile duct stones after hepaticojejunostomy, 40 consecutive patients underwent PTCS or sDBE between October 2001 and May 2013 at Okayama University Hospital, Japan. Most patients had clinical features of cholestasis or cholangitis and were referred for abdominal ultrasonography, computed tomography, or magnetic resonance cholangiopancreatography (MRCP) for further evaluation. With evident bile duct stones on imaging, treatment was immediately scheduled, and the choice of treatment depended on the date: sDBE was introduced in August 2008. In addition, patients with first-time detection of bile duct stones using cholangiography were included.

Written informed consent was obtained from all patients, and this comparative study was approved by our institutional review board.

Protocol for the percutaneous transhepatic procedure using a cholangioscope

PTCS was performed by skilled interventional radiologists with the patient in a supine position under conscious sedation, with diazepam and pethidine hydrochloride (Figure 1).

First, percutaneous transhepatic puncture of the dilated intrahepatic bile duct was usually performed with a 21-gauge needle under ultrasonographic guidance. After advancing a guidewire, a 5-French (Fr) dilation catheter was passed through the tract, and a 7-Fr to 10-Fr biliary catheter was placed into the bile duct or jejunum across the BA site.

Second, dilation of the percutaneous tract was performed stepwise using a 10-Fr to 18-Fr dilation catheter, starting approximately 1 week after percutaneous transhepatic biliary drainage (PTBD), to insert a cholangioscope.

Third, bile duct stones were usually treated under PTCS guidance (CHF-240; Olympus Medical Systems, Tokyo, Japan) using a 2.0 mm working channel. When the BAS was observed, balloon dilation (8–10 mm in diameter) was performed before stone extraction. For stone fragmentation, electrohydraulic lithotripsy (EHL) was performed under direct vision using an EHL generator

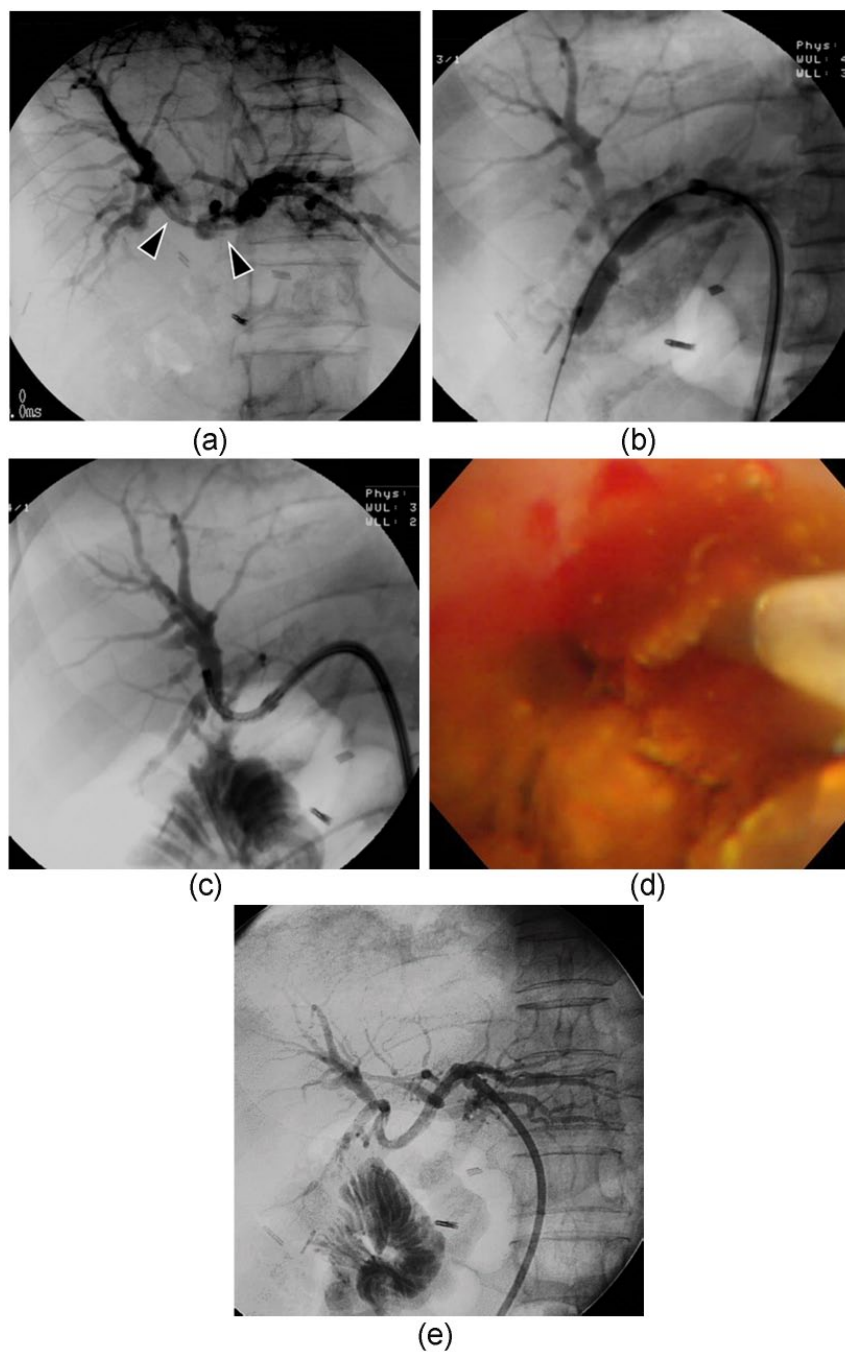


Figure 1. Percutaneous procedure using a cholangioscope.

(a) Percutaneous transhepatic biliary drainage was performed through the left hepatic bile duct. The cholangiogram shows multiple bile duct stones [arrows] with a BAS. (b) Balloon dilation for the BAS was performed over the guidewire. (c) A cholangioscope was inserted for stone extraction after creating a percutaneous biliary tract. (d) Electrohydraulic lithotripsy was performed under direct vision for stone fragmentation. (e) Following stone extraction, a biliary catheter was placed for a few days, and the catheter was removed after complete stone clearance was determined based on another cholangiography examination. BAS, bilioenteric anastomotic stricture.

(AUTOLITH® system, Northgate Technologies Inc., Elgin, IL, USA) and a 1.9-Fr BiPolar EHL Probe (Northgate Technologies Inc.,

Elgin, IL, USA). The fractured stones were flushed or pushed with the tip of the cholangioscope through the BA into the jejunum, and if

necessary, a balloon catheter and basket catheter were used. This process was repeated until the stones were determined to have completely disappeared under direct vision and cholangiography. Finally, a 10-Fr biliary catheter was placed for a few days; thereafter, the catheter was removed when the same determination was made based on another cholangiography examination.

All these steps were performed during the same admission.

Protocol for the peroral endoscopic procedure using short double-balloon enteroscopy

sDBE was performed by experienced endoscopists with the patient in a prone position under conscious sedation, with diazepam and pethidine hydrochloride (Figure 2, Supplemental video).

The sDBE (EC-450BI5 or EI-530B, Fujifilm, Tokyo, Japan) has a 152 cm working length with a 2.8 mm working channel, which enables the use of most conventional accessories, and a balloon overtube fits over the scope. In addition, the transparent hood is usually included at the sDBE tip to improve scope intubation and visibility for locating equivocal BA sites. Carbon dioxide insufflation [Domagk *et al.* 2007] and olive oil, as a lubricant for inserting accessories through the working channel, were used during the procedure.

First, the scope was perorally advanced toward the BA. Manual compression on the abdomen was sometimes performed to prevent excessive bending of the scope during the advancement. After identifying the BA site, biliary cannulation and cholangiography were generally performed using a 3.5-Fr tapered catheter (PR-V220Q; Olympus Medical Systems, Tokyo, Japan) with a 0.025-inch guidewire (Visiglide; Olympus Medical Systems). When biliary cannulation was difficult because of severe BAS, a 3-Fr tapered catheter (Contour 5-4-3 Tip; Boston Scientific, Natick, MA, USA) and a 0.018-inch guidewire (Roadrunner; Cook Medical, Tokyo, Japan) were used instead. In cases with BAS, dilation with a 6–10 mm diameter balloon dilation catheter (Quantum TTC; Cook Medical, Tokyo, Japan) was performed before stone removal. If dilation was difficult despite successful guidewire insertion, a 7-Fr Soehendra biliary dilation catheter (Cook Medical) or 7-Fr Soehendra stent retriever

(Cook Medical) was used for pre-dilation [Tsutsumi *et al.* 2013].

For stone extraction, a retrieval balloon catheter (Tri-Ex; Cook Medical), basket catheter (Flower Basket V 8-wire type; Olympus Medical Systems), and mechanical lithotripter (Crusher Catheter; Xemex, Tokyo, Japan) were usually used. For impacted stones, extracorporeal shock wave lithotripsy (ESWL) under endoscopic nasobiliary drainage (ENBD) guidance or EHL under peroral direct cholangioscopy (PDCS) using an ultra-slim gastroscope (outer diameter, 5.9 mm; EG-530NW; Fujifilm) while leaving the balloon overtube in place was planned. In some cases, with incomplete removal of bile duct stones or severe biliary stricture, 6-Fr or 7-Fr plastic stents were placed in the initial session; thereafter, sessions were repeated during readmission until stone extraction was completed or severe stricture subsided. In addition, PDCS was sometimes conducted after stone extraction. When the residual stone was detected, extraction was performed using a 5-Fr basket catheter (Memory Basket; Cook Medical) and suction after normal saline irrigation under PDCS (Figure 3) [Matsumoto *et al.* 2016].

Finally, bile duct stones were determined to have completely disappeared using a balloon-occluded cholangiography in all cases and additionally using PDCS or cholangiography with an ENBD catheter a few days later in some cases.

Follow up

Antibiotics were administered for at least 2 days, and dietary intake was started 1 day after the procedure when a good clinical course was achieved. After discharge from our hospital, laboratory and radiological tests were performed to check for stone recurrence every 3–6 months or any time patients reported symptoms suggestive of recurrence or cholangitis. All patients were followed up for >2 years after treatment completion. If necessary, objective information was also collected by contacting the patient's family doctor.

Study definitions

Initial success with biliary access was defined as the feasibility of bile duct access by successful PTBD or the BA site was reached during sDBE by using the initial treatment methods. Biliary

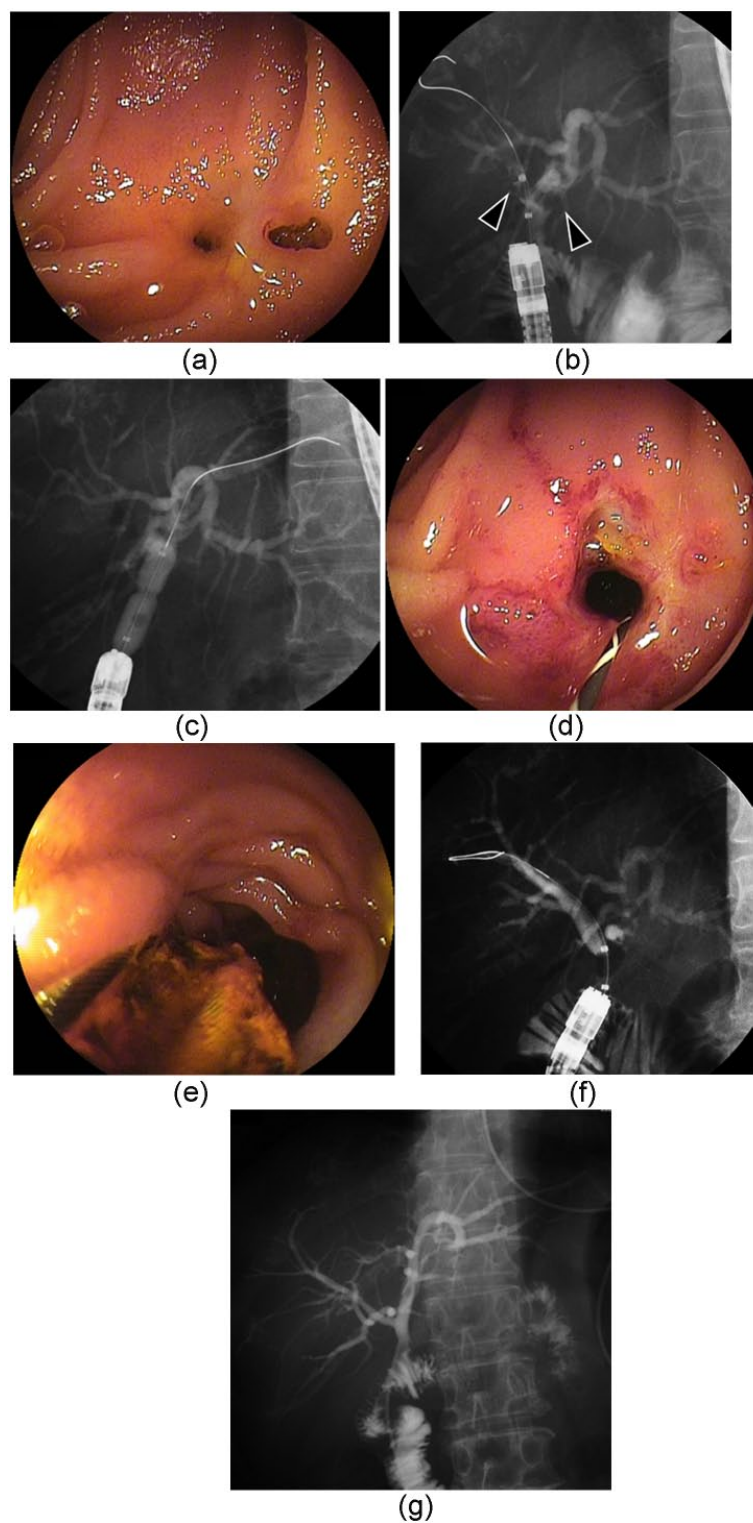


Figure 2. Peroral endoscopic procedure using a short double-balloon enteroscope. (a) Endoscopic view showing a BAS. (b) Cholangiogram showing multiple bile duct stones (arrows) at the hilum. (c) Balloon dilation for the BAS was performed over the guidewire. (d) Endoscopic view showing the resolution of BAS after dilation. (e) Stone extraction was performed using a mechanical lithotripter. (f) Balloon-occluded cholangiography was performed on each side of the bile ducts to determine complete stone clearance. (g) After a few days, the catheter was removed following the determination of complete stone clearance based on cholangiography using a nasobiliary catheter. BAS, bilioenteric anastomotic stricture.

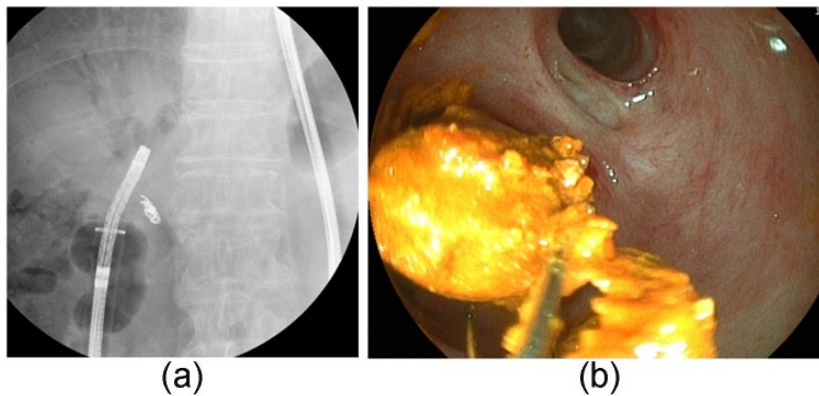


Figure 3. Overtube-assisted PDCS using an ultraslim gastroscop. (a) Following the determination of complete stone clearance by balloon-occluded cholangiography and withdrawal of the balloon enteroscop, an ultraslim gastroscop was advanced into the bile duct through the overtube that was left in place. (b) The retained stones shown were grasped by a 5-Fr basket catheter, and they were extracted under direct vision. 5-Fr, 5-French; PDCS, peroral direct cholangioscop.

intervention-related technical success was defined as the feasibility of biliary interventions such as stone extraction, stent placement, or ENBD catheter placement after successful access of the bile duct using each treatment method, irrespective of achieving complete stone clearance. Clinical success was defined as improved symptoms and laboratory data after each treatment. Adverse events were defined as those related to the procedure that occurred within 1 month after all the procedures [Cotton *et al.* 2010]. Regarding quality of life (QOL), severe postprocedural pain requiring analgesic administration was also evaluated. Residual and recurrent stones were defined as detectable stones ≤ 3 months and > 3 months after determining complete stone clearance, respectively [Hwang *et al.* 2004]. True complete stone clearance was defined as no detection of residual stones after determining complete stone clearance. The hospitalization duration was defined as the total length of hospital stay from the date of the initial hospital admission to the date of discharge after determining complete stone clearance, because no patient was treated as an outpatient in both groups. The stone-free duration was defined as the time from determining complete stone clearance to the detection of residual or recurrent stones. The follow up duration was defined as the time from the date of determining complete stone clearance to the date of the last visit.

In this study, the initial success rate for biliary access was evaluated in 8 patients with PTCS and

in 32 patients with an sDBE. Then for the following analyses, including biliary intervention-related technical success, clinical success, adverse events, true complete stone clearance, hospitalization duration, and stone-free survival, three patients in whom biliary access failed during the initial sDBE but was successful with subsequent PTCS were reassigned to undergo PTCS. Therefore, these data were analyzed in 11 patients treated with PTCS and in 29 patients treated with sDBE.

Statistical analysis

Continuous data are presented as medians (interquartile ranges). Continuous variables were compared using the Mann–Whitney U test. Frequency distribution was compared using Fisher's exact or χ^2 tests. The cumulative probability of being stone-free was assessed using the Kaplan–Meier method and compared using log-rank tests. All statistical analyses were performed with GraphPad Prism 6.0 (GraphPad Software, San Diego, CA, USA). A $p < 0.05$ was considered statistically significant.

Results

Among 40 patients, the initial success rates for biliary access were not significantly different between PTCS and sDBE [100% (8/8) *versus* 91% (29/32)]. In three patients, sDBE failed because scope insertion for BA was difficult due to severe adhesion of the intestinal limb. In two of three patients, the reconstruction method was

Table 1. Characteristics of patients with bile duct stones after hepaticojejunostomy.

	PTCS (n = 11)	sDBE (n = 29)	p-value
Sex, n (%)			
Male	4 (36)	16 (55)	0.48
Female	7 (64)	13 (45)	
Median age, years (range)	65 (30–81)	69 (4–82)	0.585
Clinical symptoms*, n			
Cholangitis	11	17	NA
Liver abscess	0	2	
Septic shock	2	0	
Abnormal LFT	0	8	
Abdominal pain	0	2	
Asymptomatic	0	2	
Primary disease for surgical operation, n			
Congenital biliary dilation	4	2	NA
Congenital bile duct atresia	1	0	
Liver failure requiring liver transplantation	0	3	
Bile duct injury in cholecystectomy	2	0	
Hepatolithiasis	0	1	
Choledocholithiasis	0	1	
Pancreatic neoplasm; benign/malignant	0/1	10/4	
Bile duct cancer	2	6	
Gastric cancer	0	1	
Liver metastasis due to colon cancer	0	1	
Unknown	1	0	
Reconstruction of the digestive tract, n (%)			
RYHJ†	8 (73)	7 (24)	0.012
Pancreatoduodenectomy	2 (18)	20 (69)	
The others	1 (9)	2 (7)	
Concomitant benign biliary stricture, n (%)			
BA	5 (45)	24 (82)	0.042
Intrahepatic bile duct	0	1 (3)	1

BA, bilioenteric anastomosis; LFT, liver function test; NA, not available; PTCS, percutaneous transhepatic procedures using a cholangioscopy; RYHJ, Roux-en-Y hepaticojejunostomy; sDBE, short double-balloon enteroscope.
 *Two patients had cholangitis with septic shock in PTCS, and two patients had cholangitis with liver abscess in sDBE.
 †Due to bile duct resection with or without hepatectomy, or living donor liver transplantation.

RYHJ. Regarding stone extraction and long-term outcomes, three patients who had been successfully treated with subsequent PTCS were re-assigned to undergo PTCS.

Patients' characteristics

Patients' characteristics are shown in Table 1. Regarding reconstruction of the digestive tract, 69% (20/29) of patients underwent pancreatoduodenectomy before the present study was conducted.

Stone characteristics

The median maximum stone size and median number of stones were larger with PTCS than with sDBE [12 (8–15) versus 8 (4–10) mm and 5 (1–6) versus 3 (1–8), respectively; Table 2]. Multiple stones in the bilateral bile ducts existed more frequently with PTCS than with sDBE [55% (6/11) versus 38% (11/29)]. Regarding the first modality to visualize the stones, the stones were initially detected using cholangiography in 24% (7/29) of the patients treated with sDBE, whereas the stones were detected using

Table 2. Bile duct stone characteristics.

	PTCS (<i>n</i> = 11)	sDBE (<i>n</i> = 29)	<i>p</i> -value
Size of stones (maximum), <i>n</i> (%)			
<10	4 (36)	18 (62)	0.173
≥10	7 (64)	11 (38)	
Number of stones, <i>n</i> (%)			
<3	4 (36)	12 (41)	0.958
3–10	5 (45)	12 (41)	
>10	2 (19)	5 (18)	
Location of stones in the bile duct, <i>n</i> (%)			
Right	0	7 (24)	0.29
Left	4 (36)	7 (24)	
Bilateral	6 (55)	11 (38)	
Common bile duct	1 (9)	4 (14)	
First modality for stone visualization, <i>n</i> (%)			
US/CT/MRCP	11 (100)	22 (76)	0.159
Cholangiography	0	7 (24)	

CT, computed tomography; MRCP, magnetic resonance cholangiopancreatography; PTCS, percutaneous transhepatic procedures using a cholangioscopy; sDBE, short double-balloon enteroscope; US, ultrasonography.

noninvasive imaging modalities in all patients treated with PTCS.

Biliary intervention-related technical success, clinical success, and treatment details

Biliary intervention-related technical success and clinical success were eventually achieved in all 40 patients (Table 3).

A total of 9 of 11 patients (82%) treated with PTCS had one biliary tract that communicated with the left intrahepatic bile duct (*n* = 8) or posterior branch (*n* = 1). One patient had two biliary tracts that communicated with B2 and B3, whereas another patient had three biliary tracts that communicated with B3, the anterior branch, and posterior branch, as access to multiple targeted bile ducts was needed because of multiple bile duct stones. A total of 10 of 11 patients (91%) required EHL for stone extraction, and fractured stones were removed by saline irrigation without the use of any accessories in 7 patients (64%).

For 29 patients treated with sDBE, the median procedure time for scope insertion to the BA was 14 (9–29) min, and the median total procedure time in the initial session was 68 (50–93) min. For stone fragmentation, a mechanical lithotripter

was required for 8 patients (28%), and ESWL was required for 1 patient (3%). In four of eight patients (50%) undergoing PDCS after complete stone clearance was determined using balloon-occluded cholangiography, retained stones were detected and could be completely extracted under direct vision. In addition, retained stones were detected using cholangiography with an ENBD catheter in another two patients, and complete stone extraction using sDBE was conducted.

Adverse events

The rate of procedure-related adverse events was significantly higher with PTCS than with sDBE (Table 3).

With PTCS, the adverse events consisted of cholangitis (*n* = 4), hemobilia (*n* = 2), and uncontrollable, severe pain resulting in treatment discontinuation (*n* = 1). One patient had cholangitis, hemobilia, and severe pain. The cholangitis and hemobilia improved with conservative treatment, and the severe pain required additional treatment for stone extraction under general anesthesia. With sDBE, the adverse events consisted of cholangitis due to residual stones (*n* = 2) and transplanted liver graft ischemia in a pediatric patient (*n* = 1) [Tsutsumi *et al.* 2014a]. Cholangitis

Table 3. Biliary intervention-related technical success, clinical success, details of treatment, and adverse events associated with treatment.

	PTCS (n = 11)	sDBE (n = 29)	p-value
Technical success, n (%)	11 (100)	29 (100)	1
Details of treatment, n.			
Balloon dilation	4	24	NA
Stone extraction	11	29	
Balloon	2	23	
Basket	3	3	
Mechanical lithotripter	0	8	
ESWL	0	1	
EHL	10	0	
EBS	0	6	
ENBD	–	13	
PDCS	–	6	
Biopsy	1	0	
Clinical success, n (%)	11 (100)	29 (100)	1
Adverse events, n (%)	*5 (45)	3 (10)	0.025
Cholangitis with/without residual stone	4/0 (36)	0/2 (14)	
Hemobilia	2 (18)	0	
Uncontrollable, severe pain resulting in the discontinuation of treatment	1 (9)	0	
Transplanted liver graft ischemia	0	1 (3)	
Severe pain necessitating analgesic administration, n (%)	8 (73)	1 (3)	<0.001

EBS, endoscopic biliary stenting; EHL, endoscopic mechanical lithotripsy; ENBD, endoscopic nasobiliary drainage; ESWL, extracorporeal shock wave lithotripsy; NA, not available; PDCS, peroral direct cholangioscopy; PTCS, percutaneous transhepatic procedures using a cholangioscopy; sDBE, short double-balloon enteroscope.
*One patient had three adverse events.

occurred at 3 or 21 days after determining complete stone clearance, and emergency sDBE was required for biliary drainage. The latter improved within 1 week of conservative treatment.

In addition, severe postprocedural pain requiring analgesia occurred significantly more often with PTCS than with sDBE.

True complete stone clearance

The rate of true complete stone clearance was similar with PTCS and sDBE (Table 4).

The median number of sessions for stone removal was similar between both treatments. However, the median number of total sessions from initial drainage to complete stone clearance was significantly higher with PTCS than with sDBE.

Overall, two patients with failed complete stone clearance with sDBE experienced cholangitis with residual stones, as described in the adverse events section.

Hospitalization duration

Median hospitalization duration for complete stone clearance was significantly shorter with sDBE than with PTCS (Table 4).

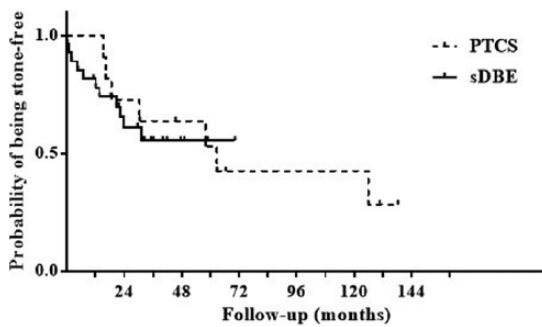
Stone-free survival

Median follow up durations after determining complete stone clearance were 7.2 (5.1–10.4) years in patients treated with PTCS and 3.1 (2.5–4.1) years in patients treated with sDBE. The probabilities of being stone-free at 1, 2, and 3 years were 100%, 73% [95% confidence interval

Table 4. Details of treatment for complete stone clearance.

	PTCS (<i>n</i> = 11)	sDBE (<i>n</i> = 29)	<i>p</i> -value
True complete stone clearance, <i>n</i> (%)	11 (100)	27 (93)	1
Total no. of sessions until complete stone removal, <i>n</i> (%)			
1 session	0	18 (67)	<0.001
≥2 sessions	11 (100)	9 (33)	
Median no. of total sessions, <i>n</i> (IQR)	5 (4–6)	1 (1–2)	<0.001
Median no. of sessions for stone extraction only, <i>n</i> (IQR)	2 (1–2)	1 (1–2)	0.121
Median total hospitalization duration, days (IQR)	35 (27–41)	10 (7–15)	<0.001

IQR, interquartile range; no., number; PTCS, percutaneous transhepatic procedures using a cholangioscopy; sDBE, short double-balloon enteroscope.

**Figure 4.** The probability of being stone-free after the determination of complete stone clearance. PTCS, percutaneous transhepatic procedures using a cholangioscopy; sDBE, short, double-balloon enteroscope.

(CI), 37–90], and 64% (95% CI, 30–84), respectively, with PTCS and 85% (95% CI, 65–94), 65% (95% CI, 43–80), and 59% (95% CI, 37–76), respectively, with sDBE ($p = 0.919$ between treatments; Figure 4). Of five patients with recurrent stones after PTCS, three were treated with PTCS, one was treated with sDBE, and one was treated conservatively due to a poor performance status. Among eight patients with recurrent stones after sDBE, seven patients were treated with sDBE, and one patient was treated conservatively owing to refusal of further treatment.

Discussion

To the best of our knowledge, this is the first study to compare PTCS and sDBE for the treatment of bile duct stones in patients with prior hepaticojejunostomy. Although sDBE was no less effective than PTCS regarding technical success, clinical success, and long-term outcomes, sDBE

was significantly superior to PTCS in terms of adverse events and the hospitalization duration.

There are only a few articles and several case reports about percutaneous transhepatic treatment of bile duct stones in patients with hepaticojejunostomy. Most of these studies focused on the treatment of BAS, with high technical success rates for these biliary interventions (94–100%) [Bonnell *et al.* 1991; Schumacher *et al.* 2001; Kim *et al.* 2003; Glas *et al.* 2008]; however, treatment details and long-term outcomes are mostly unknown. The main advantages of the percutaneous approach are the ability to accurately target the bile duct in which the stones exist when an imaging modality previously showed the stones clearly and the ability to perform repeated procedures using the percutaneous biliary tract until complete stone clearance is achieved. In addition, as bile duct stones are usually observed under direct vision with a cholangioscope, EHL could also be conducted safely and effectively [Jeng *et al.* 1989; Binmoeller *et al.* 1993; Glas *et al.* 2008] even for large, impacted stones. However, PTCS has inevitable technical disadvantages such as requiring multiple step-by-step procedures, which increases the potential for adverse events. Despite the lack of uniform standards, approximately 16 days are reportedly required to prepare for absolute and safe PTCS [Lee *et al.* 2013]. In the present study, PTCS was performed without adverse events related to the percutaneous tract, possibly as a result of the median 22 (17–30) days of preparation; however, the longer duration of hospitalization for the preparation was the result of pain and discomfort associated with the external transhepatic catheter that was experienced by most patients [Schumacher *et al.* 2001; Lee *et al.*

2013]. As the second technical disadvantage, not all bile duct segments can be accessed in a single puncture, and the management of stones in opposite bile ducts may be difficult due to the anatomy of the hepatic duct confluence; therefore, PTCS is considered highly difficult and complicated, especially for patients with multisegmental bile duct stones. Third, radiologists' hands are directly exposed to radiation when PTCS is performed using a percutaneous tract through the left bile duct. Finally, this procedure is contraindicated for patients with ascites or coagulopathy.

Recent advancements in balloon enteroscopes facilitate access to the BA site in patients with surgically altered anatomies; therefore, diagnostic and therapeutic endoscopic procedures can be performed for various postoperative biliary diseases [Aabakken *et al.* 2007; Shimatani *et al.* 2009; Itoi *et al.* 2010a; Tsujino *et al.* 2010; Siddiqui *et al.* 2013]. However, the technical outcomes for treatment of bile duct stones using balloon enteroscopes have been reported for only small samples of patients with hepaticojejunostomy [Aabakken *et al.* 2007; Shimatani *et al.* 2009; Itoi *et al.* 2010a; Parlak *et al.* 2010; Tsujino *et al.* 2010; Itokawa *et al.* 2014], and no studies have focused on the long-term or immediate outcomes. The significance of the present study was new insight regarding the treatment of all patients with the sDBE, which is characterized by a high degree of maneuverability and therapeutic potential compared with long balloon enteroscopes. Despite the short length of the sDBE, successful access to the BA site was achieved in most patients with hepaticojejunostomy. Once the scope reaches the BA site, successful cholangiography and treatment can almost always be achieved because of the availability of various conventional accessories. Diagnostic procedure using a sDBE for patients with symptoms suggestive of cholangitis can sometimes show small bile duct stones or sludge, which cannot be detected with MRCP [Macías-Gómez and Dumonceau, 2015], whereas PTBD is always used in directed therapeutics. Even with multiple bile duct orifices, successful biliary cannulation and stone extraction can be correctly and safely conducted through the BA site under direct vision [Tsutsumi *et al.* 2014b]. In addition, EHL under PDCS with an ultra-slim endoscope [Itoi *et al.* 2012] or a balloon enteroscope [Kao and Batra, 2014] can be performed and useful in selected cases. However, patients can never be treated with sDBE if the scope insertion to the BA is unsuccessful. Additionally,

stones located above severe biliary strictures through which a guidewire cannot pass cannot be extracted using an endoscopic procedure. Instead, PTCS is mandatory and may be useful in these situations.

Adverse events with PTCS, including PTBD, consist of hemobilia, cholangitis, biloma, pneumothorax, catheter migration, and pain, and they occur in 20–38.1% of patients [Clouse *et al.* 1986; Jeng *et al.* 1989; Bonnel *et al.* 1991; Yeh *et al.* 1995; Schumacher *et al.* 2001; Winick *et al.* 2001; Kim *et al.* 2003; Oh *et al.* 2007]. The rate of cholangitis after PTCS in the present study was relatively high, yet similar to that in previous reports, and no events related to the percutaneous tract occurred. The rate of adverse events with endoscopic procedures using a balloon enteroscope for pancreatobiliary disease is reportedly very low (0–8.3%); these events include bleeding, retroperitoneal air, pancreatitis, and perforation, although these did not occur in the present study. Regarding another important aspect, postprocedural pain requiring analgesic administration associated with deterioration in patients' QOL was markedly more frequent with PTCS than with sDBE; this is a minor but not a negligible disadvantage of PTCS [Jeng *et al.* 1989; Schumacher *et al.* 2001; Winick *et al.* 2001; Oh *et al.* 2007].

Residual and recurrent stones remain issues with the treatment of bile duct stones, because these stones can lead to recurrent cholangitis. In the present study, the rate of 3-year stone-free survival did not differ between PTCS and sDBE. However, regarding the means to determine complete stone clearance, balloon-occluded cholangiography in sDBE involves the risk of overlooking stone fragments by disturbing the pneumobilia [Tsuchiya *et al.* 2008]. This situation is similar to stone extraction in conventional endoscopic retrograde cholangiopancreatography; approximately 24–28.3% of patients have retained stones even after the procedure [Itoi *et al.* 2010b; Lee *et al.* 2012]. Based on our frequent detection of residual stones by PDCS, PDCS may be the more promising procedure for optimal treatment, complete stone clearance, and maintenance of stone clearance, and it may make a better contribution to stone-free survival. Further improvement in scopes, balloon overtubes, and devices is necessary to perform PDCS in all patients treated with sDBE, and studies that evaluate the long-term outcomes of endoscopic procedures combined with PDCS are warranted.

There are some limitations in this study. First, the sample size of patients treated with PTCS was small; this is related to the limited number of patients with bile duct stones after hepaticojunostomy. Therefore, when biliary intervention-related outcomes, except for initial success, were evaluated, three patients in whom access failed during the initial sDBE but was successful with subsequent PTCS were reassigned to the PTCS. Second, the treatments depended on the study period. Third, the usefulness of sDBE may be overestimated, because about two-thirds of patients treated with sDBE underwent pancreatoduodenectomy before the present study was conducted, as this is a simpler way to reach the BA site. In fact, among patients who underwent sDBE at our hospital, scope insertion to the BA site was more difficult with RYHJ [81% (73/90)] than with pancreatoduodenectomy [99% (111/112)]. However, this result suggests that approximately 80% patients with hepaticojunostomy will be initially treated with sDBE. Prospective, randomized, controlled studies with large samples are necessary to establish the optimal strategy for treating bile duct stones in patients with prior hepaticojunostomy.

In conclusion, compared with PTCS, peroral endoscopic procedures using an sDBE for managing bile duct stones in patients with prior hepaticojunostomy was useful and had low rates of adverse events, a short hospitalization, and potential cost-effectiveness. In addition, stone-free survival for 3 years was not different between the treatments. Therefore, minimally-invasive, efficacious sDBE performed by experienced endoscopists can be considered as first-line treatment for managing bile duct stones in patients with hepaticojunostomy.

Acknowledgements

Koichiro Tsutsumi: conception and design, treatment, analysis and interpretation of the data, and drafting of the article. Hironari Kato; treatment, interpretation of data, and drafting of the article. Shuntaro Yabe: treatment, interpretation of data, and critical revision of the article for important intellectual content. Sho Mizukawa: treatment, interpretation of data, and critical revision of the article for important intellectual content. Hiroyuki Seki: treatment, interpretation of data, and critical revision of the article for important intellectual content. Yutaka Akimoto: treatment, interpretation of data, and critical revision of the

article for important intellectual content. Daisuke Uchida: treatment, interpretation of data, and critical revision of the article for important intellectual content. Kazuyuki Matsumoto: treatment, interpretation of data, and critical revision of the article for important intellectual content. Takeshi Tomoda: treatment, interpretation of data, and critical revision of the article for important intellectual content. Naoki Yamamoto: treatment, interpretation of data, and critical revision of the article for important intellectual content. Shigeru Horiguchi: treatment, interpretation of data, and critical revision of the article for important intellectual content. Hirofumi Kawamoto: treatment. Hiroyuki Okada: final approval of the article.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare that there is no conflict of interest.

References

- Aabakken, L., Bretthauer, M. and Line, P. (2007) Double-balloon enteroscopy for endoscopic retrograde cholangiography in patients with a Roux-en-Y anastomosis. *Endoscopy* 39: 1068–1071.
- Binmoeller, K., Brückner, M., Thonke, F. and Soehendra, N. (1993) Treatment of difficult bile duct stones using mechanical, electrohydraulic and extracorporeal shock wave lithotripsy. *Endoscopy* 25: 201–206.
- Bonnel, D., Liguory, C., Cornud, F. and Lefebvre, J. (1991) Common bile duct and intrahepatic stones: results of transhepatic electrohydraulic lithotripsy in 50 patients. *Radiology* 180: 345–348.
- Clouse, M., Stokes, K., Lee, R. and Falchuk, K. (1986) Bile duct stones: percutaneous transhepatic removal. *Radiology* 160: 525–529.
- Cotton, P., Eisen, G., Aabakken, L., Baron, T., Hutter, M., Jacobson, B. *et al.* (2010) A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc* 71: 446–454.
- Domagk, D., Bretthauer, M., Lenz, P., Aabakken, L., Ullerich, H., Maaser, C. *et al.* (2007) Carbon dioxide insufflation improves intubation depth in double-balloon enteroscopy: a randomized, controlled, double-blind trial. *Endoscopy* 39: 1064–1067.

- Glas, L., Courbière, M., Ficarelli, S., Milot, L., Mennesson, N. and Pilleul, F. (2008) Long-term outcome of percutaneous transhepatic therapy for benign bilioenteric anastomotic strictures. *J Vasc Interv Radiol* 19: 1336–1343.
- Hwang, J., Yoon, Y., Kim, Y., Cheon, J. and Jeong, J. (2004) Risk factors for recurrent cholangitis after initial hepatolithiasis treatment. *J Clin Gastroenterol* 38: 364–367.
- Itoi, T., Ishii, K., Sofuni, A., Itokawa, F., Tsuchiya, T., Kurihara, T. *et al.* (2010a) Single-balloon enteroscopy-assisted ERCP in patients with Billroth II gastrectomy or Roux-en-Y anastomosis (with video). *Am. J. Gastroenterol* 105: 93–99.
- Itoi, T., Sofuni, A., Itokawa, F., Kurihara, T., Tsuchiya, T., Ishii, K. *et al.* (2012) Diagnostic and therapeutic peroral direct cholangioscopy in patients with altered GI anatomy. *Gastrointest Endosc* 75: 441–449.
- Itoi, T., Sofuni, A., Itokawa, F., Shinohara, Y., Moriyasu, F. and Tsuchida, A. (2010b) Evaluation of residual bile duct stones by peroral cholangioscopy in comparison with balloon-cholangiography. *Dig Endosc* 22(Suppl. 1): S85–S89.
- Itokawa, F., Itoi, T., Ishii, K., Sofuni, A. and Moriyasu, F. (2014) Single- and double-balloon enteroscopy-assisted endoscopic retrograde cholangiopancreatography in patients with Roux-en-Y plus hepaticojejunostomy anastomosis and Whipple resection. *Dig Endosc* 26(Suppl. 2): 136–143.
- Jeng, K., Chiang, H. and Shih, S. (1989) Limitations of percutaneous transhepatic cholangioscopy in the removal of complicated biliary calculi. *World J Surg* 13: 603–610.
- Kao, K. and Batra, B. (2014) Single-balloon-assisted ERCP with electrohydraulic lithotripsy for the treatment of a bile duct stone in a patient with a hepaticojejunostomy. *Gastrointest Endosc* 80: 1173
- Kim, J., Lee, S., Kim, M., Song, M., Park, D., Kim, S. *et al.* (2003) Percutaneous transhepatic cholangioscopic treatment of patients with benign bilio-enteric anastomotic strictures. *Gastrointest Endosc* 58: 733–738.
- Kondo, S., Nimura, Y., Hayakawa, N., Kamiya, J., Nagino, M., Miyachi, M. *et al.* (1995) A clinicopathologic study of primary cholesterol hepatolithiasis. *Hepatogastroenterology* 42: 478–486.
- Lee, J., Kim, H., Kang, D., Choi, C., Park, S., Kim, S. *et al.* (2013) Usefulness of percutaneous transhepatic cholangioscopic lithotomy for removal of difficult common bile duct stones. *Clin Endosc* 46: 65–70.
- Lee, Y., Moon, J., Choi, H., Min, S., Kim, H., Lee, T. *et al.* (2012) Direct peroral cholangioscopy using an ultraslim upper endoscope for management of residual stones after mechanical lithotripsy for retained common bile duct stones. *Endoscopy* 44: 819–824.
- Macías-Gómez, C. and Dumonceau, J. (2015) Endoscopic management of biliary complications after liver transplantation: an evidence-based review. *World J Gastrointest Endosc* 7: 606–616.
- Matsumoto, K., Tsutsumi, K., Kato, H., Akimoto, Y., Uchida, D., Tomoda, T. *et al.* (2016) Effectiveness of peroral direct cholangioscopy using an ultraslim endoscope for the treatment of hepatolithiasis in patients with hepaticojejunostomy (with video). *Surg Endosc* 30: 1249–1254.
- Oh, H., Lee, S., Lee, T., Kwon, S., Lee, S., Seo, D. *et al.* (2007) Analysis of percutaneous transhepatic cholangioscopy-related complications and the risk factors for those complications. *Endoscopy* 39: 731–736.
- Parlak, E., Çiçek, B., Dişibeyaz, S., Cengiz, C., Yurdakul, M., Akdoğan, M. *et al.* (2010) Endoscopic retrograde cholangiography by double balloon enteroscopy in patients with Roux-en-Y hepaticojejunostomy. *Surg Endosc* 24: 466–470.
- Schumacher, B., Othman, T., Jansen, M., Preiss, C. and Neuhaus, H. (2001) Long-term follow-up of percutaneous transhepatic therapy (PTT) in patients with definite benign anastomotic strictures after hepaticojejunostomy. *Endoscopy* 33: 409–415.
- Shah, R., Smolkin, M., Yen, R., Ross, A., Kozarek, R., Howell, D. *et al.* (2013) A multicenter, U.S. experience of single-balloon, double-balloon, and rotational overtube-assisted enteroscopy ERCP in patients with surgically altered pancreaticobiliary anatomy (with video). *Gastrointest Endosc* 77: 593–600.
- Shimatani, M., Matsushita, M., Takaoka, M., Koyabu, M., Ikeura, T., Kato, K. *et al.* (2009) Effective ‘short’ double-balloon enteroscope for diagnostic and therapeutic ERCP in patients with altered gastrointestinal anatomy: a large case series. *Endoscopy* 41: 849–854.
- Siddiqui, A., Chaaya, A., Shelton, C., Marmion, J., Kowalski, T., Loren, D. *et al.* (2013) Utility of the short double-balloon enteroscope to perform pancreaticobiliary interventions in patients with surgically altered anatomy in a US Multicenter Study. *Dig Dis Sci* 58: 858–864.
- Tazuma, S. and Nakanuma, Y. (2015) Clinical features of hepatolithiasis: analyses of multicenter-based surveys in Japan. *Lipids Health Dis* 14: 129. doi:10.1186/s12944-015-0130-2
- Tsuchiya, S., Tsuyuguchi, T., Sakai, Y., Sugiyama, H., Miyagawa, K., Fukuda, Y. *et al.* (2008)

Clinical utility of intraductal US to decrease early recurrence rate of common bile duct stones after endoscopic papillotomy. *J Gastroenterol Hepatol* 23: 1590–1595.

Tsujino, T., Yamada, A., Isayama, H., Kogure, H., Sasahira, N., Hirano, K. *et al.* (2010) Experiences of biliary interventions using short double-balloon enteroscopy in patients with Roux-en-Y anastomosis or hepaticojejunostomy. *Dig Endosc* 22: 211–216.

Tsutsumi, K., Kato, H., Okada, H., Yagi, T. and Yamamoto, K. (2014a) Transplanted liver graft ischemia caused by pediatric ERCP in the prone position. *Endoscopy* 46(Suppl. 1) UCTN: E594–E595.

Tsutsumi, K., Kato, H., Okada, H. and Yamamoto, K. (2014b) Usefulness of the rendezvous technique


for deep scope insertion during endoscopic retrograde cholangiography in a patient with a Roux-en-Y hepaticojejunostomy. *Endoscopy* 46(Suppl. 1) UCTN: E619–E620.

Tsutsumi, K., Kato, H., Sakakihara, I., Yamamoto, N., Noma, Y., Horiguchi, S. *et al.* (2013) Dilation of a severe bilioenteric or pancreatoenteric anastomotic stricture using a Soehendra stent retriever. *World J Gastrointest Endosc* 5: 412–416.

Winick, A., Waybill, P. and Venbrux, A. (2001) Complications of percutaneous transhepatic biliary interventions. *Tech Vasc Interv Radiol* 4: 200–206.

Yeh, Y., Huang, M., Yang, J., Mo, L., Lin, J. and Yueh, S. (1995) Percutaneous trans-hepatic cholangioscopy and lithotripsy in the treatment of intrahepatic stones: a study with 5-year follow-up. *Gastrointest Endosc* 42: 13–18.

Visit SAGE journals online
<http://tag.sagepub.com>

 SAGE journals