Clin J Gastroenterol (2017) 10:297–311
DOI 10.1007/s12328-017-0754-z

CLINICAL REVIEW

Endoscopic management of biliary strictures after living donor liver transplantation

Takeshi Tsujino[1,2] · Hiroyuki Isayama[2,3] · Hirofumi Kogure[2] · Tatsuya Sato[2] · Yousuke Nakai[2] · Kazuhiko Koike[2]

Received: 11 May 2017 / Accepted: 1 June 2017 / Published online: 9 June 2017

Abstract Living donor liver transplantation (LDLT) is an effective alternative to deceased liver transplantation (DDLT) for end-stage liver disease. Although advances in surgical techniques, immunosuppressive management, and post-transplant care have improved the overall outcomes of LDLT, biliary strictures remain the major unsolved problem. Endoscopic retrograde cholangiopancreatography (ERCP) is currently considered the first-line therapy for biliary strictures following LDLT with duct-to-duct reconstruction, with percutaneous and surgical interventions reserved for patients with unsuccessful management via ERCP. Endoscopic management of biliary strictures is technically more challenging in LDLT than in DDLT because of the complexity of the biliary anastomosis, in addition to the tortuous and angulated biliary system. Placement of one or more plastic stents after balloon dilation has been the standard strategy for post-LDLT stricture, but this requires multiple stent exchange to prevent stent occlusion until stricture resolution. Inside stents might prevent duodenobiliary reflux and thus have longer stent patency, obviating the need for multiple ERCPs. Newly developed covered self-expandable metallic stents with anti-migration systems are alternatives to the placement of multiple plastic stents. With the advent of deep enteroscopy, biliary strictures in LDLT patients with Roux-en-Y hepaticojejunostomy are now treatable endoscopically. In this review, we discuss the short- and long-term outcomes of endoscopic management of post-LDLT strictures as well as recent advances in this field.

Keywords Living donor liver transplantation · Biliary complication · Biliary stricture · Endoscopic retrograde cholangiopancreatography · Biliary stent

✉ Takeshi Tsujino
tsujinot3915@gmail.com

1 Miyuki Clinic, 1-8-3 Renko-ji, Tama, Tokyo 2060021, Japan

2 Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

3 Department of Gastroenterology, Graduate School of Medicine, Juntendo University, Tokyo, Japan

Abbreviations

LDLT	Living donor liver transplantation
DDLT	Deceased donor liver transplantation
RYHJ	Roux-en-Y hepaticojejunostomy
DD	Duct-to-duct
ERCP	Endoscopic retrograde cholangiopancreatography
BAS	Biliary anastomotic stricture
RCT	Randomized controlled trial
US	Ultrasonography
MRCP	Magnetic resonance cholangiopancreatography
DIC-CT	Drip-infusion cholangiography with CT
PTBD	Percutaneous transhepatic biliary drainage
PS	Plastic stent
EST	Endoscopic sphincterotomy
SEMS	Self-expandable metallic stent

Introduction

Liver transplantation is the treatment of choice for selected patients with end-stage liver disease and hepatocellular carcinoma, and can offer the hope of survival to patients in danger of imminent death. Because of the scarcity of deceased-donor organs as well as the increasing number of patients on the waiting list, living donor liver transplantation (LDLT) is performed as an alternative to deceased donor liver transplantation (DDLT) [1]. Compared to DDLT using a whole liver, LDLT is technically more complex and challenging. Although refinements in surgical techniques, immunosuppressive management, and post-operative care have led to improved outcomes for LDLT [2–4], biliary complications, particularly biliary strictures, still develop in a substantial proportion of LDLT patients [5–12]. Biliary strictures affect long-term LDLT recipient outcomes and quality of life and can cause graft loss and even mortality [12, 13].

Roux-en-Y hepaticojejunostomy (RYHJ) was previously the standard biliary reconstruction technique used in LDLT patients. However, in recent years, duct-to-duct (DD) biliary reconstruction has been the preferred method over RYHJ [6, 14–16] because of its simplicity, rapid gastrointestinal recovery, lower risk of bacterial colonization of the biliary tract, and preservation of physiological bilioenteric and bowel continuity [4, 15]. In addition, DD biliary reconstruction allows easier endoscopic access to the biliary system for the evaluation and management of biliary strictures following liver transplantation. Thus, endoscopic retrograde cholangiopancreatography (ERCP) is currently performed as the first-line treatment modality for post-LDLT biliary strictures [17]. Nevertheless, endoscopic management of biliary strictures is technically more difficult in LDLT than in DDLT, principally because of the difference in the type of graft used (partial vs whole size) and the method of biliary reconstruction. Compared to DDLT, the DD biliary anastomosis is more peripheral, smaller, and more complex in LDLT [5, 16, 18], and the reconstructed bile duct in LDLT is sometimes tortuous and angulated due to hypertrophy of the transplanted liver [19]. Therefore, the strategies and outcomes of endoscopic management of biliary strictures after DDLT cannot be applied to LDLT patients [13, 19].

In this review, we focus on the status of endoscopic management of biliary strictures after LDLT. We also summarize recent advances in endoscopic techniques for management of this complication.

Incidence and risk factors of biliary strictures after LDLT

Overall biliary complications remain the most common complications after LDLT, with a reported incidence of 20–43%; biliary strictures and leakages are two major biliary complications that occur in 13–36 and 5–26% of cases, respectively (Table 1) [5–11]. While identification of the causative factors of biliary complications and subsequent refinements in reconstruction techniques might reduce the incidence of these complications in some institutions [20–22], the rate of biliary complications, particularly biliary strictures, does not seem to significantly decrease with experience [7, 8, 19, 23]. Kyoto University divided LDLT recipients into three groups according to case experience (Group 1, cases 1–100; Group 2, cases 101–200; and Group 3, cases 201–335), and found that while the rate of bile leakage significantly decreased with experience (25% in Group 1, 14% in Group 2, and 13% in Group 3, $p = 0.021$), there were no differences in the development of biliary strictures among the three groups (19, 28, 26%, respectively, $p = 0.290$) [7]. Shah et al. at the University of Toronto did not find a significant difference in the incidence of biliary stricture in the first 65 cases compared to the last 65 cases [8]. At the University of Tokyo and the University of Hong Kong, two high-volume LDLT centers, biliary strictures developed at a rate of approximately one in every four to five LDLTs [9, 24]. These results suggest that various factors, in addition to technical factors, play an important role in the development of biliary strictures [25].

Biliary strictures usually occur at the anastomosis (biliary anastomotic stricture; BAS), and non-BAS after LDLT is relatively rare. At Kyoto University, non-BAS occurred in 5 of 273 right-liver LDLT patients (2%), accounting for 6% of all biliary strictures [18]. Chang et al. reported that among 339 patients undergoing right-liver LDLT, all of the biliary strictures and non-BAS developed in 121 (36%) and 11 (10%), respectively [10]. At the Mayo Clinic Hospital in Arizona, ischemic-type strictures were observed in 3 of 110 LDLT patients (3%) [26].

Etiologies and risk factors for biliary strictures after LDLT

Biliary strictures occur more frequently after LDLT than after DDLT [12, 27–29]. Compared to DDLT, a partial graft has a smaller bile duct diameter and sometimes multiple biliary openings, rendering biliary reconstruction in LDLT complex and technically demanding. In a systematic review by Akamatsu et al., while there were no significant differences in the incidence of bile leakage between LDLT and DDLT (9.5 vs 7.8%), the incidence of BAS was significantly higher in LDLT patients than in DDLT patients (19 vs 12%) [12].

Various factors may be associated with the development of post-LDLT biliary strictures. These include recipient, graft, technical, inflammatory, ischemic, and immunological factors, which may act independently or synergistically in stricture development. Because bile duct epithelial cells (cholangiocytes) are vulnerable to ischemic and reperfusion injury [30], local ischemic change around the biliary anastomosis, particularly due to devascularization of the

Table 1 Incidence of biliary complications after LDLT

References	*n*	Overall biliary complications	Biliary strictures	Biliary leaks
Gondolesi et al. [5]	96	39 (41%)	22 (23%)	21 (22%)
Hwang et al. [6]	259	53 (20%)	42 (16%)	12 (5%)
Morioka et al. [7]	335	110 (33%)	82 (24%)	56 (17%)
Shah et al. [8]	128	41 (32%)	19 (15%)	22 (17%)
Kyoden et al. [9]	310	111 (36%)	70 (23%)	53 (17%)
Chang et al. [10]	339	147 (43%)	121 (36%)	44 (13%)
Zimmerman et al. [11]	356	141 (40%)	46 (13%)	91 (26%)

LDLT living donor liver transplantation

bile duct at the hilar dissection of the graft, is believed to be a major contributor to BAS. Another important risk factor for BAS is bile leakage [11, 23, 31, 32], which causes peribiliary inflammation and subsequent fibrosis, leading to stricture formation at the anastomosis.

Other risk factors for BAS identified in multivariate analyses include donor age >50 years [8], preoperative MELD score ≥35 [27], urgency of the surgery [33], bile duct diameter [34], a graft with multiple bile ducts [31], graft cold ischemia time [24, 34], hepatic artery stenosis [31], and acute cellular rejection [24]. Whether the biliary reconstruction technique affects the development of BAS is controversial. A retrospective study of 310 adult LDLTs at the University of Tokyo identified DD biliary reconstruction as the only significant risk factor for biliary strictures by univariate analyses [9]. The Kyoto group also reported that the biliary stricture rate was significantly higher in DD biliary reconstruction [35]. Both Seoul University [31] and Hong Kong University [24] studies, however, found no significant difference between DD biliary reconstruction and RYHJ in terms of the incidence of biliary strictures by multivariate analyses. A prospective randomized control trial (RCT) is needed to clarify this issue.

Hepatic artery thrombosis or stenosis is considered an important risk factor for non-BAS [36]. Immunological factors (e.g., ABO blood type incompatibility [37, 38] and cytomegalovirus infection [39]) are also associated with non-BAS formation. Because cholangiocytes play an important role in mucosal immunity in the biliary system [40, 41], they are the primary targets of immune attack, which leads to stricture formation.

The surgeon's experience might affect biliary strictures after LDLT. The Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL), a multicenter study conducted in the United States [29], found that liver transplant recipients at centers with higher volumes of LDLT were less likely to develop biliary strictures. Kim et al. at Samsung Medical Center, however, found no significant differences in the incidence of biliary stricture with experience, while they showed that bile leakage occurred more frequently in the LDLT patients of the junior surgeon than those of the senior surgeon [42].

Diagnosis of biliary strictures after LDLT

The majority of biliary strictures develop within the first year after transplantation, but their onset can be delayed for many years after LDLT [12]. The clinical presentation of biliary strictures is highly variable; patients may remain asymptomatic despite the presence of biliary strictures [31], or present with anorexia, pruritus, fever, abdominal pain, or jaundice. In asymptomatic LDLT patients, abnormal liver function tests, such as elevated bilirubin and alkaline phosphatase, should raise suspicion of biliary strictures. In LDLT patients with cholestasis, the priority is to differentiate biliary obstruction from liver parenchymal causes including acute or chronic rejection, recurrence of the primary disease, and drug-induced liver injury.

Diagnosis of biliary strictures is based on imaging studies. Transabdominal ultrasonography (US) is the first-line modality when biliary strictures are suspected. Dilatation of the intrahepatic bile ducts on US indicates blockage of bile flow, but US has relatively low sensitivity for detection of biliary obstruction in liver transplant recipients [43, 44]. Nevertheless, US with Doppler should be the initial modality for the evaluation of major vascular complications (e.g., hepatic artery thrombosis), which require urgent management. Magnetic resonance cholangiopancreatography (MRCP) has replaced ERCP as a noninvasive diagnostic modality for suspected post-LDLT biliary strictures, because its sensitivity and accuracy in the evaluation of biliary complications following transplantation are comparable to those of ERCP [45, 46]. Unnecessary ERCP can be avoided in LDLT recipients when there is no evidence of biliary strictures on MRCP [47]. Drip-infusion cholangiography with computed tomography (DIC-CT) is another noninvasive imaging technology for evaluating the entire biliary system in LDLT patients. Its spatial resolution is higher than that of MRCP, enabling DIC-CT to produce better images of second-order bile ducts [48, 49]. The advantages of both MRCP and DIC-CT over direct cholangiography (ERCP and percutaneous transhepatic cholangiography) is that they allow delineation of the bile ducts both proximal and distal to the stricture even in complete biliary obstruction, thereby providing important anatomic information on the complex biliary system in LDLT recipients (Fig. 1) [17]. The disadvantages of DIC-CT include the risk of severe adverse reactions to the biliary contrast media, and poor images of the biliary system in patients with severe jaundice, and radiation exposure [48]. Therefore, DIC-CT is not routinely performed in many institutions. At the University of Tokyo, MRCP is the first-line modality for the diagnosis of biliary strictures, with DIC-CT reserved for cases in which MRCP is inconclusive. Because neither MRCP nor DIC-CT is a useful imaging modality for diagnosis of small stones in the biliary tract [50], we routinely perform intraductal US during ERCP. Intraductal US facilitates detection of biliary stones, sludge, casts, and foreign bodies, even in cases lacking a discrete filling defect on a direct cholangiogram [19, 51, 52].

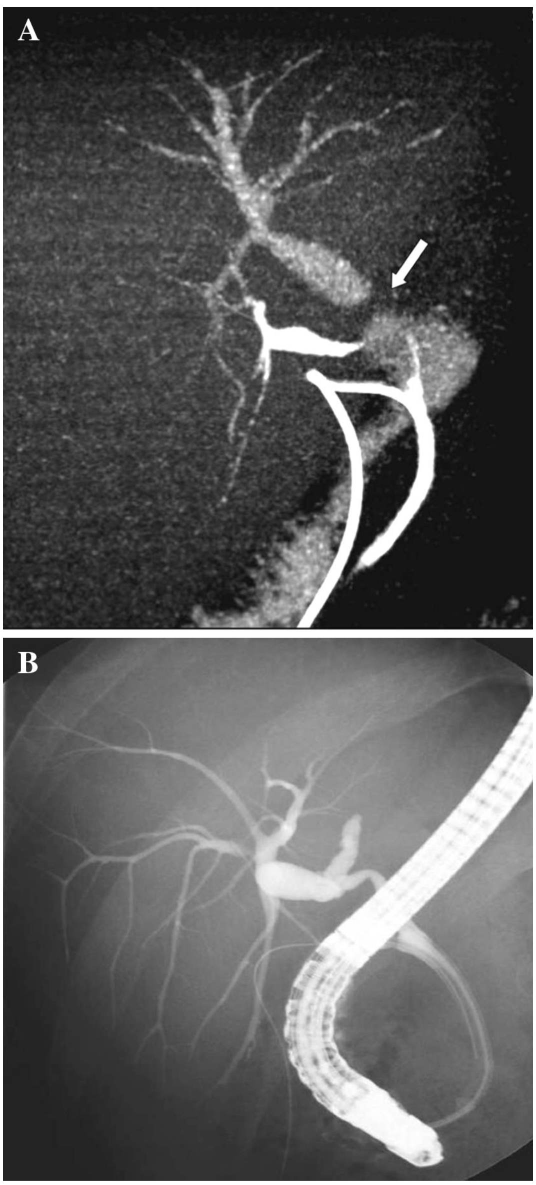


Fig. 1 **a** Drip-infusion cholangiography with CT showing obstruction of the anastomosis at the right anterior branch (*arrow*). **b** Initial endoscopic retrograde cholangiography demonstrating the right posterior branch. Note the absence of opacification of the right anterior branch

Endoscopic management of biliary strictures after LDLT

ERCP has become the first-line modality for the management of biliary strictures after LDLT; percutaneous transhepatic biliary drainage (PTBD) and surgery are reserved for cases in which an endoscopic approach is unsuccessful or the biliary reconstruction is RYHJ [13]. With the recent advent of balloon-assisted enteroscopy, biliary complications in LDLT patients with RY anastomosis are now endoscopically treatable. Before performing ERCP, it is mandatory for endoscopists to review the details of the biliary reconstruction record as well as MRCP and/or CT performed prior to ERCP [17]. In addition, endoscopists must understand the normal anatomy and potential variation in the biliary system [53]. Such knowledge will decrease the procedure time and increase the success rate of complex endoscopic procedures.

Endoscopic management of biliary strictures consists of passing the stricture with a guide wire, balloon dilation, and placement of one or more stents. Passing the stricture with a guide wire is a fundamental prerequisite for technical success of endoscopic stricture management. In LDLT patients, the strictures are often very tight and twisted due to the presence of dense fibrotic tissue and the hypertrophic transplanted liver, rendering this procedure challenging. At the University of Okayama, a guide wire could not be traversed across the stricture in 7 (17%) of 41 patients with biliary stricture [54]. The Seoul National University [31] and Mayo Clinic Hospital in Arizona [26] reported that the incidence of failed guide wire passage through the stricture was 38% (10/26 patients) and 16% (6/38 patients), respectively. At the University of Tokyo, it was impossible to pass various guide wires through the stricture in 3 (18%) of 17 patients with BAS and non-BAS [19]. Combination use of a bendable ERCP catheter (SwingTip cannula; Olympus EndoTherapy, Tokyo, Japan) and an angle-tip hydrophilic guide wire with high torque control (e.g., Radifocus Guidewire; Terumo, Tokyo, Japan) can assist negotiation of difficult strictures. In LDLT patients with difficult-to-pass strictures by conventional methods, a single-operator peroral cholangioscopy (SpyGlass System; Boston Scientific, Natick, MA, USA) may enable passage of a guide wire through the stricture under direct visualization [55, 56]. Woo et al. reported that the SpyGlass was helpful in passage of a guide wire in 9 (60%) of 15 LDLT patients with unsuccessful conventional methods [56]. Interestingly, a recent report suggests that cholangioscopic findings help predict the response to endoscopic management of post-DDLT BAS [57].

After successful passage of a guide wire, a balloon catheter is advanced and positioned across the stricture. The balloon size should be determined based on the diameter of the bile duct just proximal and distal to the stricture. Because both donor and recipient ducts are not generally very dilated in LDLT patients, a 4–8 mm diameter balloon is employed. When a severe stricture does not allow passage of a balloon catheter, a Soehendra Biliary Dilation Catheter (Cook Medical, Winston-Salem, NC, USA) or a Soehendra stent retriever (Cook Medical) is effective for traversing the stricture [58].

Plastic stent placement

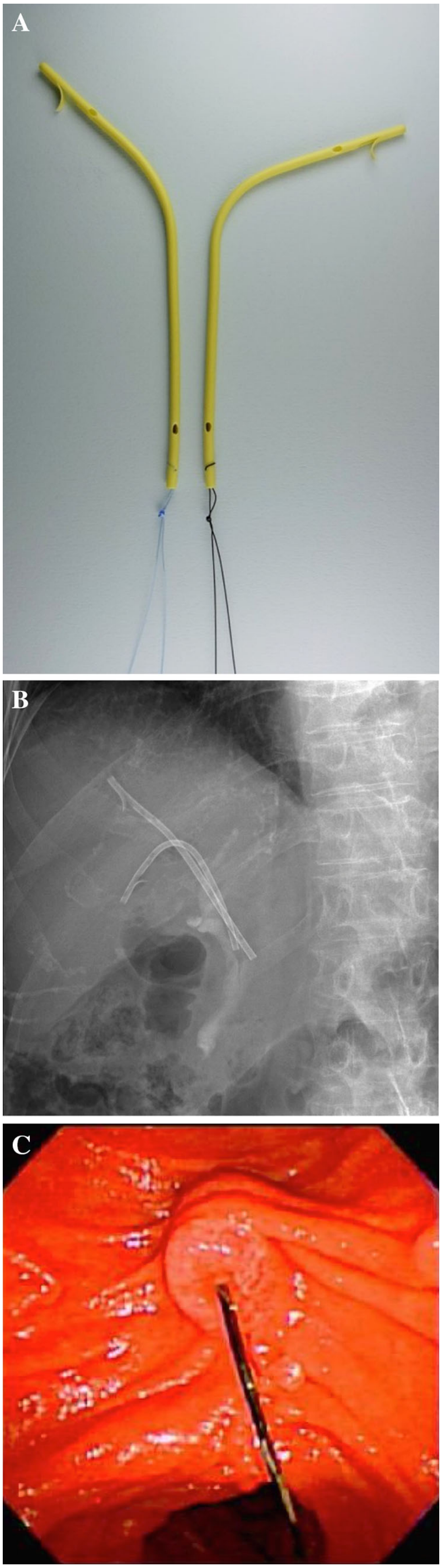
For the endoscopic management of BAS, temporary placement of single or multiple 7–11.5 Fr plastic stents (PSs) is generally recommended after balloon dilation based on the results of DDLT studies, which indicate that balloon dilation alone is less effective for BAS than balloon dilation followed by PS placement [59–61]. Endoscopic sphincterotomy (EST) is performed at many institutions to prevent post-ERCP pancreatitis, particularly when multiple PSs are placed across the papilla. Similar to the protocols for benign biliary strictures in non-transplanted patients, PSs are usually exchanged every 3 months to prevent stent occlusion and subsequent acute cholangitis. In the majority of patients with BAS, PSs are placed for at least 1 year. All of the PSs are removed after a cholangiogram shows that the BAS has resolved.

The results of balloon dilation followed by PS placement for BAS have been variable, with technical endoscopic and final endoscopic success rates ranging from 40−84% and from 20−100%, respectively [26, 28, 31, 33, 54, 62–64]. Technical endoscopic success is defined as successful placement of biliary stents without the aid of a percutaneous procedure (i.e., rendezvous technique), and final endoscopic success is resolution of BAS after stent removal. To achieve final success, an average of 2.2–6.3 ERCPs was required during an average period of 4.1–14.5 months [26, 31, 54, 62–64]. At Okayama University, an institution dedicated to endoscopic management of complex malignant hilar obstruction [65, 66], technical endoscopic success and final endoscopic success were achieved in 31 (76%) and 21 (51%) of 41 LDLT patients with BAS, respectively [54]. Their management strategy appeared to be relatively conservative; among 35 patients with eventual endoscopic success, they placed a single PS in 26 patients and two PSs in the remaining 9 because of technical difficulty as well as concern over the risk of stent-induced cholangitis/abscess. Hsieh et al. recently reported that a more aggressive strategy with PSs after EST and balloon dilation had an 84% (32/38 LDLT patients with strictures) technical endoscopic success rate and a 100% final endoscopic success rate [26]. In their study, the interval between LDLT and BAS development was relatively short (median 2.1 months), which might be related to the outcome [64, 67]. Their impressive result has not been reproduced, likely because the small donor bile duct and angulated biliary system in LDLT patients often preclude the deployment of multiple PSs [19, 54].

Inside stent placement

In general, PSs are placed across the papilla, with their distal end exposed into the duodenum. This provokes free reflux of duodenal contents through the stent, which is considered the main cause of stent occlusion [68, 69]. Therefore, PSs usually require prophylactic exchange every 2–4 months, particularly in immunocompromised LDLT patients, causing increased cost and patient burden. In addition, EST is generally performed prior to placement of a large-bore PS or multiple PSs to prevent obstruction of pancreatic outflow with resultant acute pancreatitis. EST results in permanent loss of sphincter of Oddi function [70, 71], leading to subsequent duodenobiliary reflux and bacterial colonization of the biliary system [72]. Consequently, EST can diminish one of the advantages of DD biliary reconstruction in LDLT patients.

To prolong stent patency and maintain the advantages of DD biliary reconstruction, some Japanese groups have placed PSs completely in the bile duct (inside stents) for post-LDLT biliary complications [18, 19, 73–75]. Because the distal end of an inside stent is located in the bile duct, duodenobiliary reflux is theoretically prevented. In addition, multiple inside stents do not obstruct the pancreatic orifice, obviating the need for EST. Traditionally, modified Amsterdam-type biliary stents (e.g., Flexima Biliary Stent; Boston Scientific) are used as inside stents, but a PS dedicated to inside stenting is now commercially available (Gadelius Medical, Tokyo, Japan) (Fig. 2). In a recent report from the Kyoto group, inside stents were successfully placed across the strictures in 94 (80%) of 118 LDLT patients with biliary strictures [74]. Resolution of biliary strictures was observed in 81 patients (69%). Of note, an average of 1.4 ERCP sessions was required to resolve the strictures by inside stents, and the median inside stent



◀**Fig. 2** **a** Inside stents (Gadelius Medical, Tokyo, Japan) (*left* stent for the right liver; *right* stent for the left liver). The suture thread is tied to the distal end of the stent. **b** Endoscopic retrograde cholangiography showing two inside stents placed across the strictures. **c** Endoscopic image of the papilla after inside stent deployment; the nylon thread is visible

patency was 189 days. At the University of Tokyo, we place inside stents in cases in which stricture resolution is not achieved by balloon dilation, followed by nasobiliary catheter (NBC) placement [19]. Among 63 LDLT recipients who underwent inside stent placement, 25 (40%) achieved stricture resolution [unpublished data]. The median interval of inside stent exchange was 161 days, and the cumulative incidence of stent dysfunction was 7.8% at 3 months, 12.3% at 6 months, and 18.1% at 12 months. These data suggest that inside stent placement has the potential to be the first-line strategy for post-LDLT strictures. A prospective RCT is needed to compare inside stent placement with conventional PS placement in terms of efficacy and safety.

Balloon dilation and nasobiliary catheter placement

Balloon dilation followed by NBC placement also preserves the function of the sphincter of Oddi. At the University of Tokyo, strictures are dilated with a 4–8 mm balloon, followed by placement of a 7 Fr NBC across the stricture to maintain patency [19]. Repeat balloon is performed 5–7 days later and an NBC is left in situ for 1–5 days. We used this protocol as the first-line therapy in 36 (39%) of 93 LDLT patients with biliary strictures [unpublished data]. The cumulative recurrence rate after balloon dilation and NBC placement was high (38.9% at 6 months, 44.4% at 1 year, and 59.9% at 3 years). However, a small number of patients with post-LDLT biliary stricture (15/93; 16% patients) experienced stricture resolution without recurrence using this strategy, which could prevent unnecessary additional ERCPs. Therefore, the patients with post-LDLT strictures that will benefit from balloon dilation and NBC placement should be identified. Disadvantages of NBC placement include patient discomfort, risk of tube withdrawal, prolonged hospitalization, and fluid/electrolyte imbalance.

Rendezvous technique

When endoscopic access to biliary strictures fails, PTBD, rather than surgery, is performed as a rescue procedure. The stricture can subsequently be dilated using a 12–14 Fr PTBD catheter [76]. A large-bore PTBD catheter may not only cause patient discomfort but also put LDLT patients at risk for injury to the liver parenchyma and vessels (the hepatic artery and the portal vein) [47]. The combined percutaneous-endoscopic technique (rendezvous technique) [77] requires a small (7–8 Fr) PTBD catheter, thereby reducing the risk of liver injury. After the guide wire has traversed the stricture via the PTBD route, endoscopic stent placement is relatively easy (Fig. 3) [78–80]. In cases with a completely obstructed BAS, in which identification of the anastomosis is difficult, we perform simultaneous cholangiogram via both an NBC and a PTBD tube to ensure the correct direction toward the anastomosis while attempting to pass a guide wire through the anastomosis via the PTBD route (Fig. 4) [47]. During the rendezvous technique, a hydrophilic guide wire is usually used to negotiate the stricture, but this procedure

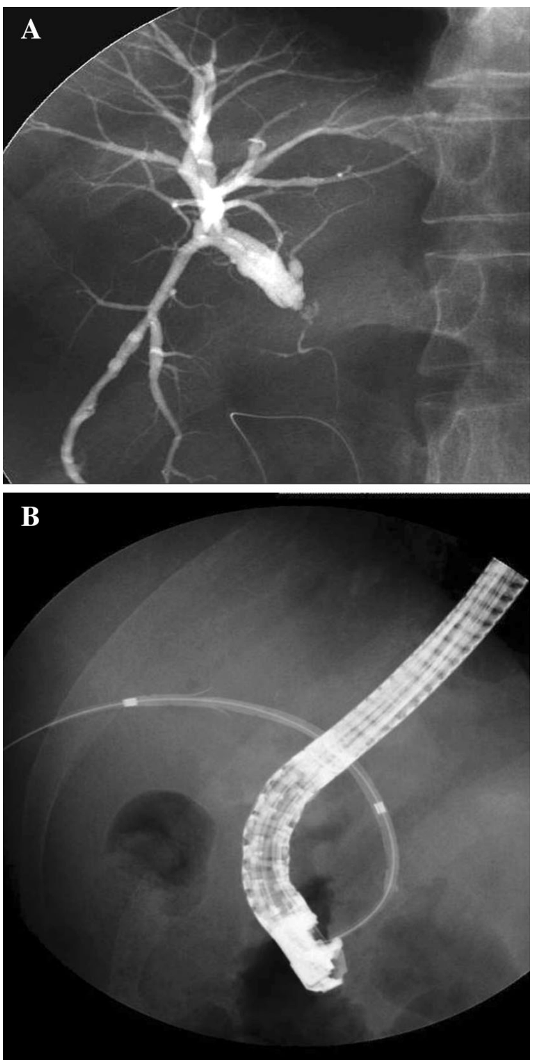


Fig. 3 **a** Percutaneous transhepatic cholangiography showing a severe anastomotic stricture at the right anterior branch. **b** Rendezvous technique (combined percutaneous-endoscopic technique). A 10 Fr plastic stent was inserted endoscopically over the guide wire, which had been passed via the percutaneous tract

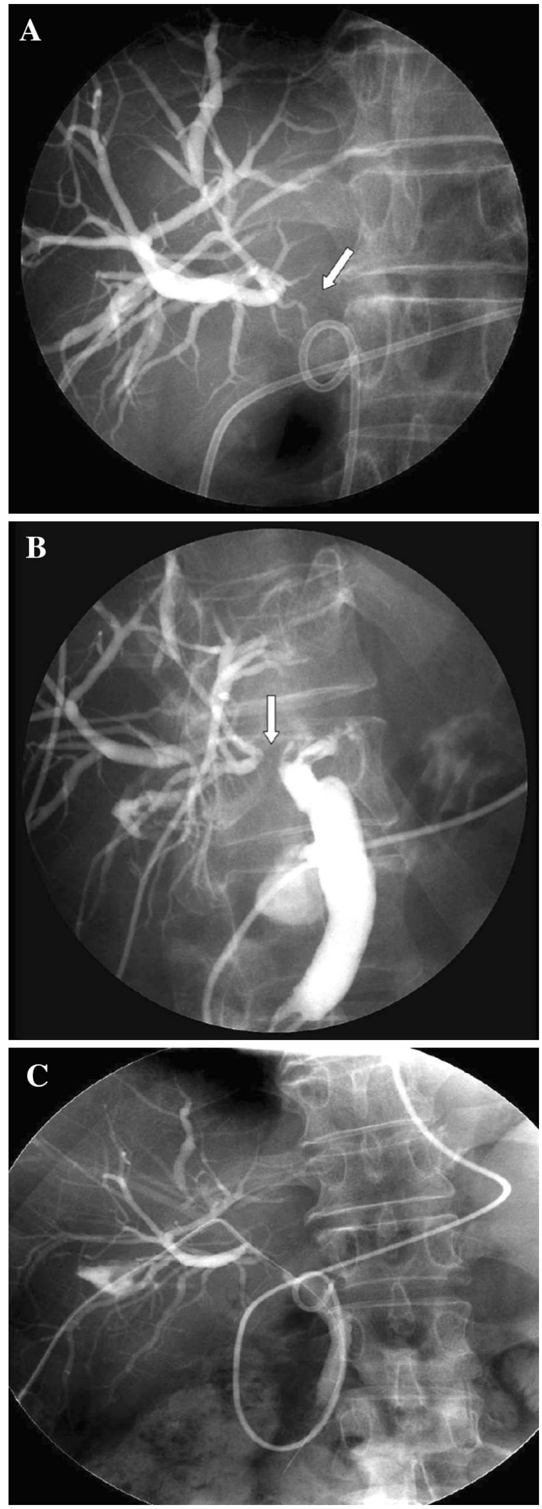


Fig. 4 **a** Percutaneous transhepatic cholangiography showing complete obstruction of the anastomosis (*arrow*). **b** Cholangiography via a percutaneous and endoscopic nasobiliary drainage tube. Location of the stricture is evident (*arrow*). **c** A guide wire could be passed through the stricture percutaneously

can be challenging and time-consuming in sharply angulated/twisted biliary strictures. Chang et al. reported that the Kumpe (KMP) catheter might be more effective than a guide wire in terms of facilitating stent placement [80].

Self-expandable metallic sent placement

Self-expandable metallic stents (SEMS) were initially developed to overcome the disadvantage of PSs (short stent patency due to small caliber). SEMS with a larger diameter (30 Fr or 10 mm), equivalent to three 10 Fr PSs, have significantly longer patency than PSs for palliation of malignant biliary obstruction. The small pre-deployment diameter of the delivery system facilitates insertion of SEMS. These advantages of SEMS over PSs have resulted in their use for benign biliary strictures. Initial experience of uncovered SEMS for this indication, however, yielded disappointing results because of stent-induced complications such as hyperplastic tissue ingrowth and overgrowth resulting in stent occlusion [81–83]. Once uncovered SEMS become embedded into the tissue, their endoscopic removal is technically very difficult or impossible [84]. Occluded SEMS further result in biliary stone/sludge formation and recurrent cholangitis [85]. In addition, SEMS present for years in the biliary system might cause serious vascular complications in liver transplant patients [86]. Consequently, uncovered SEMS placement is contraindicated for benign biliary strictures [87].

Fully covered SEMS are designed to prevent tissue ingrowth through the mesh and have shown efficacy for malignant distal biliary obstruction [88, 89]. Because they are readily removed from the bile duct during ERCP [90], covered SEMS are more appropriate for benign biliary strictures. In two recent RCTs of covered SESM versus multiple PSs for biliary strictures after DDLT, stricture resolution rates were similar, but covered SEMS required significantly fewer ERCPs to resolve the strictures [91, 92].

A disadvantage of covered SEMS is stent migration [93]. A German RCT demonstrated a 33% incidence of covered SEMS migration in post-DDLT strictures [91]. According to a recent systematic review by Kao et al., the overall SEMS migration rate was 16% [94]. Interestingly, liver transplant patients are more likely to have stent migration than biliary strictures due to other benign causes [95]. Other factors likely to be associated with stent migration include a stricture close to the hilum, a large bile duct below the stricture, and a short stricture [95]. While stent migration occurred spontaneously without the need for further interventions in some cases [91], it could result in severe consequences [95]. Stent migration might have a negative impact on stricture resolution [96]. Another problem is duodenobiliary reflux when placing a large-diameter covered SEMS across the papilla, which disturbs the physiological status of the biliary system. In addition, EST is required to prevent post-ERCP pancreatitis prior to covered SEMS placement [92], resulting in loss of sphincter of Oddi function [70, 71].

Few reports have focused on the clinical use of covered SEMS for post-LDLT biliary strictures [97–99]. Jang et al. retrospectively evaluated the efficacy and safety of covered SEMS in 35 LDLT patients with refractory biliary strictures [99]. The authors placed a short, fully covered SEMS with a central waist as an anti-migration system (Kaffes®; Taewoong Medical, Seoul, Korea [100]) (Fig. 5). The stent had a long, radiopaque-marked string, which enables removal of the stent by pulling the string, even when placed above the papilla. Their results were impressive, i.e., after 3-month placement of a covered SEMS, complete resolution of the stricture was achieved in 83% of this challenging group of LDLT patients [99]. Stent migration was observed in 2 (6%) of 35 patients. When a covered SEMS is used for post-LDLT biliary strictures, which are usually located near the hilum, the risk of blockage of bile duct branches by its cover is a reasonable concern. We place inside stents together with a covered SEMS to maintain the patency of side branches (Fig. 6).

Endoscopic management of biliary strictures after RYHJ

Traditionally, PTBD or surgery is indicated in biliary complications after LDLT with RYHJ because gaining access to the bilioenteric anastomosis with a conventional duodenoscope is generally impossible. Deep enteroscopy techniques (double-balloon enteroscopy, single-balloon enteroscopy, and spiral overtube-assisted enteroscopy), however, enable access to the anastomosis and subsequent endoscopic management of biliary strictures in LDLT patients with RYHJ, thus obviating the need for more invasive interventions [78, 101–104]. Sanada et al. evaluated the efficacy of double-balloon enteroscopy in 25 pediatric LDLT patients with bilioenteric anastomotic stricture [102]. The overall success rate in terms of reaching the anastomosis was 68% (16/25) before 2008, but dramatically improved after 2009 (93% [27/29]), suggesting that there is a learning curve for this innovative technology. They successfully treated bilioenteric anastomotic strictures with double-balloon enteroscopy in 84% (36/43) of patients. In a study by Tomoda et al., short-type double-balloon enteroscopy reached the anastomosis in 17 (85%) of 20 LDLT patients with RYHJ, and 14 of the 17 patients achieved successful endoscopic management of their biliary stricture [104]. The disadvantages of conventional enteroscopies include the lack of an elevator and a small working channel (2.8 mm), which limits the use of

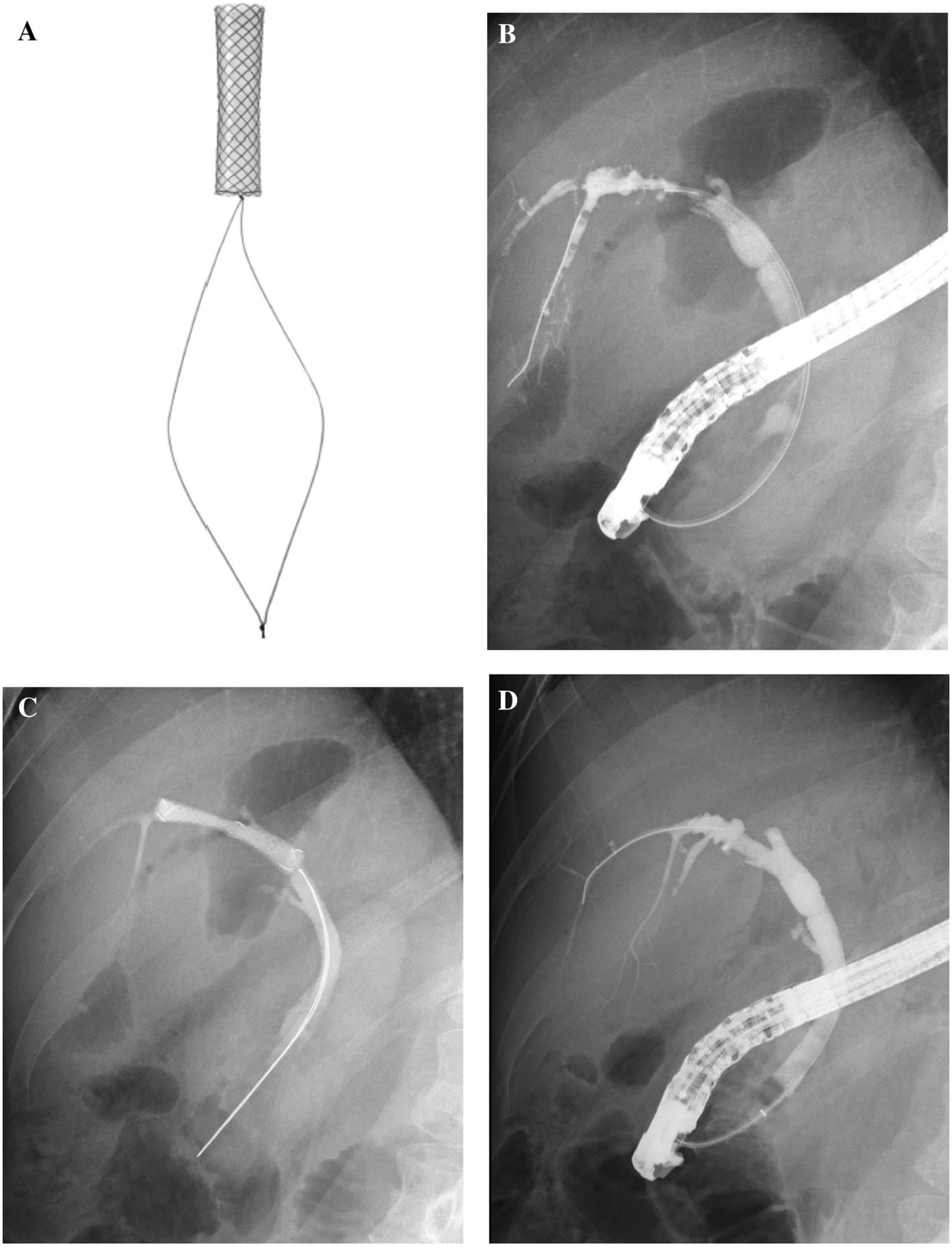
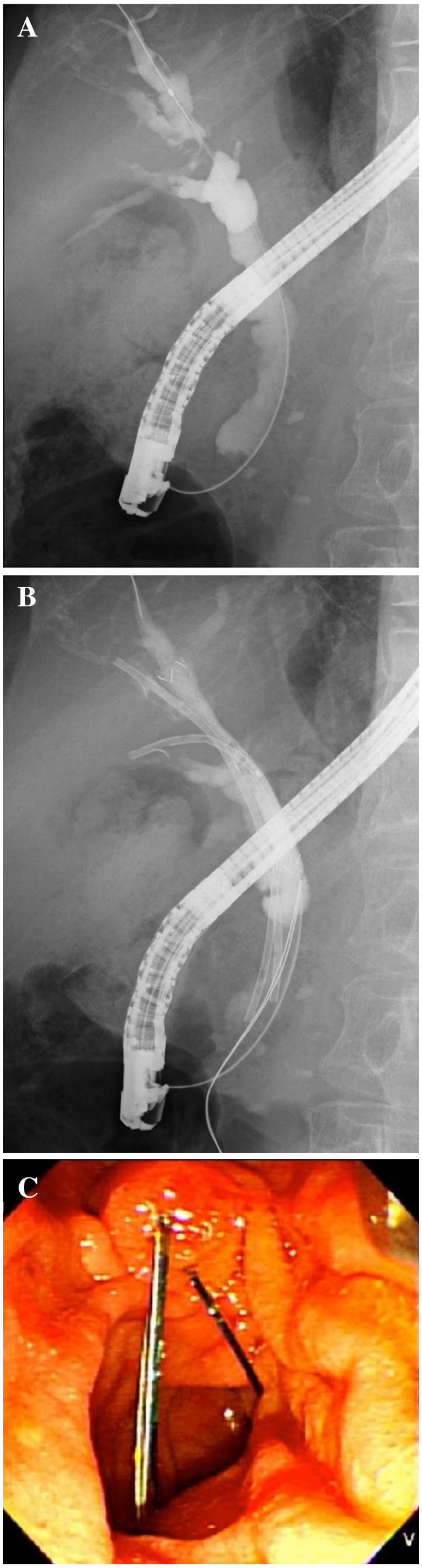


Fig. 5 **a** Fully covered self-expandable metallic stent (Kaffes®; Taewoong Medical, Seoul, Korea). The stent has a waist at the middle portion as an anti-migration system and a long, platinum, radiopaque-marked retrieval string. **b** Cholangiogram showing a biliary anastomotic stricture after right-liver LDLT. **c** Cholangiogram showing a covered self-expandable metallic stent. Note the radiopaque-marked retrieval string. **d** Cholangiogram 90 days after stent placement demonstrating resolution of the anastomotic stricture

therapeutic accessories [17]. Recently, a prototype short-type double-balloon enteroscopy with advanced force transmission and adaptive bending was developed for ERCP (EI-580BT; Fujifilm Medical, Tokyo, Japan). This innovative enteroscopy has a 3.2 mm working channel, which allows use of most ERCP devices including SEMS and facilitates insertion and exchange in ERCP devices



◀**Fig. 6** **a** Cholangiogram demonstrating complex biliary anastomotic strictures in right-liver LDLT. **b** Cholangiogram showing a fully covered self-expandable metallic stent and two inside stents placed across the strictures. **c** Endoscopic view of the papilla; the platinum, radiopaque-marked retrieval string and the nylon threads are visible

[105]. We have successfully treated three LDLT patients with RYHJ using this enteroscope (Fig. 7) [106].

Risk factors or failed endoscopic management of post-LDLT biliary strictures

Identification of risk factors for failure of endoscopic management is not only helpful for patient risk stratification but also enables use of other treatment modalities (i.e., PTBD or surgery) after unsuccessful management via ERCP. There is general agreement that non-BASs are intractable to endoscopic management [10, 18]. Endoscopic therapy may be more likely to fail in LDLT patients with a history of hepatic artery stenosis [10] and surgery for bleeding during the first month after liver transplantation [107], which are potentially related to ischemia, leading to non-BAS formation.

Morphological changes in the biliary tree as well as stricture are strongly associated with the outcome of endoscopic intervention [28, 67, 108, 109]. The Kyoto group found that the crane-neck deformity, sharp angulation of the anastomotic bile duct caused by a severely bent common bile duct, resulted in a poor outcome [108]. In a study by Chok et al., stricture morphology was identified as a significant risk factor for failed endoscopic management of post-LDLT BAS in a multivariate analyses; pouched (round tip) BAS had a significantly lower success rate than other types of BAS (i.e., intermediately pouched and triangular types) [109]. Gomez et al. found that none of the LDLT patients with pouched-type BAS ($n = 2$) or the crane-neck deformity ($n = 3$) achieved endoscopic stricture resolution [28]. In addition, Lee et al. [67] and Kim et al. [76] showed that LDLT patients with a pouched stricture were at higher risk of endoscopic management failure. It is worth noting that Chok et al. reported a significant association between bile leakage and pouched BAS [109]. Kato et al. identified bile leakage as a risk factor for endoscopic stent deployment failure [54]. Although bile duct kinking rarely occurs in adult LDLT patients with DD biliary anastomosis, it might require surgical intervention (e.g., conversion to RYHJ) [110].

The timing of endoscopic management, the interval between LDLT and ERCP or between stricture and ERCP, also predicts endoscopic outcome [64, 67]. A delay in the onset or diagnosis of stricture after LDLT might cause a

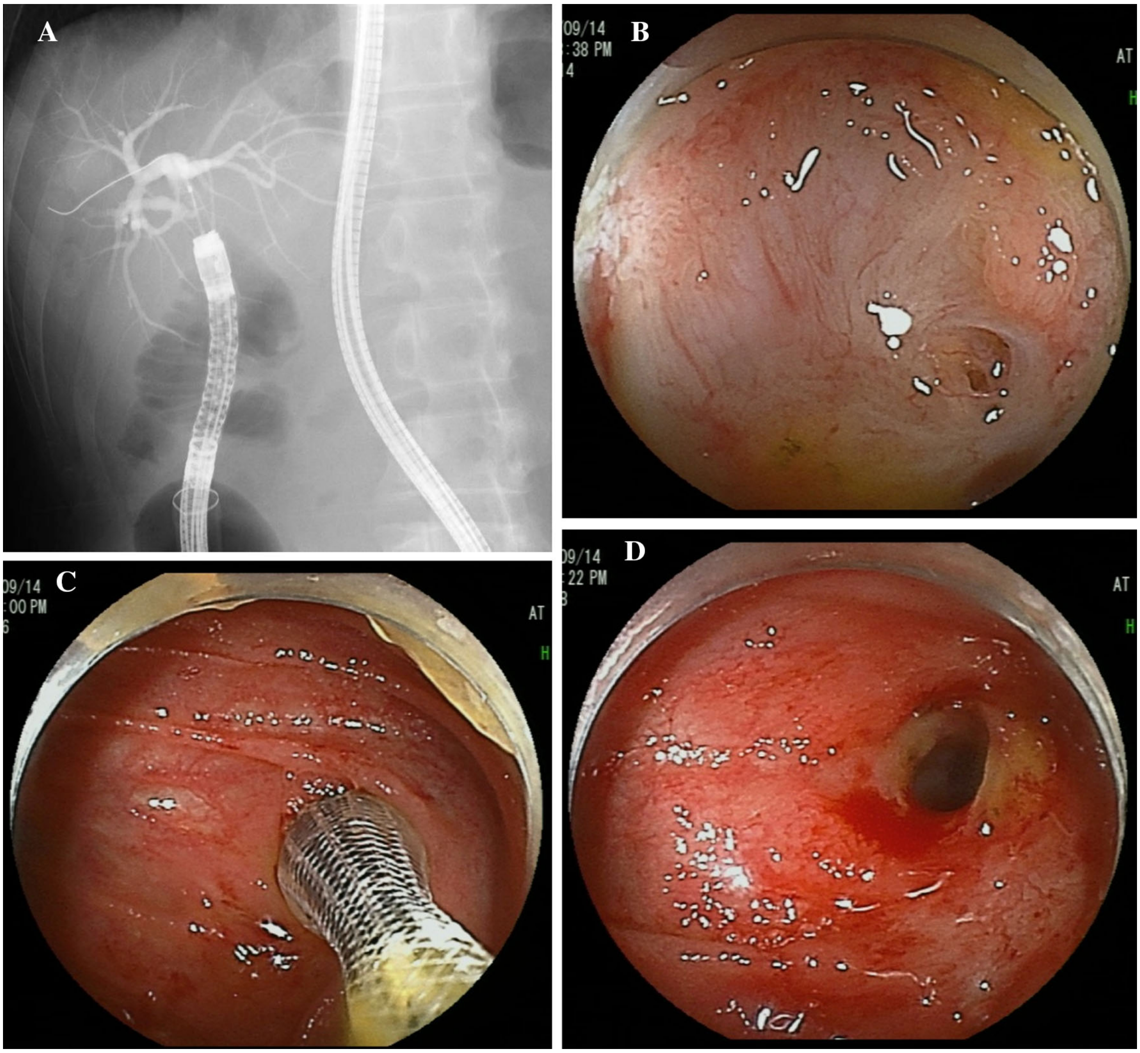


Fig. 7 **a** Cholangiogram using a double-balloon enteroscopy showing the biliary anastomotic stricture in LDLT with Roux-en-Y reconstruction. **b** Endoscopic view of the bilioenteric stricture. **c** Endoscopic view of balloon dilation of the bilioenteric stricture. **d** Endoscopic view of the bilioenteric stricture after balloon dilation

tight stricture, rendering endoscopic management difficult. In addition, experience in endoscopic management in LDLT patients has an impact on stricture resolution by ERCP [11, 33, 64].

Long-term outcomes of endoscopic management of post-LDLT biliary strictures

Because endoscopic management of post-LDLT biliary stricture is a relatively new topic, its long-term outcomes are not fully understood. Among LDLT patients undergoing balloon dilation and/or conventional PS placement, the rate of stricture recurrence has been reported to be 12–30% during a median follow-up period of 9.5–70 months [26, 31, 54, 63, 64]. The majority of recurrent strictures developed within the first year after stent removal. While most recurrent strictures were successfully retreated via ERCP, a small number of patients required PTBD or surgical revision. Hsieh et al., who adopted maximal PS therapy, reported that 79% of patients had no evidence of stricture recurrence during an average follow-up period of 70 months after initial management [26]. In their study, recurrent stricture was observed in eight patients (21%), all of whom were successfully re-treated with the same endoscopic strategy. According to Seo et al., the duration of stent placement was significantly shorter in the recurrence than in the non-recurrence group (11.8 vs 29.0 weeks, $p = 0.004$) [31].

The Kyoto group evaluated the long-term outcome of inside stent placement. In their study, once stricture resolution was achieved with inside stents, 90% (73/81) of patients were free of recurrence during a median follow-up of 53.0 months [74]. Strictures recurred in eight patients (10%). Management of recurrent stricture included repeat inside stent ($n = 5$), endoscopic balloon dilation ($n = 1$), PTBD ($n = 1$), and retransplantation ($n = 1$). At the University of Tokyo, we observed recurrent stricture in 1 (4%) of 25 patients with stricture resolution with inside stents over a median period after stent removal of 52 months [unpublished data].

If strictures are treated adequately, the development of BAS does not affect overall survival after LDLT [9, 24, 31, 33]. Chok et al. reported that there were no significant differences in 1-, 3-, and 5-year graft survival rates between patients with and without BAS [24]. The University of Tokyo also showed that the 3- and 5-year overall survival rates in LDLT patients with biliary complications were not significantly different from those without biliary complications [9].

Conclusions

Biliary complications remain the Achilles' heel of LDLT. Despite recent refinements in surgical techniques, immunosuppressive management, and post-LDLT care, biliary strictures still develop in a substantial number of LDLT patients. ERCP is the first-line modality for the management of biliary strictures in LDLT patients with DD biliary reconstruction. Multiple PS placement after balloon dilation is the procedure of choice for post-LDLT biliary strictures, and placement of inside stents is an alternative with longer stent patency. Covered SEMS may be useful particularly in LDLT patients with refractory biliary strictures. Unfortunately, the majority of the reported series in this topic is retrospective and includes small number of LDLT patients with strictures. In addition, there is considerable heterogeneity among centers regarding patient characteristics, biliary reconstruction methods, and endoscopic strategies, making it difficult to give standardized recommendations. RCTs are needed to determine the optimum endoscopic strategy for this challenging group of patients.

Compliance with ethical standards

Conflict of interest Drs. Tsujino, Isayama, Kogure, Sato, Nakai, and Koike declare that they have no conflict of interest.

Human rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from all patients for being included in the study.

References

1. Trotter JF, Wachs M, Everson GT, Kam I. Adult-to-adult transplantation of the right hepatic lobe from a living donor. N Engl J Med. 2002;346:1074–82.
2. Sugawara Y, Makuuchi M. Advances in adult living donor liver transplantation: a review based on reports from the 10th anniversary of the adult-to-adult living donor liver transplantation meeting in Tokyo. Liver Transpl. 2004;10:715–20.
3. Chan SC, Cheung TT, Chan AC, et al. New insights after the first 1000 liver transplantations at The University of Hong Kong. Asian J Surg. 2016;39:202–10.
4. Chok KS, Lo CM. Biliary complications in right lobe living donor liver transplantation. Hepatol Int. 2016;10:553–8.
5. Gondolesi GE, Varotti G, Florman SS, et al. Biliary complications in 96 consecutive right lobe living donor transplant recipients. Transplantation. 2004;77:1842–8.
6. Hwang S, Lee SG, Sung KB, et al. Long-term incidence, risk factors, and management of biliary complications after adult living donor liver transplantation. Liver Transpl. 2006;12:831–8.
7. Morioka D, Egawa H, Kasahara M, et al. Outcomes of adult-to-adult living donor liver transplantation: a single institution's experience with 335 consecutive cases. Ann Surg. 2007;245:315–25.
8. Shah SA, Grant DR, McGilvray ID, et al. Biliary strictures in 130 consecutive right lobe living donor liver transplant recipients: results of a Western center. Am J Transplant. 2007;7:161–7.
9. Kyoden Y, Tamura S, Sugawara Y, et al. Incidence and management of biliary complications after adult-to-adult living donor liver transplantation. Clin Transplant. 2010;24:535–42.
10. Chang JH, Lee IS, Choi JY, et al. Biliary stricture after adult right-lobe living-donor liver transplantation with duct-to-duct anastomosis: long-term outcome and its related factors after endoscopic treatment. Gut Liver. 2010;4:226–33.
11. Zimmerman MA, Baker T, Goodrich NP, et al. Development, management, and resolution of biliary complications after living and deceased donor liver transplantation: a report from the adult-to-adult living donor liver transplantation cohort study consortium. Liver Transpl. 2013;19:259–67.
12. Akamatsu N, Sugawara Y, Hashimoto D. Biliary reconstruction, its complications and management of biliary complications after adult liver transplantation: a systematic review of the incidence, risk factors and outcome. Transpl Int. 2011;24:379–92.
13. Sharma S, Gurakar A, Jabbour N. Biliary strictures following liver transplantation: past, present and preventive strategies. Liver Transpl. 2008;14:759–69.
14. Ishiko T, Egawa H, Kasahara M, et al. Duct-to-duct biliary reconstruction in living donor liver transplantation utilizing right lobe graft. Ann Surg. 2002;236:235–40.
15. Sugawara Y, Sano K, Kaneko J, et al. Duct-to-duct biliary reconstruction for living donor liver transplantation: experience of 92 cases. Transplant Proc. 2003;35:2981–2.
16. Dulundu E, Sugawara Y, Sano K, et al. Duct-to-duct biliary reconstruction in adult living-donor liver transplantation. Transplantation. 2004;78:574–9.
17. Arain MA, Attam R, Freeman ML. Advances in endoscopic management of biliary tract complications after liver transplantation. Liver Transpl. 2013;19:482–98.
18. Yazumi S, Yoshimoto T, Hisatsune H, et al. Endoscopic treatment of biliary complications after right-lobe living-donor liver transplantation with duct-to-duct biliary anastomosis. J Hepatobiliary Pancreat Surg. 2006;13:502–10.

19. Tsujino T, Isayama H, Sugawara Y, et al. Endoscopic management of biliary complications after adult living donor liver transplantation. Am J Gastroenterol. 2006;101:2230–6.
20. Fan ST, Lo CM, Liu CL, et al. Biliary reconstruction and complications of right lobe live donor liver transplantation. Ann Surg. 2002;236:676–83.
21. Soejima Y, Taketomi A, Yoshizumi T, et al. Biliary strictures in living donor liver transplantation: incidence, management, and technical evolution. Liver Transpl. 2006;12:979–86.
22. Vij V, Makki K, Chorasiya VK, et al. Targeting the Achilles' heel of adult living donor liver transplant: corner-sparing sutures with mucosal eversion technique of biliary anastomosis. Liver Transpl. 2016;22:14–23.
23. Chan SC, Fan ST. Biliary complications in liver transplantation. Hepatol Int. 2008;2:399–404.
24. Chok KS, Chan SC, Cheung TT, et al. Bile duct anastomotic stricture after adult-to-adult right lobe living donor liver transplantation. Liver Transpl. 2011;17:47–52.
25. Seehofer D, Eurich D, Veltzke-Schlieker W, Neuhaus P. Biliary complications after liver transplantation: old problems and new challenges. Am J Transplant. 2013;13:253–65.
26. Hsieh TH, Mekeel KL, Crowell MD, et al. Endoscopic treatment of anastomotic biliary strictures after living donor liver transplantation: outcomes after maximal stent therapy. Gastrointest Endosc. 2013;77:47–54.
27. Liu CL, Fan ST, Lo CM, et al. Operative outcomes of adult-to-adult right lobe live donor liver transplantation: a comparative study with cadaveric whole-graft liver transplantation in a single center. Ann Surg. 2006;243:404–10.
28. Gómez CM, Dumonceau JM, Marcolongo M, et al. Endoscopic management of biliary complications after adult living-donor versus deceased-donor liver transplantation. Transplantation. 2009;88:1280–5.
29. Samstein B, Smith AR, Freise CE, et al. Complications and their resolution in recipients of deceased and living donor liver transplants: findings from the A2ALL cohort study. Am J Transplant. 2016;16:594–602.
30. Noack K, Bronk SF, Kato A, Gores GJ. The greater vulnerability of bile duct cells to reoxygenation injury than to anoxia. Implications for the pathogenesis of biliary strictures after liver transplantation. Transplantation. 1993;56:495–500.
31. Seo JK, Ryu JK, Lee SH, et al. Endoscopic treatment for biliary stricture after adult living donor liver transplantation. Liver Transpl. 2009;15:369–80.
32. Melcher ML, Pomposelli JJ, Verbesey JE, et al. Comparison of biliary complications in adult living-donor liver transplants performed at two busy transplant centers. Clin Transplant. 2010;24:E137–44.
33. Na GH, Kim DG, Choi HJ, et al. Interventional treatment of a biliary stricture after adult right-lobe living-donor liver transplantation with duct-to-duct anastomosis. HPB (Oxford). 2014;16:312–9.
34. Park JB, Kwon CH, Choi GS, et al. Prolonged cold ischemic time is a risk factor for biliary strictures in duct-to-duct biliary reconstruction in living donor liver transplantation. Transplantation. 2008;86:1536–42.
35. Kasahara M, Egawa H, Takada Y, et al. Biliary reconstruction in right lobe living-donor liver transplantation: comparison of different techniques in 321 recipients. Ann Surg. 2006;243:559–66.
36. Dacha S, Barad A, Martin J, Levitsky J. Association of hepatic artery stenosis and biliary strictures in liver transplant recipients. Liver Transpl. 2011;17:849–54.
37. Song GW, Lee SG, Hwang S, et al. ABO-incompatible adult living donor liver transplantation under the desensitization protocol with rituximab. Am J Transplant. 2016;16:157–70.
38. Song GW, Lee SG, Hwang S, et al. Biliary stricture is the only concern in ABO-incompatible adult living donor liver transplantation in the rituximab era. J Hepatol. 2014;61:575–82.
39. Gotthardt DN, Senft J, Sauer P, et al. Occult cytomegalovirus cholangitis as a potential cause of cholestatic complications after orthotopic liver transplantation? A study of cytomegalovirus DNA in bile. Liver Transpl. 2013;19:1142–50.
40. Mocchegiani F, Vincenzi P, Lanari J, et al. Immunological risk factors in biliary strictures after liver transplantation. Ann Transpl. 2015;20:218–24.
41. Syal G, Fausther M, Dranoff JA. Advances in cholangiocyte immunobiology. Am J Physiol Gastrointest Liver Physiol. 2012;15:G1077–86.
42. Kim JM, Cho W, Kwon CH, et al. Bile duct reconstruction by a young surgeon in living donor liver transplantation using right liver graft. Medicine (Baltimore). 2014;93:e84.
43. Kok T, Van der Sluis A, Klein JP, et al. Ultrasound and cholangiography for the diagnosis of biliary complications after orthotopic liver transplantation: a comparative study. J Clin Ultrasound. 1996;24:103–15.
44. Zoepf T, Maldonado-Lopez EJ, Hilgard P, et al. Diagnosis of biliary strictures after liver transplantation: which is the best tool? World J Gastroenterol. 2005;11:2945–8.
45. Katz LH, Benjaminov O, Belinki A, et al. Magnetic resonance cholangiopancreatography for the accurate diagnosis of biliary complications after liver transplantation: comparison with endoscopic retrograde cholangiography and percutaneous transhepatic cholangiography – long-term follow-up. Clin Transplant. 2010;24:E163–9.
46. Garg B, Rastogi R, Gupta S, et al. Evaluation of biliary complications on magnetic resonance cholangiopancreatography and comparison with direct cholangiography after living-donor liver transplantation. Clin Radiol. 2017;72:518.e9–15.
47. Tsujino T, Sugawara Y, Omata M. Management of biliary strictures after living donor liver transplantation. Gastrointest Endosc. 2009;70:599–600.
48. Hyodo T, Kumano S, Kushihata F, et al. CT and MR cholangiography: advantages and pitfalls in perioperative evaluation of biliary tree. Br J Radiol. 2012;85:887–96.
49. McSweeney SE, Kim TK, Jang HJ, Khalili K. Biliary anatomy in potential right hepatic lobe living donor liver transplantation (LDLT): the utility of CT cholangiography in the setting of inconclusive MRCP. Eur J Radiol. 2012;81:6–12.
50. Kondo S, Isayama H, Akahane M, et al. Detection of common bile duct stones: comparison between endoscopic ultrasonography, magnetic resonance cholangiography, and helical-computed-tomographic cholangiography. Eur J Radiol. 2005;54:271–5.
51. Tsujino T, Sugawara Y, Kawabe T, et al. Foreign body (suture thread) in the bile duct after living donor liver transplantation. Liver Transpl. 2007;13:1065–6.
52. Tsujino T, Isayama H, Tada M, et al. Intraductal US in biliary cast after living donor liver transplantation (with video). Gastrointest Endosc. 2008;67:540–1.
53. Yazumi S, Chiba T. Biliary complications after a right-lobe living donor liver transplantation. J Gastroenterol. 2005;40:861–5.
54. Kato H, Kawamoto H, Tsutsumi K, et al. Long-term outcomes of endoscopic management for biliary strictures after living donor liver transplantation with duct-to-duct reconstruction. Transpl Int. 2009;22:914–21.
55. Parsi MA, Guardino J, Vargo JJ. Peroral cholangioscopy-guided stricture therapy in living donor liver transplantation. Liver Transpl. 2009;15:263–5.

56. Woo YS, Lee JK, Noh DH, et al. SpyGlass cholangioscopy-assisted guidewire placement for post-LDLT biliary strictures: a case series. Surg Endosc. 2016;30:3897–903.
57. Balderramo D, Sendino O, Miquel R, et al. Prospective evaluation of single-operator peroral cholangioscopy in liver transplant recipients requiring an evaluation of the biliary tract. Liver Transpl. 2013;19:199–206.
58. Mohamed E, Kröner PT, Kumar U, Mönkemüller K. Use of a Soehendra stent retriever in dilation of an anastomotic biliary stricture in a post-liver transplant patient. Endoscopy. 2016;48(Suppl 1):E35–6.
59. Schwartz DA, Petersen BT, Poterucha JJ, Gostout CJ. Endoscopic therapy of anastomotic bile duct strictures occurring after liver transplantation. Gastrointest Endosc. 2000;51:169–74.
60. Zoepf T, Maldonado-Lopez EJ, Hilgard P, et al. Balloon dilatation vs. balloon dilatation plus bile duct endoprostheses for treatment of anastomotic biliary strictures after liver transplantation. Liver Transpl. 2006;12:88–94.
61. Graziadei IW, Schwaighofer H, Koch R, et al. Long-term outcome of endoscopic treatment of biliary strictures after liver transplantation. Liver Transpl. 2006;12:718–25.
62. Shah JN, Ahmad NA, Shetty K, et al. Endoscopic management of biliary complications after adult living donor liver transplantation. Am J Gastroenterol. 2004;99:1291–5.
63. Zoepf T, Maldonado-Lopez EJ, Hilgard P, et al. Endoscopic therapy of posttransplant biliary stenoses after right-sided adult living donor liver transplantation. Clin Gastroenterol Hepatol. 2005;3:1144–9.
64. Kim TH, Lee SK, Han JH, et al. The role of endoscopic retrograde cholangiography for biliary stricture after adult living donor liver transplantation: technical aspect and outcome. Scand J Gastroenterol. 2011;46:188–96.
65. Kawamoto H, Tsutsumi K, Fujii M, et al. Endoscopic 3-branched partial stent-in-stent deployment of metallic stents in high-grade malignant hilar biliary stricture (with videos). Gastrointest Endosc. 2007;66:1030–7.
66. Kawamoto H, Tsutsumi K, Harada R, et al. Endoscopic deployment of multiple JOSTENT SelfX is effective and safe in treatment of malignant hilar biliary strictures. Clin Gastroenterol Hepatol. 2008;6:401–8.
67. Lee YY, Gwak GY, Lee KH, et al. Predictors of the feasibility of primary endoscopic management of biliary strictures after adult living donor liver transplantation. Liver Transpl. 2011;17:1467–73.
68. van Berkel AM, van Marle J, Groen AK, Bruno MJ. Mechanisms of biliary stent clogging: confocal laser scanning and scanning electron microscopy. Endoscopy. 2005;37:729–34.
69. Weickert U, Venzke T, König J, et al. Why do bilioduodenal plastic stents become occluded? A clinical and pathological investigation on 100 consecutive patients. Endoscopy. 2001;33:786–90.
70. Yasuda I, Tomita E, Enya M, et al. Can endoscopic papillary balloon dilation really preserve sphincter of Oddi function? Gut. 2001;49:686–91.
71. Isayama H, Komatsu Y, Inoue Y, et al. Preserved function of the Oddi sphincter after endoscopic papillary balloon dilation. Hepatogastroenterology. 2003;50:1787–91.
72. Bergman JJ, van Berkel AM, Groen AK, et al. Biliary manometry, bacterial characteristics, bile composition, and histologic changes fifteen to seventeen years after endoscopic sphincterotomy. Gastrointest Endosc. 1997;45:400–5.
73. Hisatsune H, Yazumi S, Egawa H, et al. Endoscopic management of biliary strictures after duct-to-duct biliary reconstruction in right-lobe living-donor liver transplantation. Transplantation. 2003;76:810–5.
74. Kurita A, Kodama Y, Minami R, et al. Endoscopic stent placement above the intact sphincter of Oddi for biliary strictures after living donor liver transplantation. J Gastroenterol. 2013;48:1097–104.
75. Kobayashi N, Kubota K, Shimamura T, et al. Complications of the treatment of endoscopic biliary strictures developing after liver transplantation. J Hepatobiliary Pancreat Sci. 2011;18:202–10.
76. Kim ES, Lee BJ, Won JY, et al. Percutaneous transhepatic biliary drainage may serve as a successful rescue procedure in failed cases of endoscopic therapy for a post-living donor liver transplantation biliary stricture. Gastrointest Endosc. 2009;69:38–46.
77. Dowsett JF, Vaira D, Hatfield AR, et al. Endoscopic biliary therapy using the combined percutaneous and endoscopic technique. Gastroenterology. 1989;96:1180–6.
78. 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;14:385–7.
79. Chang JH, Lee IS, Chun HJ, Choi JY, et al. Usefulness of the rendezvous technique for biliary stricture after adult right-lobe living-donor liver transplantation with duct-to-duct anastomosis. Gut Liver. 2010;4:68–75.
80. Chang JH, Lee IS, Chun HJ, et al. Comparative study of rendezvous techniques in post-liver transplant biliary stricture. World J Gastroenterol. 2012;18:5957–64.
81. Diamond NG, Lee SP, Niblett RL, et al. Metallic stents for the treatment of intrahepatic biliary strictures after liver transplantation. J Vasc Interv Radiol. 1995;6:755–61.
82. Culp WC, McCowan TC, Lieberman RP, et al. Biliary strictures in liver transplant recipients: treatment with metal stents. Radiology. 1996;199:339–46.
83. Dumonceau JM, Devière J, Delhaye M, et al. Plastic and metal stents for postoperative benign bile duct strictures: the best and the worst. Gastrointest Endosc. 1998;47:8–17.
84. Kahaleh M, Tokar J, Le T, Yeaton P. Removal of self-expandable metallic Wallstents. Gastrointest Endosc. 2004;60:640–4.
85. Togawa O, Kawabe T, Isayama H, et al. Management of occluded uncovered metallic stents in patients with malignant distal biliary obstructions using covered metallic stents. J Clin Gastroenterol. 2008;42:546–9.
86. Harada N, Shirabe K, Soejima Y, et al. Intrahepatic artery pseudoaneurysm associated with a metallic biliary stent after living donor liver transplantation: report of a case. Surg Today. 2013;43:678–81.
87. Siriwardana HP, Siriwardena AK. Systematic appraisal of the role of metallic endobiliary stents in the treatment of benign bile duct stricture. Ann Surg. 2005;242:10–9.
88. Isayama H, Komatsu Y, Tsujino T, et al. A prospective randomised study of "covered" versus "uncovered" diamond stents for the management of distal malignant biliary obstruction. Gut. 2004;53:729–34.
89. Isayama H, Yasuda I, Ryozawa S, et al. Results of a Japanese multicenter, randomized trial of endoscopic stenting for non-resectable pancreatic head cancer (JM-test): covered Wallstent versus DoubleLayer stent. Dig Endosc. 2011;23:310–5.
90. Togawa O, Isayama H, Tsujino T, et al. Management of dysfunctional covered self-expandable metallic stents in patients with malignant distal biliary obstruction. J Gastroenterol. 2013;48:1300–7.
91. Tal AO, Finkelmeier F, Filmann N, et al. Multiple plastic stents versus covered metal stent for treatment of anastomotic biliary strictures after liver transplantation: a prospective, randomized,

multicenter trial. Gastrointest Endosc. 2017. doi:10.1016/j.gie.2017.03.009..
92. Martins FP, De Paulo GA, Contini MLC, Ferrari AP. Metal versus plastic stents for anastomotic biliary strictures after liver transplantation: a randomized controlled trial. Gastrointest Endosc. 2017. doi:10.1016/j.gie.2017.04.013.
93. Isayama H, Nakai Y, Kogure H, et al. Biliary self-expandable metallic stent for unresectable malignant distal biliary obstruction: which is better: covered or uncovered? Dig Endosc. 2013;25(Suppl 2):71–4.
94. Kao D, Zepeda-Gomez S, Tandon P, Bain VG. Managing the post-liver transplantation anastomotic biliary stricture: multiple plastic versus metal stents: a systematic review. Gastrointest Endosc. 2013;77:679–91.
95. Coté GA, Slivka A, Tarnasky P, et al. Effect of covered metallic stents compared with plastic stents on benign biliary stricture resolution: a randomized clinical trial. JAMA. 2016;315:1250–7.
96. Park JS, Lee SS, Song TJ, et al. Long-term outcomes of covered self-expandable metal stents for treating benign biliary strictures. Endoscopy. 2016;48:440–7.
97. Curcio G, Traina M, Miraglia R, et al. Treatment of a refractory biliary stricture after living donor liver transplantation, with a short fully covered metal stent with a long string. Endoscopy. 2012;44(Suppl 2):E74–5.
98. Moon JH, Choi HJ, Koo HC, et al. Feasibility of placing a modified fully covered self-expandable metal stent above the papilla to minimize stent-induced bile duct injury in patients with refractory benign biliary strictures (with videos). Gastrointest Endosc. 2012;75:1080–5.
99. Jang SI, Sung SY, Park H, et al. Salvage therapy using self-expandable metal stents for recalcitrant anastomotic strictures after living-donor liver transplantation. Ther Adv Gastroenterol. 2017;10:297–309.
100. Kaffes A, Griffin S, Vaughan R, et al. A randomized trial of a fully covered self-expandable metallic stent versus plastic stents in anastomotic biliary strictures after liver transplantation. Ther Adv Gastroenterol. 2014;7:64–71.
101. Haruta H, Yamamoto H, Mizuta K, et al. A case of successful enteroscopic balloon dilation for late anastomotic stricture of choledochojejunostomy after living donor liver transplantation. Liver Transpl. 2005;11:1608–10.
102. Sanada Y, Mizuta K, Yano T, et al. Double-balloon enteroscopy for bilioenteric anastomotic stricture after pediatric living donor liver transplantation. Transpl Int. 2011;24:85–90.
103. Kamei H, Imai H, Onishi Y, et al. Considerable risk of restenosis after endoscopic treatment for hepaticojejunostomy stricture after living-donor liver transplantation. Transpl Proc. 2015;47:2493–8.
104. Tomoda T, Tsutsumi K, Kato H, et al. Outcomes of management for biliary stricture after living donor liver transplantation with hepaticojejunostomy using short-type double-balloon enteroscopy. Surg Endosc. 2016;30:5338–44.
105. Tsutsumi K, Kato H, Okada H. Impact of a newly developed short double-balloon enteroscope on stent placement in patients with surgically altered anatomies. Gut Liver. 2017;11:306–11.
106. Kogure H, Yamada A, Isayama H, et al. Newly developed short double-balloon endoscope for pancreaticobiliary interventions in patients with surgically altered anatomy. Gastrointest Endosc. 2016;83:AB139.
107. Buxbaum JL, Biggins SW, Bagatelos KC, Ostroff JW. Predictors of endoscopic treatment outcomes in the management of biliary problems after liver transplantation at a high-volume academic center. Gastrointest Endosc. 2011;73:37–44.
108. Yoshimoto T, Yazumi S, Hisatsune H, et al. Crane-neck deformity after right lobe living donor liver transplantation. Gastrointest Endosc. 2006;64:271.
109. Chok KS, Chan SC, Cheung TT, et al. A retrospective study on risk factors associated with failed endoscopic treatment of biliary anastomotic stricture after right-lobe living donor liver transplantation with duct-to-duct anastomosis. Ann Surg. 2014;259:767–72.
110. Wan P, Xia Q, Zhang JJ, et al. Bile duct kinking after adult living donor liver transplantation: case reports and literature review. J Dig Dis. 2015;16:610–5.