Diagn Interv Radiol 2021; 27:546-552

INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Role of percutaneous radiological treatment in biliary complications associated with adult left lobe living donor liver transplantation: a single-center experience

Sinan Karatoprak
Ramazan Kutlu
Sezai Yılmaz

PURPOSE
Biliary complications develop at a higher rate in living donor liver transplantation (LDLT) compared with cadaveric liver transplantation. Almost all studies about biliary complications after LDLT were made with the right lobe. The aim of this study was to determine the frequency of biliary complications developing after adult left lobe LDLT and to evaluate the efficacy of the algorithm followed in diagnosis and treatment, particularly percutaneous radiological treatment.

METHODS
A total of 2185 LDLT operations performed in our center between May 2009 and December 2019 were retrospectively reviewed and patients receiving left lobe LDLT were analyzed regarding biliary complications and treatments. Biliary complications were treated via percutaneous drainage under ultrasound (US) guidance, endoscopic retrograde cholangiopancreatography (ERCP), and percutaneous transhepatic cholangiography (PTC)/ percutaneous transhepatic biliary drainage (PTBD). Patient demographics, ERCP procedures before percutaneous treatment, and percutaneous treatment indications were analyzed.

RESULTS
A total of 69 adult patients received left lobe LDLT. Biliary complications requiring endoscopic and/or percutaneous treatment developed in 28 patients (40%). Of these patients, 4 had bile leakage (14%), 20 had anastomosis stricture (72%), and 4 had both leakage and anastomosis stricture (14%). External drainage treatment under ultrasound guidance was sufficient for 2 of 4 patients with bile leakage, and these cases were accepted as minor bile leakage (7%). Overall, 26 patients underwent ERCP; of these, 8 were referred for PTC/PTBD because the guidewire and/or balloon-stent could not pass the anastomosis stricture (n=7) and common bile duct cannulation could not be obtained because of duodenal diverticulum (n=1). Diagnostic PTC was performed in 10 patients, 8 were referred after inadequate/failed ERCP procedure and two were referred directly without ERCP. Anastomosis stricture was found in 7 patients and anastomosis stricture and bile leakage in 3. In 7 patients determined to have stricture, balloon dilatation was applied and then biliary drainage was performed. In 3 patients who had leakage and anastomosis stricture, balloon dilatation was applied for stricture; after dilatation, an IEBD catheter was placed through the leakage region in 2 patients, while a covered metallic stent passing through the leakage region was placed in one patient.

CONCLUSION
Generally, ERCP is the first preferred method in biliary complications of LDLT; however, in cases where a response cannot be obtained by endoscopic treatment or require complex and/or aggressive treatment, percutaneous radiological treatment should be the treatment of choice before surgery in left lobe LDLT.

From the Department of Radiology (S.K. ✉ *snnkrtprk@hotmail.com*, R.K.), Department of General Surgery (S.Y.), Inonu University Faculty of Medicine, Malatya, Turkey.

Received 5 July 2020; revision requested 21 July 2020; last revision received 18 August 2020; accepted 28 August 2020.

Published online 18 February 2021.

DOI 10.5152/dir.2021.20523

Liver transplantation is a life-saving treatment method for end-stage liver disease and hepatocellular carcinoma (1–3). As cadaveric liver transplantation is limited, especially in Asian countries, or in situations where there is no time to wait for a suitable liver from a cadaver, living donor liver transplantation (LDLT) is an appropriate alternative method (4, 5). The first successful LDLT was performed by Strong et al. (6) in 1989, using segments 2-3 of left lobe in a child with biliary atresia. In 1993, Ichida et al. (7) performed adult-to-adult transplantation using the left lobe in a female with primary biliary cirrhosis. The first right lobe LDLT was performed by Tanaka et al. (8) in 1994.

You may cite this article as: Karatoprak S, Kutlu R, Yılmaz S. Role of percutaneous radiological treatment in biliary complications associated with adult left lobe living donor liver transplantation: a single-center experience. Diagn Interv Radiol 2021; 27:546-552

Initially, because of the risks to the donor, left lobe transplantation was considered to be the only option in adult LDLT. However, as the left lobe grafts are thought to meet only 30%–50% of the metabolic needs of adult recipients, potentially leading to small-for-size syndrome, left lobe donation was limited (9). Although the current use of right lobe LDLT has resolved the problem of graft size in the recipient, it has caused an increase in the risks for donors. Recent studies have shown that left lobe LDLT have shifted the donor risks to the recipients (10).

In previous studies, biliary complications in the recipient patient group have ranged as 10%–15% in cadaveric liver transplantation and 9%–37% in LDLT. Of the biliary complications that develop after LDLT, bile leakage constitutes 5%–19% and biliary stricture 4%–37% (11–14).

The management of biliary complications includes endoscopic, radiological and surgical procedures. Endoscopic methods are generally the first step in treatment, and success rates after LDLT have been reported as 60%–75% in anastomotic strictures and 25%–33% in non-anastomotic strictures. Percutaneous radiological methods are the second step in treatment, with a reported success rate of 50%–75% (15).

Almost all studies on biliary complications biliary complications following LDLT have been made with right lobe. The aim of the current study was to determine the frequency of biliary complications developing after adult left lobe LDLT and to evaluate the efficacy of the algorithm followed in diagnosis and percutaneous radiological treatment.

Methods

Approval for this retrospective study was granted by the Scientific Research and Publication Ethics Committee of Malatya Inonu University (decision no:2019/9-19). From May 2009 to December 2019, a total of 2185 LDLT operations were performed in the Liver Transplantation Institute of Inonu University. The parameters used in graft selection were donor morbidity and mortality, residual liver volume and the size of the recipient liver; when the recipient standard liver volume was >30% of the graft volume (GV/SLV), left lobe grafts were preferred. In the scope of this study, a total of 69 adult patients who received left lobe graft transplantation and developed biliary complications during the follow-up period were evaluated.

Management of biliary complications

Patients developing biliary complications were treated by percutaneous drainage under ultrasound (US) guidance, endoscopic retrograde cholangiopancreatography (ERCP), and percutaneous transhepatic cholangiography (PTC)/ percutaneous transhepatic biliary drainage (PTBD); patients who received percutaneous radiological treatment were the subject of this study. The patients were evaluated with respect to demographic data, transplantation indications, ERCP procedures before percutaneous treatment, percutaneous treatment indications and treatment efficacy. The Clavien classification system, modified in 2004, as the most widely used system, was used to evaluate the complications that developed following surgery (16, 17) (Table 1). The patients evaluated in the scope of this study were those evaluated as Clavien grade III-IV, requiring interventional treatment.

In patients with abnormal liver function tests, or when biliary complications such as bile leakage or stricture were suspected in the presence of symptoms such as itching, jaundice, or fever, noninvasive methods such as (US), computed tomography (CT), magnetic resonance cholangiopancreatography, or cholangiography from a feeding catheter were applied first. In patients determined to have fluid collection within the abdomen on imaging methods, a sample was taken under US guidance. In patients diagnosed with bile leakage, percutaneous drainage was applied as the first treatment step.

Patients with suspected stricture on imaging methods and patients who did not respond to percutaneous drainage treatment were referred for ERCP. In case common bile duct cannulation could not be achieved during the ERCP procedure or the guidewire could not pass through the narrow segment or in patients with continuing biliary problems despite stent placement, PTC/PTBD was applied as the second step treatment before surgery (Fig. 1).

PTC/PTBD

Following antibiotic prophylaxis, PTC was applied under general anesthesia or sedation, using diluted contrast material (Iohexol, Omnipaque 300™, 647 mg iohexol/mL, GE Healthcare) targeting the peripheral bile

Main points

- Although the right lobe is generally preferred for LDLT, left lobe could be used in cases where it is sufficient, with an intent to decrease donor complications.
- Biliary complications are frequent in left lobe LDLT, and percutaneous biliary interventions should be tried before surgical treatments when endoscopic procedures fail.
- Percutaneous biliary interventions in left lobe LDLT are effective and problem-solving methods.

Table 1. Modified Clavien Dindo classification

Degree	Definitions
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs such as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic or radiological intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
IV	Life-threatening complication (including CNS complications)* requiring IC/ICU-management
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
V	Death of a patient

CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.
*Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks.

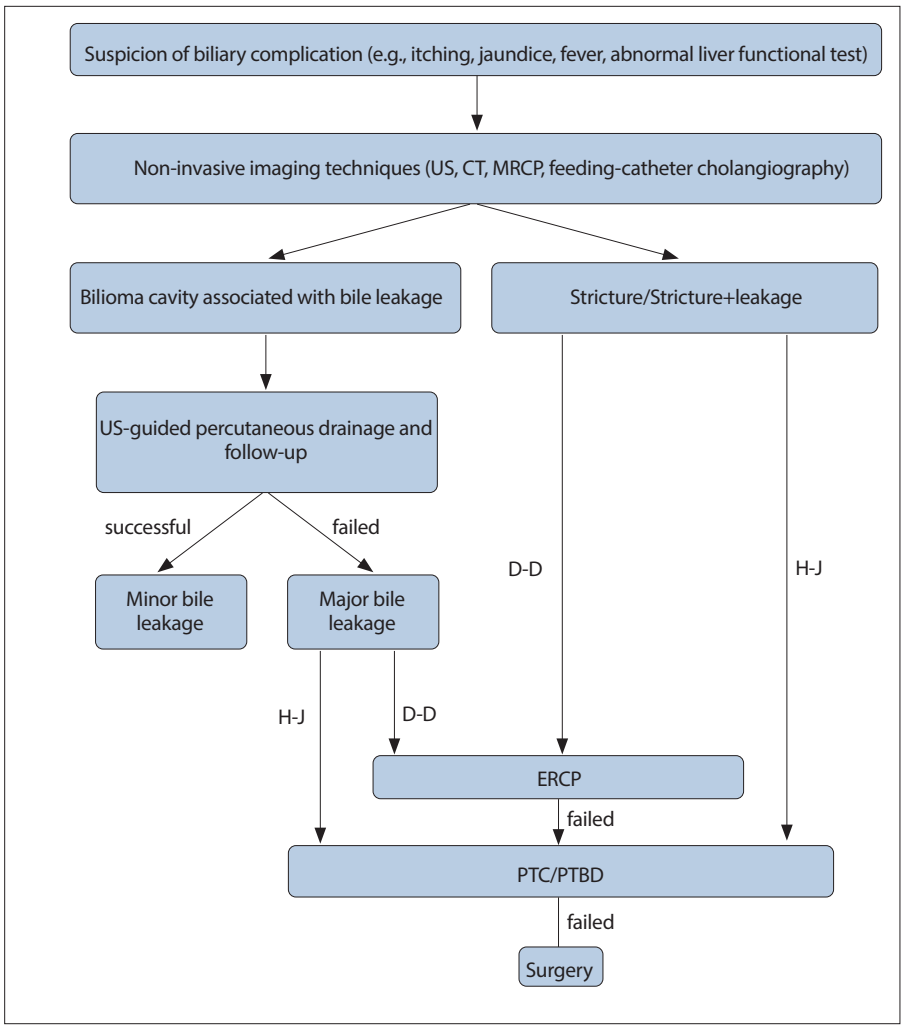

Figure 1. Treatment algorithm of biliary complications after adult left lobe living donor liver transplantation (LDLT) in our center. US, ultrasound; CT, computed tomography; MRCP, magnetic resonance cholangiopancreatography; D-D, duct-to-duct anastomosis; H-J, hepaticojejunostomy; ERCP, endoscopic retrograde cholangiopancreatography; PTC/PTBD, percutaneous transhepatic cholangiography/ percutaneous biliary drainage.

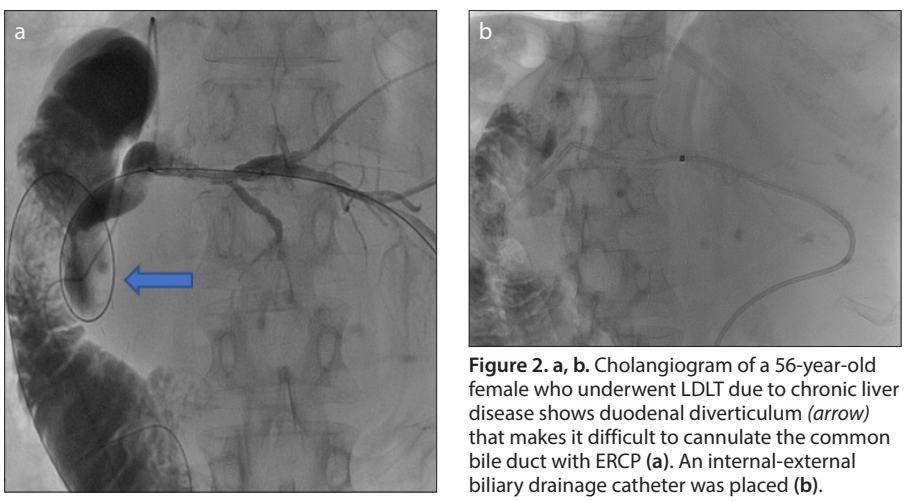

Figure 2. a, b. Cholangiogram of a 56-year-old female who underwent LDLT due to chronic liver disease shows duodenal diverticulum *(arrow)* that makes it difficult to cannulate the common bile duct with ERCP **(a)**. An internal-external biliary drainage catheter was placed **(b)**.

ducts with a 21 G Chiba needle (Boston Scientific) or Micropuncture Access Set (Cook Medical) under US and fluoroscopy guidance. Then the bile ducts were catheterized using the AccuStick™ Introducer System (Boston Scientific). The stricture and/or leakage level was negotiated with a 0.035-inch stiff-type hydrophilic guidewire (Boston Scientific) and various diagnostic catheters. When there was a stricture requiring dilatation, an introducer (Shunmei Medical) was placed and dilatation was applied 2 or 3 times for at least 1 minute with balloon catheters of various dimensions (5 to 10 mm diameter) according to the size of bile duct. Then, an internal-external biliary drainage (IEBD) catheter (Flexima catheters, Boston Scientific) extending from the bile ducts to the common bile duct and duodenum passing the stricture or leakage region was placed and biliary drainage was achieved.

If the PTC/PTBD procedure was not successful (e.g., the bile ducts could not be filled with contrast material or could not be catheterized, the catheter could not be placed, sufficient drainage could not be obtained despite catheter placement), these patients were referred for surgical treatment as the final treatment step. In this study, surgical treatment was not required in any of the patients for biliary drainage.

Results

A total of 69 adult patients received left lobe LDLT in our center between May 2009 and December 2019. Of these patients, biliary complications (Clavien grade III-IV) requiring endoscopic and/or percutaneous treatment developed in 28 (40%).

Of these 28 patients: 4 had bile leakage (14%), 20 had anastomosis stricture (72%), and 4 had both leakage and anastomosis stricture (14%). External drainage treatment under US guidance was sufficient in 2 of 4 patients with bile leakage, and these cases were accepted as minor bile leakage (7%).

Overall, 26 patients underwent ERCP. Of these 26 patients, 8 were referred for PTC/PTBD, due to failure to pass the guidewire and/or balloon-stent through the anastomosis stricture (n=7) and failure to cannulate the common bile duct because of a duodenal diverticulum (n=1) (Fig. 2).

Diagnostic PTC was performed in 10 patients; eight patients were referred after inadequate/ failed ERCP procedure, while two patients were referred directly without ERCP (Table 2). Anastomosis stricture and associated intrahepatic bile duct dilatation was determined in 7 patients (70%) and anastomosis stricture and bile leakage in 3 patients (30%).

In 7 patients determined with only stricture, balloon dilatation was applied by

Table 2. Results of 10 patients who underwent percutaneous treatment for biliary complications after left lobe LDLT

Patient no.	Gender	Age (years)	Biliary complication	ERCP before PTC	PTC indication	Treatment
1	F	26	L+S	+	Could not pass the narrow segment in ERCP	B-D, IEBD catheter
2	F	56	S	+	Could not cannulate the common bile duct because of diverticulum	B-D, IEBD catheter
3	F	27	S	+	Could not pass the narrow segment in ERCP	B-D, IEBD catheter, C-M stent
4	F	31	S	+	Could not pass the narrow segment in ERCP	B-D, R
5	M	69	S	+	Could not pass the narrow segment in ERCP	B-D, IEBD catheter, C-M stent
6	F	41	L+S	+	Could not pass the narrow segment in ERCP	B-D, IEBD catheter, C-M stent
7	F	65	S	-	IHBD dilatation and suspected anastomosis stricture	B-D, IEBD catheter
8	M	19	L+S	+	Could not pass the narrow segment in ERCP	B-D, covered metallic stent
9	M	64	S	+	Could not pass the narrow segment in ERCP	B-D, IEBD catheter
10	M	43	S	-	IHBD dilatation and suspected anastomosis stricture	B-D, IEBD catheter

F, female; M, male; L, leakage; S, stricture; ERCP, endoscopic retrograde cholangiopancreatography; PTC, percutaneous transhepatic cholangiography; B-D, balloon dilatation; IEBD, internal-external biliary drainage; C-M, custom-made; R, rendezvous procedure; IHBD, intrahepatic bile duct.

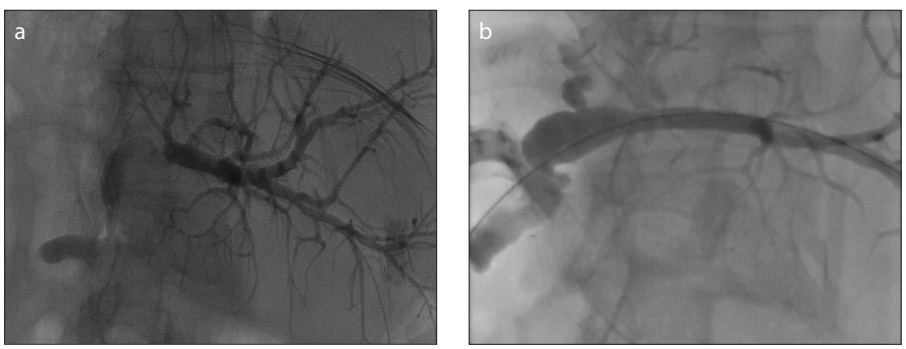

Figure 3 a, b. Cholangiogram of a 31-year-old female who underwent LDLT due to cirrhosis and hepatocellular carcinoma shows anastomosis stricture and intrahepatic bile duct dilatation **(a)**. Stricture disappeared after balloon dilatation **(b)**.

passing the narrow segment with various guidewires and catheter manipulations (Fig. 3) and then biliary drainage was performed. For tight strictures, dilatation was performed 2 or 3 times for at least 1 minute. Minor strictures were negotiated at first trial. In one case, following balloon dilatation, a 5 F diagnostic catheter was placed and the patient was referred to ERCP, where a stent was placed by aid of this diagnostic catheter (i.e., Rendezvous procedure).

In 3 patients who had biliary leakage and anastomosis stricture, balloon dilatation was applied for stricture. After dilatation, an IEBD catheter was placed through the leakage region in 2 patients. For the remaining patient, a covered metallic stent was placed passing through the leakage region (Fig. 4).

Three patients showed regression of bile duct dilatation and/or bile leakage and a return to normal laboratory values after percutaneous biliary drainage; a custom-made plastic biliary stent obtained from the IEBD catheter was placed in these patients (Fig. 5) and they were followed with stent revisions by ERCP as needed.

In the patient with initially failed common bile duct cannulation because of duodenal diverticulum, in the follow-up with ERCP after percutaneous biliary drainage, the plastic biliary stent which was revised in the previous ERCP session was discovered to be stuck over the anastomosis and the patient was referred to PTC. In the diagnostic PTC, the stent was observed to be within the diverticulum. Initial attempt to remove it with the aid of a snare failed, and it was eventually removed with the aid of a balloon by squeezing inside the introducer (Fig. 6). Biliary drainage was then achieved with the placement of an IEBD catheter.

None of the 10 patients required surgery for biliary complication after PTC/PTBD.

Discussion

Liver transplantation, which is the only curative treatment for end-stage chronic liver disease, has become more widespread in recent years. While there is an increase in the number of end-stage liver disease patients who are candidates for organ transplantation, cadaveric organ donation has not increased at the same rate to meet this need, and LDLT has come to prominence. Right lobe graft transplantation is preferred to meet the metabolic needs of adult recipients, but this has increased morbidity and mortality in the donor group. In a study by Barr et al. (18), the mortality risk was reported as 0.5% in donors undergoing right hepatectomy and as 0.1% in donors undergoing left hepatectomy. Left lobe LDLT has been gaining popularity in consideration

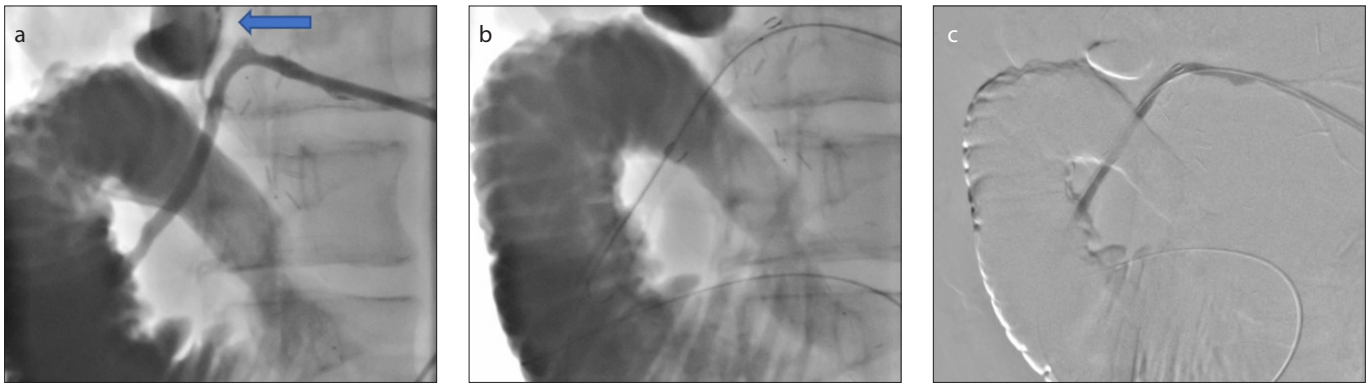

Figure 4. a–c. Cholangiogram of a 19-year-old male who underwent LDLT due to Wilson's disease shows bile leakage *(arrow)* from cystic canal to cut surface **(a)**. A covered metallic biliary stent was implanted to cover the cystic duct leakage area **(b)**. Control cholangiogram shows the disappearance of leakage **(c)**.

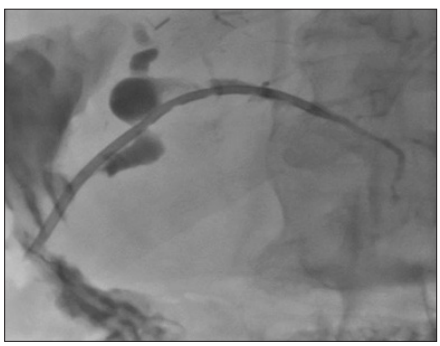

Figure 5. Cholangiogram of a 61-year-old male who underwent LDLT due to hepatitis B virus and hepatocellular carcinoma shows custom-made biliary stent, obtained from IEBD catheter.

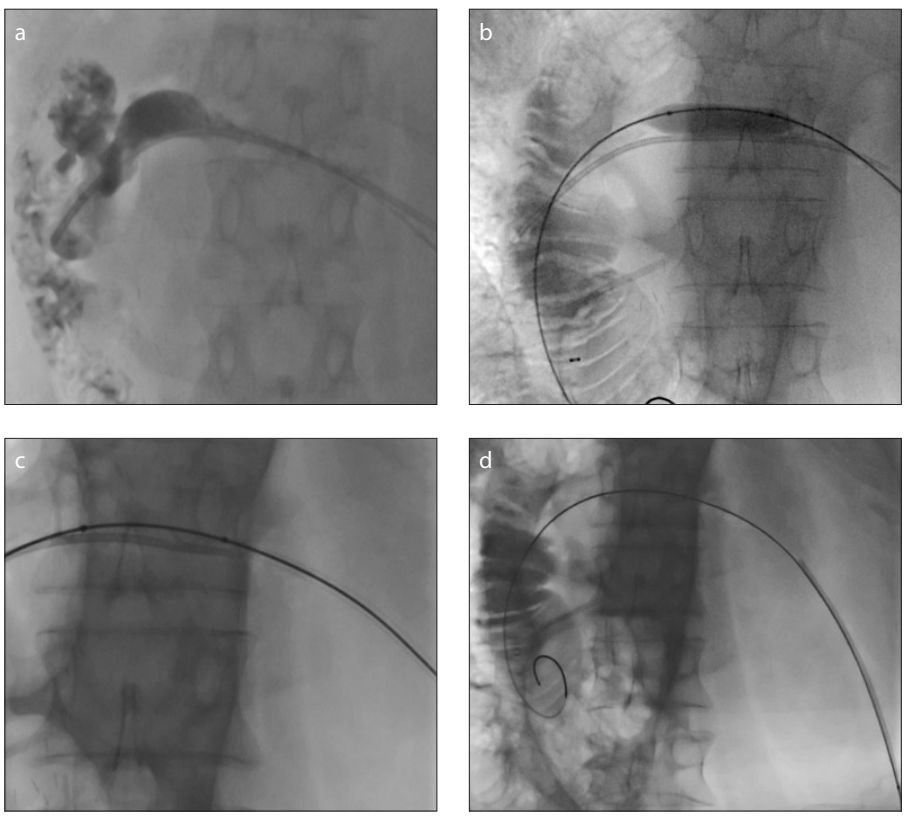

Figure 6. a–d. Cholangiogram of a 56-year-old female shows the distal part of plastic biliary stent in the diverticulum **(a)**. Stent was removed with the aid of a balloon catheter percutaneously, by squeezing inside the introducer **(b–d)**.

of donor safety; however, the rate of biliary complications in left graft recipients has been reported as 47% which is greater compared to right graft recipients (19). From a review of literature, no definitive diagnostic algorithm could be found for biliary complications developing after left lobe LDLT in particular. The treatment planning for these types of patients in our center is made by a multidisciplinary council including an interventional radiologist, gastroenterologist and transplant surgeons, and treatment is started with ERCP, which is the least invasive method. Success rates of endoscopic treatment methods after cadaveric liver transplantation have been reported in the literature as 70%–100% in anastomosis strictures and 50%–75% in non-anastomotic strictures. However, in LDLT, these rates fall to 60%–75% and 25%–33%, respectively (15). When ERCP is insufficient or unsuccessful, patients are referred for PTC/PTBD as a second-line treatment before resorting to surgery (15). The success rate of PTC/PTBD has been reported as 50%–75%, although the studies conducted have been mostly dealing with biliary complications following right lobe LDLT.

In this study, we evaluated the outcome of left lobe LDLT in particular; of the 28 patients who developed Clavien grade III–IV biliary complications, ERCP was applied to 26, while 8 patients were referred for PTC/PTBD following insufficient or unsuccessful treatment. Successful biliary drainage was achieved in all of these patients and surgical treatment was not required in any patient.

In a study by Kulkarni et al. (20), 17 LDLT recipients (4 left lobe, 13 right lobe) with biliary complications were treated with PTC/PTBD and the rendezvous procedure, and the percutaneous treatment technique was successful in 70.6%. All left lobe receipients, 1 with hepatico-jejunostomy (H-J) and 3 with duct-to-duct anastomosis, were successfully treated with balloon dilatation and biliary drainage. Jegadeesan et al. (21) conducted a single-center study of

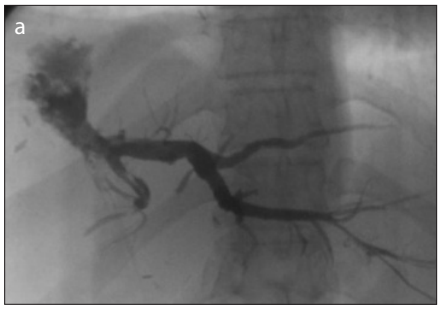

Figure 7. a, b. Cholangiogram of a 56-year-old female who underwent LDLT due to chronic liver failure associated with hepatitis B virus shows bile leakage from anastomosis to cut surface **(a)**. Two wide diameter plastic biliary stents were placed percutaneously to cover the leakage region. An external drainage catheter was placed into the proximal part of the stents **(b)**.

81 LDLT recipients (3 left lobe, 78 right lobe) who developed biliary stricture. ERCP was applied to 75 of these patients, and 39 (2 left, 37 right) were referred for PTC, because of ERCP failure in 33 and H-J anastomosis in 6. Overall, 29 patients were treated with a rendezvous procedure and 5 with external biliary drainage catheter. Percutaneous treatment was not successful in 5 patients and technical success was reported as 87%. Finally, PTBD was performed in two left lobe recipients in total; one patient following failed ERCP and the other with continued bleeding precluding ERCP, with full technical success achieved in both cases. In our study, 69 adult left lobe LDLT patients were evaluated; out of 10 cases undergoing percutaneous intervention for biliary complications (8 because of ERCP failure, 2 direct referral), technical success was achieved in all 10 (100%).

Another important biliary complication seen after LDLT is bile leakage. The management of bile leakage is similar to that of biliary stricture and includes percutaneous drainage treatment. Cases not responding to percutaneous drainage are referred for ERCP. In a recent review by Akamatsu et al. (22), the incidence of bile leakage after LDLT was reported as 9.5%, and 34% of patients determined with bile leakage were followed up conservatively or with percutaneous drainage only, without any aggressive treatment. In our study, fluid collection was determined on imaging methods in 10 of the 69 patients applied with left lobe LDLT, sampling was performed for suspected bile leakage and a drainage catheter was placed. Minor bile leakage was diagnosed in 4 patients (5.7%) who responded to treatment without need for aggressive treatment methods.

In patients who do not respond to percutaneous drainage treatment, first-line treatment is ERCP. The aim of ERCP is both to lower bile duct pressure with external sphincterotomy and to prevent leakage with the placement of a stent that will pass the leakage region (23). When there is no response to endoscopic treatment, percutaneous treatment is recommended again before surgery. In a study by Jong et al. (24), 63 patients who developed postoperative bile leakage underwent PTBD with 90.5% technical success and 69.8% clinical success. In a study by Kulkarni et al. (20), 4 left lobe LDLT recipients, two with stricture and two with bile leakage, underwent percutaneous drainage. The two patients with leakage were successfully treated, one by drainage and glue embolization and the other by biliary drainage and external drainage. In our study, 3 patients had both stricture and leakage. In one patient, biliary drainage was obtained with IEBD catheter, two wide diameter plastic biliary stents (7F and 10F) were placed percutaneously to cover the leakage region, and an external drainage catheter was left proximal to the stent (Fig. 7). In the second patient, the bile leakage was stopped with the IEBD catheter and the catheter was removed. Follow-up of both these patients was made with ERCP. In the third patient, a covered metallic stent was placed and the leakage disappeared.

The rendezvous technique, which was first defined in 1987, classically involves the use of two access routes as a combination of at least two of the surgical, endoscopic and percutaneous approaches to reach a point in the body. This technique is generally preferred when ERCP or PTBD alone are not sufficient in the treatment of hepatobiliary dysfunctions such as bile leakage, biliary stricture, bile duct damage, or stones (25). Two methods are generally preferred in the rendezvous procedure: the first involves an endoscopically placed guidewire caught with the aid of a snare by an interventional radiologist from a percutaneous entry route. In the other method, the guidewire placed with the percutaneous route is caught endoscopically with a snare (26). The rendezvous technique is used in biliary complications following LDLT. In our study, endoscopic biliary stent placement in a 5 F diagnostic catheter guide placed after balloon dilatation to the anastomotic stricture with the percutaneous route, was applied successfully.

In our center, PTBD was applied to a total of 10 adult left lobe LDLT recipients, 8 of whom switching to percutaneous treatment after failed ERCP procedure. Of these patients, custom-made biliary stents obtained from the IEBD catheter were placed percutaneously in 3 patients. The stent revisions of these patients were made using endoscopic methods. In addition, in 2 patients where the drainage catheter was removed before stent placement, a need for biliary intervention developed again later and biliary drainage was achieved endoscopically in these patients. In other words, biliary complications which could not be treated endoscopically because the stricture could not be passed or cannulation could not be achieved, became treatable with the less invasive method of ERCP following percutaneous radiological treatment. If these patients had been referred for surgical treatment, the chance for endoscopic treatment would have been lost because bilio-enteric anastomosis (H-J) would have been applied.

There were some limitations to this study, primarily that it was retrospective and the number of patients was low because of the low preference for left lobe LDLT in our center compared with the right lobe.

In conclusion, generally, ERCP is the first preferred method in biliary complications which develop after LDLT. In cases where a response cannot be obtained by endoscopic treatment or require complex and/or aggressive treatment, percutaneous radiological treatment should be the treatment of choice before surgery in left lobe LDLT. Nevertheless, further studies with greater number of patients are needed to draw definitive conclusions.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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