External Biliary Drainage in Living Donor Liver Transplantation Using Duct-to-Duct Anastomosis


ABSTRACT

Purpose. This study compared the incidence of biliary complication (BC) in adult living donor liver transplant recipients who underwent right-lobe duct-to-duct anastomosis (DDA) with or without external biliary drainage (EBD) and intended to optimize EBD tube clamping.

Methods. This study consisted of a retrospective assessment of EBD effect and a prospective trial for EBD tube-clamping optimization. The retrospective study included the EBD group (n = 208) and the non-EBD group (n = 145). The prospective study included 60 patients with EBD.

Results. In the retrospective study, single DDA was performed in 83.7% of the EBD group and 80.7% of the non-EBD group (P = .47). One-year overall incidence of BC was 14.4% in the EBD group and 16.8% in the non-EBD group (P = .48). The incidence of early anastomotic bile leakage was 1.0% in the EBD group and 4.8% in the non-EBD group (P = .036). In the prospective study, there was no difference in tube-clamping success rates between low- and high-output EBD groups. There was also no statistical difference between the success and failure groups in terms of graft duct size, liver function tests, and post-transplant days at tube clamping.

Conclusions. The size of our EBD tube was too small for the graft duct size, therefore its main role appeared to be early biliary decompression, which helped prevent bile leakage and also simplified the route of cholangiogram in detecting early BC. Hence, EBD is worthy of performing in selected patients with a high risk of anastomotic bile leak.

Biliary complication (BC) is well known as the most common and intractable complication of adult living donor liver transplantation (LDLT) [1,2]. Biliary reconstruction of adult LDLT has innately overt disadvantages such as frequent multiple duct openings of the right lobe graft, a relatively small graft duct compared with the edematous bowel wall, arterial hypoperfusion of the liver graft secondary to portal hypertension, and chronic inflammation of the recipient’s proximal bile duct. As a natural consequence, most transplantation centers reported considerably high rates of BC following adult LDLT [1-6].

Since early 2000, we have performed duct-to-duct anastomosis (DDA) with the expectation of reducing BC and achieving technical simplicity and functional restoration of natural biliary drainage [1]. However, we have found that the incidence of BC was not decreased to an acceptably low level despite refined surgical techniques and thus have performed various other surgical methods to reduce the incidence of BC. The present study is evidence of one such trial where we evaluated the use of DDA with external biliary drainage (EBD). However, the EBD procedure...
induced patient discomfort due to prolonged maintenance of EBD at the abdomen.

In this study, we compared the incidence of BC in adult LDLT recipients who underwent DDA with or without EBD. In addition, we intended to optimize the management protocol for EBD tube clamping during the early post-transplant period in LDLT recipients.

PATIENTS AND METHODS

This study consisted of 2 parts: a retrospective study on assessment of EBD effect and a prospective study for optimization of EBD tube clamping.

A Retrospective Study on Assessment of EBD Effect

The EBD group was selected from the adult LDLT pool throughout the year of 2010. The inclusion criteria were right lobe graft implantation, DDA with EBD, and exclusion of salvage liver transplantation, by which 218 patients were selected. After further exclusion of perioperative mortality (n = 10; 4.6%), 208 patients were finally selected for the EBD group. The historical control group was selected from the adult LDLT pool over a 3-year period from 2001 to 2003. With the application of similar conditions and DDA without EBD (no stent or internal biliary stent only), 145 subjects were selected as the non-EBD group.

The EBD techniques consisted of placement of a thin Silastic tube (0.7–1.5 mm external diameter) across the anastomotic line, penetration of the common bile duct wall with absorbable transfixation sutures, and percutaneous placement with fixation sutures at the skin. This tube was naturally drained for the first 1 to 3 weeks and then clamped. A tube cholangiogram was obtained during the operation and 1 to 3 weeks after the LDLT. The tube was removed after 6 to 12 months to minimize the risk of tract-related bile leakage.

The medical records of our 2 subject groups were retrospectively reviewed with a particular focus on BC in the first year. In this study, the definition of BC was biliary stenosis and bile leakage that required radiologic or endoscopic intervention.

A Prospective Study for Optimization of EBD Tube Clamping

This part of study was prospectively performed with particular attention paid to early successful clamping of the EBD tube. The study subjects were selected from an adult LDLT population during a 4-month period from January 2011 to April 2011. The selection criteria were right-lobe graft implantation, single DDA, DDA with EBD, with exclusion of salvage liver transplantation; 60 patients were finally selected for the EBD group.

The protocol for EBD tube clamping during the early post-transplant period in LDLT recipients.

The patient profile is summarized in Table 1, showing comparable clinical features between the EBD and non-EBD groups.

A single DDA was performed in 174 of 208 (83.7%) patients in the EBD group and 117 of 145 (80.7%) patients in the non-EBD group (P = .47). Unification ductoplasty was performed in 53 (25.5%) patients in the EBD group and 32 (22.1%) patients in the non-EBD group (P = .46). Hepatic artery complications occurred in only two cases in each group (1.0% versus 1.4%; P > .99).

The 1-year overall incidence of BC was 14.4% (n = 31) in the EBD group and 16.8% (n = 22) in the non-EBD group, showing no statistical difference (P = .48). In contrast, early bile leakage at the anastomotic site occurred in 2 patients (1.0%) in the EBD group and 7 patients (4.8%) in the non-EBD group (P = .036). Early anastomotic stenosis was detected through comparison of the intraoperative and follow-up tube cholangiogram findings.

Treatment modalities for BC comprised an endoscopic approach (endoscopic nasobiliary drainage [ENBD] or endoscopic retrograde biliary drainage [ERBD]) in 10 patients, percutaneous transhepatic biliary drainage (PTBD) in 8 patients, and sequential ENBD and PTBD in 13 patients from the EBD group. In contrast, treatment modalities for BC involved ENBD in 2 patients and PTBD in 22 patients from the non-EBD group. The preference for the endoscopic approach was greatly increased from 9.1% in the non-EBD group to 74.2% in the EBD group.

In the EBD group, the EBD tube was accidentally removed too early in 11 patients (5.3%), most of whom then required in-hospital supportive care due to unexpected bile leakage from the bile duct hole. In other patients, the EBD

| Table 1. Demographics of the 353 Adult Patients Who Underwent LDLT Using a Right Liver Graft and Duct-to-Duct Anastomosis With or Without EBD |
|-----------------|-----------------|-----------------|
| Age (y) | EBD Group (n = 208) | Non-EBD Group (n = 145) | P Value |
| 50.3 ± 6.8 | 49.3 ± 7.1 | .18 |
| Male gender | 165 (79.3%) | 114 (78.6%) | .87 |
| Primary diagnosis | | | .19* |
| Hepatitis B virus-associated liver cirrhosis | 165 (79.3%) | 123 (84.8%) | |
| Hepatitis C virus-associated liver cirrhosis | 12 (5.8%) | 7 (4.8%) | |
| Alcoholic liver cirrhosis | 14 (6.7%) | 5 (3.5%) | |
| Fulminant hepatic failure | 8 (3.9%) | 6 (4.1%) | |
| Others | 9 (4.3%) | 4 (2.8%) | |
| Model for End-stage Liver Disease score | | | .37 |
| ≤20 | 96 (46.2%) | 60 (41.4%) | |
| >20 | 112 (53.8%) | 85 (58.6%) | |
| Concurrent hepatocellular carcinoma | 69 (33.2%) | 35 (24.1%) | .067 |

Abbreviation: EBD, external biliary drainage.

*Hepatitis B virus-associated liver cirrhosis versus all other diseases.

RESULTS

Assessment of EBD Effect

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In the EBD group, the EBD tube was accidentally removed too early in 11 patients (5.3%), most of whom then required in-hospital supportive care due to unexpected bile leakage from the bile duct hole. In other patients, the EBD
tube was removed uneventfully during the 6- to 12-month period after LDLT.

Optimization of EBD Tube Clamping

The primary diseases in the 60 study patients were hepatitis B virus-associated liver cirrhosis (n = 43), alcoholic liver disease (n = 6), acute liver failure (n = 5), hepatitis C virus-associated liver cirrhosis (n = 4), autoimmune hepatitis (n = 1), and primary sclerosing cholangitis (n = 1). The mean patient age was 50.4 ± 8.9 years (range, 20–64). Forty of the patients were male. All of these LDLT recipients received a right liver graft with a single DDA and EBD.

For 35 patients in the study cohort showing low-output bile drainage (<300 mL/d), a rapid clamping exercise for 2 to 3 days was successfully achieved at the first attempt in 30 cases (85.7%). The remaining 5 patients, however, underwent delayed clamping trials due to an initial rise in liver enzyme levels. There was no statistical difference found between the success and failure groups in terms of graft duct size (6.2 ± 1.6 mm vs 7.0 ± 2.5 mm, P = .26). The levels of serum aspartate transaminase (AST; 46.3 ± 20.1 IU/L vs 44.1 ± 13.5 IU/L, P = .81), serum alanine transaminase (ALT; 137.2 ± 105.3 IU/L vs 111.4 ± 37.2 IU/L, P = .48), serum total bilirubin (2.0 ± 0.9 mg/dL vs 2.1 ± 1.0 mg/dL, P = .93), and serum alkaline phosphatase (80.1 ± 36.9 IU/L vs 96.2 ± 26.5 IU/L, P = .36), or posttransplant days (13.4 ± 9.8 days vs 12.9 ± 8.9 days, P = .85) at the time of EBD tube clamping.

For 25 patients in our LDLT cohort showing high-output bile drainage (≥300 mL/d), a rapid clamping exercise for 2 to 3 days was successfully achieved at the first trial in 17 cases (68%). The remaining 5 patients underwent delayed clamping trials due to an initial rise in the liver enzyme or bilirubin levels. There was no statistically significant difference between the success and failure groups in terms of graft duct size (6.6 ± 2.3 mm vs 6.1 ± 3.1 mm, P = .68), levels of serum AST (44.9 ± 22.6 IU/L vs 55.1 ± 24.5 IU/L, P = .28), serum ALT (1182.9 ± 962.2 IU/L vs 1287.7 ± 106.7 IU/L, P = .25), serum total bilirubin (1.8 ± 0.6 mg/dL vs 1.6 ± 0.5 mg/dL, P = .56), and serum alkaline phosphatase (92.1 ± 54.2 IU/L vs 76.9 ± 21.5 IU/L, P = .45), or posttransplant days (17.9 ± 11.7 days vs 14.8 ± 5.6 days, P = .39) at the time of EBD tube clamping.

There was no difference in the success rates of clamping between the low- and high-output EBD groups (P = .10). The transfixed external tube was released after 6 months and removed during the 6- to 12-month period after the LDLT operation. Bile peritonitis from bile leak after spontaneous or incidental removal of the catheter occurred in 2 patients who required in-hospital treatment.

DISCUSSION

The results of current study confirm that BC is the most frequent and intractable complication in the years following adult LDLT [1–6] and that anastomotic bile leakage during the early postoperative period dramatically decreases after the application of EBD.

The primary mechanism by which EBD prevents early bile leakage after DDA is decompression of the bile duct tree. After transection of the common bile duct, intrinsic control of the sphincter of Oddi may be impaired and loss of autonomic control leads to an unwanted increase in the pressure of the biliary tree, unless the sphincter is patulous following sphincterotomy. Based on our present observations, the return of sphincter tone control requires 1 to 3 weeks in about two-thirds of DDA cases. Our procedure for determining the status of the sphincter of Oddi employs saline injected into the transected common bile duct and then checking of the drainage pressure. If the sphincter is patulous, free passage of water can be felt. In the case of a spastic sphincter, a sudden rise of luminal pressure is palpable during water injection.

Prevention of early bile leakage is clinically important because such a complication can lead to infectious complications as well as to a late biliary stricture. Although the incidence of early bile leakage was found to be greatly decreased after EBD, the overall incidence of BC was not decreased significantly. We speculate that this is due to a higher early detection rate of biliary stenosis in the EBD group than in the non-EBD group. In the study period for the non-EBD group, our primary treatment modality for BC was PTBD, which is known to be more invasive than an endoscopic approach. Hence, we were rather reluctant to perform PTBD in patients without significant clinical manifestations [1]. On the other hand, in the period of EBD, a routine EBD tube-cholangiogram has been found to increase the detection rate of subclinical BC, and the endoscopic approach is preferentially performed [2,5,7,8]. Thus, we do not think that EBD itself did not work as an effective modality to decrease BC. In fact, the size of the EBD tube we used was too small for the graft duct size and its main role thus appears to be biliary decompression to prevent early bile leakage and to provide a simple route of cholangiogram to detect early BC.

The usefulness of a small-caliber internal biliary stent across DDA is also doubtful, and we think that its main purpose is to prevent accidental catch of the posterior wall, but not to prevent stenosis [1,9]. One of the characteristic features of anastomotic stenosis after LDLT is multiplicity or long involvement of the stenosis area. It is rather similar to the biliary stenosis of an ischemic origin rather than a focal stricture. While harvesting a right lobe graft, there is some possibility of blood flow damage at the graft duct stump [1,10]. In addition, it is hard to think that the recipient's bile duct stump can be a good arterial collateral source across DDA. These findings implicate that the graft duct stump is eventually vulnerable to ischemia even without significant disturbance of right hepatic arterial flow. We presume that delayed-onset multiple stenoses may emerge from subclinical mild stenosis if this potential ischemia is combined with the small-sized graft duct.
Although EBD appears to be a useful procedure, it induces patient discomfort due to maintenance of EBD tube at the abdomen as well as due to EBD drainage until successful tube clamping and EBD removal.

In the prospective part of study, we aimed to uncover factors that would facilitate early or rapid EBD tube clamping but were not successful. A daily EBD output of more than 300 mL/d showed a lower success rate of EBD tube clamping, but this was not statistically significant. Hence, EBD clamping should be attempted on a case-by-case basis. Based on the results of this study, our current protocol appears to be an effective and practical method for uneventful clamping of the EBD tube regardless of daily EBD output, which in turn minimizes patient discomfort.

Since our success rate at the first tube-clamping attempt was 85.7% in the low-output EBD group, we conclude that it is reasonable to apply rapid EBD clamping protocol routinely in such cases. In contrast, this rate decreased to 68% in the high-output EBD group, indicating that it may be better to wait for several days or even a few weeks before initiating an EBD clamping trial due to the patient’s condition. Our protocol for EBD tube clamping is similar to T-tube clamping after deceased donor liver transplantation or choledochotomy for choledocholithiasis patients [11].

If the EBD tube can be replaced with removable intraductal stenting, patient discomfort will be greatly diminished. It has been reported that a custom-made segment of a T-tube was placed into the bile duct when the diameter of the graft bile duct was smaller than 5 mm [12]. This tube was removed endoscopically at 4 to 8 months post-transplantation. No technical failures and no procedure-related complications were recorded during the drain removal.

In summary, we do not think that EBD should be routinely performed for every DDA because it discomforts the patient and its preventive effect for BC is not evident. The size of our EBD tube was too small for the graft duct size, therefore its main role appeared to be early biliary decompression, which helped to prevent bile leakage and simplified the route of cholangiogram in detecting early BC. Hence, EBD is worthy of performing in selected patients with a high-risk of anastomotic bile leak.

REFERENCES