**RAPID COMMUNICATION**

**Risk factors and prevention of biliary anastomotic complications in adult living donor liver transplantation**

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**Abstract**

**AIM:** To evaluate risk factors of biliary anastomotic complications (BACs) and outcomes according to type of biliary reconstruction.

**METHODS:** A total of 33 consecutive adult living donor liver transplantation (LDLT) were reviewed, 17 of which had undergone Duct-to-Duct anastomosis (D-D). The remaining 16 patients received Roux-en-Y anastomosis (R-Y). The perioperative factors, such as the type of graft and the number of graft bile ducts, were analyzed retrospectively.

**RESULTS:** The overall incidence of BACs was 39.4%. The incidence of BACs was significantly higher in the patients with than without neoadjuvant chemotherapy (71.4% vs 10%, \( P = 0.050 \)). There was no significant difference in the incidence of biliary leakage in patients with D-D vs those with R-Y. The incidence of biliary strictures following the healing of biliary leakage was significantly higher in D-D (60%) than in R-Y (0%) (\( P = 0.026 \)). However, the incidence of BACs related bacteremia was significantly higher in R-Y than in D-D (71.4% vs 0%, \( P = 0.008 \)). In D-D, use of T-tube stent remarkably reduced the incidence of BACs, compared with straight tube stent (0% vs 50%, \( P = 0.049 \)).

**CONCLUSION:** Our experience showed an increase of BACs related bacteremia in the patients with R-Y. Therefore, D-D might be a preferred biliary reconstruction. However, the surgical refinement of D-D should be required because of the high incidence of biliary strictures. Use of the T-tube stent might lead to a significant reduction of BACs in D-D.

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R-Y for biliary reconstruction. However, since middle 2001, we switched from R-Y to D-D because of its advantages. Through the end of the study period, 18 patients have undergone the D-D and 17 patients have undergone the R-Y. Two patients, who died within one month after surgery, were excluded from the study. The causes of the death were persistent bacteremia (existing prior to operation) and cerebral hemorrhage. The demographic characteristics of the 33 consecutive recipients included in this study are shown in Table 1. We analyzed etiologic factors affecting BACs and evaluated the differences in the incidence of BACs between the patients having received D-D and those treated with a R-Y.

**Donor operations**

Healthy individuals aged 19 to 62 years were eligible donors. The selection of the left versus right liver lobe was based on donor graft liver volume as measured through computer-assisted tomography scans (CT scans). Essentially, whichever lobe had a graft-to-recipient body weight ratio (GRWR) greater than 0.7% was used as the graft liver. However, when the right liver lobe exceeded 65% of the donor's whole liver volume, the left lobe was occasionally selected with fully informed consent even if the GRWR was less than 0.7%. All donor patients preoperatively underwent DIC-CT scanning to measure graft liver volume and to evaluate the bile duct.

Donor lobectomy was performed as described previously in detail. After cholecystectomy, cystic duct cholangiography was performed to confirm the transection line. Hilar dissection was then performed. The left or right hepatic ducts were transected sharply and parenchymal transection was performed. The peribiliary plexus was preserved as much as possible. After systemic heparinization with 1000 units of heparin, the graft was flushed via the portal vein with three times the graft weight of histidine-tryptophan-ketoglutarate (HTK) at 4°C.

To decompress the biliary tract, C-tubes were routinely positioned in the common bile duct via the cystic duct in all donor cases. Recipient total heptectomy was performed with preservation of the inferior vena cava (IVC). After anastomosis of the hepatic vein, significant large accessory veins (> 5 mm) were also anastomosed to the sidewall of the IVC. The donor portal vein was anastomosed to the recipient’s main portal vein. After reperfusion of the graft, arterial anastomosis was completed through surgical microscopy between the donor hepatic artery and the recipient right, left or proper hepatic artery in most cases.

**Biliary reconstruction**

R-Y was performed in 16 patients, 6 with a right liver lobe and 10 with a left liver lobe. The bile duct was anastomosed to the Roux-en-Y limb of the jejunum by using a 6-0 PDS suture in an interrupted fashion. The 4-, 6-, or 8-Fr straight tubes were routinely inserted and introduced via the R-Y limb of the jejunum as a stent tube. Seventeen patients underwent D-D. For cases with D-D anastomosis, the recipient bile duct was dissected at the hilar plate with as much surrounding tissue attached as possible. An end-to-end anastomosis was performed with the placement of an external stent by using a 6-0 PDS suture in an interrupted fashion in cases whose underlying hepatobiliary disease allowed us to use this technique. Initially, a 4-, 6-, or 8-Fr straight tube was routinely positioned in the intrahepatic bile duct via the remnant cystic duct or the sidewall of the common bile duct. We have recently begun using a 9- or 12-Fr T-tube for an external stent to reduce BACs. We remove the T-tube between 3 and 6 mon after the LDLT.

**Diagnosis of posttransplant complications**

When we found a discharge of bilirubin occurring through the drains, we confirmed anastomotic leakages by performing cholangiography using external stent tubes.

Biliary stricture is primarily suspected with an increase of liver function tests or a presence of jaundice. Confirmation of intrahepatic bile duct dilatation using abdominal ultrasonography or CT scan was possible in most of the cases.

The patient was diagnosed with bacteremia when the presence of bacteria was showed in the patient’s blood. We concluded that the bacteremia was associated with BACs whatever the same bacterial species were found in the patient bile and blood.

**Statistical analysis**

Values were given as means ± SD. Data was analyzed by the chi-square test and the Mann-Whitney U-test. Patient survivals after LDLT were determined by the Kaplan-Meier method and compared among groups using Log-rank test. A difference was considered statistically significant when probability was less than 0.05.

**RESULTS**

**Rates of patient survival**

The mean follow-up period of the 33 patients was 47.2 ± 28.9 mo. Eight study patients died, and the overall survival
rate of the 33 patients was 75.8%. The causes of death were systemic infection resulting in liver graft failure at 3 mo, 5 mo, or 7 mo (n = 3); heart failure following amyloidosis at 7 mo (n = 1); and the recurrence of hepatocellular carcinoma (HCC) at 6 mo, 8 mo, or 10 mo (n = 3). In two of three patients died due to systemic infection, the infection contributed to repeated reflux cholangitis after biliary leakage. The cumulative patient survival rate tended to be lower in patients without than with BACs (Figure 1).

Rates and risk factors of biliary anastomotic complications

The overall incidence of BACs was 39.4% (13/33). Biliary leakage developed in 11 patients, while biliary stricture occurred in 2 patients. We analyzed the risk factors of BACs by comparing patients with and without BACs (Table 2). The patients with neoadjuvant chemotherapy (NAC) for hepatocellular carcinoma (HCC) showed significantly higher incidence of BACs than those without NAC (71.4% vs 10%, P = 0.050, Table 2A). Seven patients underwent NAC, of which 5 experienced BACs (71.4%). NAC was defined as systemic immunochemotherapy or transarterial chemoembolization (TACE) performed within three months before LDLT.

Cold ischemia time, hepatic artery thrombosis or CMV infection, which has been identified as a cause of BACs in the previous reports, was not observed in any recipients in this series (Table 2B, 2C), neither was there an ABO-incompatible case (Table 2A). Several recent reports have shown that multiple biliary orifices, which present a further hurdle in biliary reconstruction, significantly increased the incidence of BACs. However, in our study, although the number of BACs was increased in cases multiple bile ducts, the difference failed to reach statistical significance due to the low number of cases. The incidence of post-transplant bacteremia was significantly higher in patients with than without BACs (53.8% vs 10%, P = 0.006, Table 2C). There was no significant difference in any of the other risk factors between patients with and without BACs.

Analysis of biliary anastomotic complications according to the type of biliary reconstruction

In the 33 adult LDLT patients, there were 13 BACs, in-

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**Table 2A Preoperative risk factor for biliary anastomotic complications in adult living donor liver transplantation**

| Biliary anastomotic complications | Absent (n = 20) | Present (n = 13) | P value |
|-----------------------------------|-----------------|-----------------|---------|
| Age (yr)                          | 50.4 ± 12.8     | 46.2 ± 16.4     | NS      |
| Gender                            |                 |                 |         |
| Male                              | 10              | 7               |         |
| Female                            | 10              | 6               |         |
| CTP                               | 10.4 ± 3.2      | 10.0 ± 3.2      | NS      |
| MELD                              | 18.5 ± 8.0      | 16.8 ± 7.4      | NS      |
| ABO matching                      |                 |                 |         |
| Identical                         | 15              | 10              |         |
| Compatible                        | 2               | 3               |         |
| Incompatible                      | 3               | 0               |         |
| NAC                               |                 |                 |         |
| Yes                               | 2               | 5               |         |
| No                                | 18              | 2               |         |
| Donor age (yr)                    | 38.4 ± 11.6     | 33.8 ± 13.5     | NS      |

CTP: Child-Turcotte-Pugh; MELD: model for end-stage liver disease; NAC: neoadjuvant chemotherapy; NS: not significant.

**Table 2B Intraoperative risk factor for biliary anastomotic complications in adult living donor liver transplantation**

| Biliary anastomotic complications | Absent (n = 20) | Present (n = 13) | P value |
|-----------------------------------|-----------------|-----------------|---------|
| WIT (min)                         | 47.8 ± 9.1      | 46.0 ± 7.7      | NS      |
| CIT (min)                         | 61.7 ± 52.9     | 47.1 ± 32.9     | NS      |
| Post PVP (mmHg)                   | 163.2 ± 40.7    | 182.3 ± 42.5    | NS      |
| Graft                             |                 |                 | NS      |
| Right                             | 4               | 4               |         |
| Left                              | 16              | 9               |         |
| GRWR (%)                          | 0.834 ± 0.211   | 0.843 ± 0.261   | NS      |
| Number of bile duct              |                 |                 |         |
| Single                           | 16              | 8               |         |
| Multiple                         | 4               | 5               |         |

WIT: warm ischemia time; CIT: cold ischemia time; PVP: portal venous pressure; GRWR: graft volume/recipient body weight ratio; NS: not significance.

**Table 2C Postoperative risk factor for biliary anastomotic complications in adult living donor liver transplantation**

| Biliary anastomotic complications | Absent (n = 20) | Present (n = 13) | P value |
|-----------------------------------|-----------------|-----------------|---------|
| HAT                               |                 |                 |         |
| Yes                               | 0               | 0               | NS      |
| No                                | 20              | 13              |         |
| ACR                               |                 |                 |         |
| Yes                               | 10              | 6               |         |
| No                                | 10              | 7               |         |
| CMV                               |                 |                 |         |
| Yes                               | 10              | 6               |         |
| No                                | 10              | 7               |         |
| Bacteremia                        |                 |                 | 0.006   |
| Yes                               | 2               | 7               |         |
| No                                | 18              | 6               |         |

HAT: hepatic arterial thrombosis; ACR: acute cellular rejection; CMV: cytomegalovirus; NS: not significant.
Table 3 Incidence of biliary anastomotic complications according to type of biliary reconstructions

|                        | Stricture |
|------------------------|-----------|
|                        | Leakage   | Leakage (+) |
| Duct-to-Duct (n = 17)  | 5         | 1           |
| Roux-en-Y (n = 16)     | 6         | 0           |

Table 4 Incidence of bacteremia associated with biliary anastomotic complications according to type of biliary reconstructions

|                        | Absent | Present | P value |
|------------------------|--------|---------|---------|
| Duct-to-Duct (n = 6)   |        |         |         |
| Roux-en-Y (n = 7)      | 2      | 5       | 0.008   |

Table 5 Incidence of biliary anastomotic complications according to type of external stent tubes in Duct-to-Duct anastomoses

|                        | Absent | Present | P value |
|------------------------|--------|---------|---------|
| Straight tube (n = 12) |        | 6       |         |
| T tube (n = 5)         | 5      | 0       | 0.049   |

The stent tube was usually left in place for at least 3 mo after LDLT and then removed after confirming the integrity of the bile duct by a cholangiogram. There was no biliary complication associated with the insertion or removal of T-tube, such as bile leakage at the T-tube insertion and biliary peritonitis after T-tube removal.

**DISCUSSION**

Although surgical, technological, and immunological treatments have advanced greatly in the field of liver transplantation, biliary anastomotic complications remain an important cause of morbidity and mortality, as confirmed by our series.

In our study, there was no difference in the incidence of BACs between the D-D and the R-Y. However, the incidence of biliary strictures following the healing of biliary leakage was significantly higher in the D-D (60%) than in the R-Y (0%). This finding emphasizes that ischemia is an important cause of BACs. Although the Roux-en-Y limb of the jejunum receives an adequate arterial blood flow, ischemia might occur easily in the recipient’s bile duct because of lysis of porta hepatis. Therefore, in comparison with R-Y, D-D has to be monitored closely in order to preserve the peribiliary plexus of the recipient's left, right, or common hepatic duct as well as the donor’s right or left hepatic duct. The high incidence of biliary strictures in D-D probably might originate in a little longer sticture caused by ischemic change in both sides of the stoma.

However, D-D has several advantages over R-Y. First, D-D can reduce the duration of surgery. Second, D-D allows easier access for endoscopic treatments of the biliary tract and may reduce reflux cholangitis because of preservation of the normal physiologic sphincter mechanism. Third, D-D can be converted to R-Y in cases where biliary strictures cannot be resolved by percutaneous transhepatic biliary anastomotic dilatations. Moreover, in our study, the incidence of bacteria associated with BACs was significantly lower in the D-D than in the R-Y cases. Therefore, D-D is our technique of choice for biliary reconstruction. However, surgical refinement of D-D anastomosis should be performed because of the high incidence of biliary strictures, as reported previously [20]. Early in our study period, a 4- or 6-Fr straight tube was used as an external...
stent in D-D, as in R-Y. However, stent tubes of these sizes often caused obstruction; several patients who had been given the narrow hepatic duct experienced biliary congestion or cholangitis after the external stent tube was clamped. Since January 2003, we started using a T-tube of 9- or 12-Fr in diameter, which suits the hepatic duct exactly, as an external stent. Previously, Randall demonstrated that the use of the T-tube did not reduce the biliary complication rate in liver transplantation[21]. However, in LDLT, the D-D anastomosis is a hepaticohepaticostomy, in which a narrow stoma and peristomal ischemia may easily occur. As reported previously, the incidence of BACs should be higher in LDLT than in whole liver transplantation. Actually, our experience showed that there were no such complications in the biliary tract in 5 LDLT patients with T-tube drainage, while patients with straight tube drainage experienced high incidence of BACs. Hashimoto also reported that use of T tube in LDLT might reduce the incidence of biliary stricture and can be an effective therapeutic option when endoscopic treatment is unsuccessful[33]. Therefore, we expect that the use of the T-tube may reduce the incidence of BACs, especially biliary strictures in LDLT. More experience is needed to confirm this.

Heffron and Reichert reported a high incidence of BACs in reduced-size liver transplantation or LDLT in comparison with cadaveric whole liver transplantation[4,7,26,27]. Prolonged cold ischemia, chronic rejection and cytomegalovirus infection have been proposed as important risk factors for BACs after liver transplantation[4,26,27]. However, in LDLT, there have not been so many reports regarding the incidence of BACs.

We analyzed the risk factors between patients with BACs and those without. The incidence of BACs was significantly higher in the patients with NAC. Previously, Kim and Kemeny reported ischemic change in the bile duct after TACE[26,27]. Ischemia is the most important cause of BACs as described above. It is possible that LDLT patients with HCC have suffered from ischemic bile duct injury following NAC and thus are more likely to undergo BACs after LDLT. In the future, a larger group of patients should be studied to verify this hypothesis.

In this series, the overall incidence of BACs was 39.4%. It is true that the incidence rate seems to be slightly higher than that in previous reports (18.2%-4.3%)[3,5,26,28,29]. However, these reports described little of a correlation between BACs and NAC. The high incidence of BACs in our study may be due to the inclusion of many patients with NAC.

Recently, a few authors found that multiple bile ducts in the graft are strongly correlated with a high risk of BACs[4,30,31]. Multiple bile ducts showed an increased occurrence of BACs also in our study. Among the nine patients with multiple bile ducts, five had BACs (55.6%), whereas among 25 patients with single bile duct, BACs occurred only in eight (32%). This difference was not statistically significant due to the low number of cases, and needs to be confirmed in the future by larger studies.

Although there was no significant difference in the incidence of BACs between the left-lobe and right-lobe patients, the patients with the right-lobe graft clearly had increased BACs, compared with those with the left-lobe (50% vs 36%). Marcos has previously reported that the incidence of multiple bile ducts or anatomical variations is very high in right-lobe graft. In our series, the incidence of multiple bile ducts was significantly higher in the right lobe graft than in the left lobe graft (60% vs 12%, P = 0.014, data not shown). The increased incidence of BACs in the right lobe graft might reflect the high incidence of BACs in patients with multiple bile ducts.

In summary, our experience showed an increase of bacteremia associated with BACs in the patients having received R-Y. Therefore, D-D might be a preferred and safer biliary reconstruction than R-Y. However, the surgical refinement of D-D should be required because of the high incidence of biliary strictures. Use of the T-tube stent might lead to a significant reduction of BACs in D-D.

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