

Risk Factors for Biliary Complications After Living-Donor Liver Transplant: A Single-Center Experience

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Abstract

Objectives: Biliary complications remain a major concern in living-donor liver transplant. They can lead to patient and graft loss. In this study, we retrospectively analyzed patients' records to identify factors that increase the frequency of biliary complications in living-donor liver transplant with an aim toward decreasing this frequency.

Materials and Methods: We performed 53 living-donor liver transplants between November 2002 and September 2007. Five cases were excluded because of graft or patient loss within 2 weeks resulting in 48 cases available for analysis. The effect of the following variables on the frequency of biliary complications was analyzed: recipient age, liver lobe used, number of graft bile ducts, number of biliary anastomoses, type of biliary anastomosis, and bile duct diameter 4 mm or smaller.

Results: Biliary complications were seen in 14 cases (29.1%). These included 9 biliary strictures, 3 bile leaks, and 2 bile leaks eventually healing as biliary strictures. The presence of more than 1 graft bile duct increased the frequency of biliary complications ($P = .03$). The other variables did not have a statistically significant effect on the frequency of biliary complications.

Conclusions: The rate of complications in our experience is comparable to that already published. The presence of more than 1 bile duct in the graft is

a risk factor for biliary complications in living-donor liver transplant. A review of the data suggests additional risk factors.

Key words: *Transplantation, Relative risk, Liver grafting, Hepatic, Biliary tract disease*

Introduction

Biliary complications remain a major concern in living-donor liver transplant. These complications include anastomotic biliary strictures and bile leaks. A bile leak from the cut surface of the graft is usually self limiting. Management of biliary complications is demanding, both for the patient and the transplant center and can lead to adverse effects on the quality of life after transplant. These complications also can lead to graft and patient loss. It is therefore important to identify factors that lead to an increased frequency of biliary complications. Patients with small-for-size grafts or patients in a deteriorated state before the transplant are particularly susceptible to increased mortality if they develop these complications (1). In this study, we retrospectively analyzed patients' records to identify factors that increase the frequency of biliary complications in living-donor liver transplant with an aim toward decreasing this frequency.

Materials and Methods

This work was approved by the ethics committee and conforms to the research guidelines implemented at King Faisal Specialist Hospital and Research Center. This work did not involve any experimental activities on patients; rather, it was the product of data analyses. Between November 2002 and September 2007, 53 living-donor liver transplants were performed at our center. Five cases were excluded because of patient or

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graft loss within 2 weeks, resulting in 48 cases being included in this study. The number of adult patients was 38; the number of the pediatric patients (ie, those aged < 12 years) was 10. The number of patients who had a right lobe graft was 36, while 7 patients had a left lateral segment graft, and 5 patients had a whole left lobe graft. Of these grafts, 40 had a single duct; double ducts were present in 7 grafts; and triple ducts were present in 1 graft. Regarding biliary anastomoses, 44 patients had a single anastomosis, and 4 patients had a double anastomosis. A duct-to-duct anastomosis was performed in 39 patients, and a Roux-en-Y anastomosis was performed in 9 patients. The total number of bile duct orifices to be constructed was 57 orifices in 48 grafts. Bile duct diameter 4 mm or smaller was present in 34 cases, while a diameter of more than 4 mm was present in 23 cases. A ductoplasty (joining 2 ducts together) was used in 5 grafts with more than 1 bile duct. Graft and technical variables are summarized in Table 1.

The demographics of the patients including the underlying causes of liver disease are summarized in Table 2. Bile leak was diagnosed by 1 or more of the

following: postoperative bilious drainage in the abdominal drains confirmed by high bilirubin content in the drainage fluid, drainage of abdominal fluid with a high bilirubin concentration, hepato-aminodiacetic acid scanning that confirmed a bile leak, or a leak diagnosed by endoscopic retrograde cholangiography or percutaneous transhepatic cholangiography. In the first 3 clinical situations, the leak was confirmed by either endoscopic retrograde cholangiography or by percutaneous transhepatic cholangiography. In 1 patient, the bile leak was caused by a missed bile duct in the graft.

Biliary strictures were usually suspected by elevated levels of bilirubin, alkaline phosphatase, and gamma glutamyl transferase. Strictures also were suspected by finding dilated intrahepatic biliary ducts upon graft imaging. Strictures were confirmed by magnetic resonance cholangiography and later on, by either percutaneous transhepatic cholangiography or by endoscopic retrograde cholangiography (Figure 1). We used the chi-square test to compare categorical variables and the Fisher exact test when necessary. The *t* test was used to compare means.

Table 1. Graft and technical variables.

| | |
|----------------------------|----|
| Right lobe graft | 36 |
| Whole left lobe | 5 |
| Left lateral segment graft | 7 |
| 1 duct | 40 |
| 2 ducts | 7 |
| 3 ducts | 1 |
| Total number of ducts | 57 |
| Bile duct (≤ 4 mm) | 34 |
| Bile duct (> 4 mm) | 23 |
| One anastomosis | 44 |
| More than 1 anastomosis | 4 |
| Duct-to-duct anastomosis | 39 |
| Roux-en-Y anastomosis | 9 |

Table 2. Demographics of 52 patients who had living-donor liver transplants.

| | |
|------------------------------|------------------|
| Average age, years | 39.16 \pm 19.9 |
| Male / female | 34 / 18 |
| MELP / PELD | 16.5 \pm 6.1 |
| Adult / pediatric | 42 / 10 |
| Primary Liver Disease | |
| HCV | 17 |
| HCV+HCC | 7 |
| Cryptogenic | 6 |
| HBV | 5 |
| Primary hyperoxaluria | 4 |
| Wilson's disease | 4 |
| HBV + HCC | 3 |
| Other causes | 6 |

Abbreviations: HCV, hepatitis C virus; HCC, hepatocellular carcinoma; HBV, hepatitis B virus; MELD, model for end-stage liver disease; PELD, pediatric end-stage liver disease.



Figure 1. Endoscopic retrograde cholangiography showing 2 biliary strictures in a graft with double duct-to-duct anastomosis.

Results

Biliary complications were encountered in 14 patients (29.1%). These included biliary strictures in 9 patients (18.75%), bile leak in 3 (6.25%), and 2 patients (4.16%) with an initial bile leak that evolved into biliary strictures. Biliary complications were

encountered in 5 of 8 grafts with more than 1 bile duct (63%) and in 9 of 40 grafts with a single duct (23%). More than 1 biliary anastomosis was needed in 4 cases, and 2 of these had biliary complications (50%); 12 of 44 cases with a single anastomosis had biliary complications (27%). Regarding the rest of the variables, 32% of adult patients had biliary complications, and 20% of pediatric patients had biliary complications; 31% of patients with right lobe grafts had biliary complications, while 25% of patients with left lobe grafts had biliary complications; 33% of patients with a Roux-en-Y anastomosis had biliary complications, and 28% of patients with a duct-to-duct anastomosis had biliary complications; 26% of the grafts with a bile duct diameter 4 mm or smaller had biliary complications, and 22% of the grafts with bile duct diameter larger than 4 mm developed biliary complications. The effect of each variable on the frequency of biliary complications is shown in Table 3.

All cases of bile leak were diagnosed within 1 month of transplant, and most biliary strictures were detected within the first 6 months after transplant. Two of our patients developed biliary strictures more than 2 years after transplant. These 2 biliary strictures were difficult to manage endoscopically and percutaneously, eventually requiring surgical correction.

Table 3. The effect of different variables on the incidence of biliary complications.

| Variable | Total number of patients | Number of patients with complications | Percentage of patients with complication | P value |
|---|--------------------------|---------------------------------------|--|---------|
| Age group | | | | |
| Pediatric | 10 | 2 | 20 | > .05 |
| Adult | 38 | 12 | 32 | |
| Lobe used | | | | |
| Right | 36 | 11 | 31 | > .05 |
| Whole left lobe or left lateral segment | 12 | 3 | 25 | |
| Number of ducts | | | | |
| 1 | 40 | 9 | 23 | .03 |
| > 1 | 8 | 5 | 63 | |
| Number of anastomoses | | | | |
| 1 | 44 | 12 | 27 | > .05 |
| > 1 | 4 | 2 | 50 | |
| Type of anastomosis | | | | |
| Duct-to-duct | 39 | 11 | 28 | > .05 |
| Roux-en-Y | 9 | 3 | 33 | |
| Duct diameter | | | | |
| ≤ 4 mm | 34 | 9 | 26 | > .05 |
| > 4 mm | 23 | 5 | 22 | |

All biliary complications were initially treated with either endoscopic retrograde cholangiography or percutaneous transhepatic cholangiography; none was treated surgically. Resolution was achieved in 7 of 14 patients with a success rate of 50%. Surgical correction was eventually needed in 7 cases, and resolution was achieved in 5 cases with a success rate of 71%. Endoscopic retrograde cholangiography and percutaneous transhepatic cholangiography were used when surgical correction failed.

Of 53 living-donor liver transplant procedures performed at our center, 44 patients are currently alive at a median follow-up of 968 days (range, 1344-690 days). Kaplan-Meier patient and graft survival rates were 86.2% and 78.5% at 1 year and 80.3% and 75.4% at 5 years. Causes of death were primary graft nonfunction (n=2), portal vein thrombosis (n=1), aspiration pneumonia (n=1), tumor recurrence (n=1), hepatitis C virus recurrence (n=1), death on the operating table (n=1), sepsis (n=1), and invasive tuberculosis (n=1).

Discussion

Biliary complications remain the major concern in patients undergoing living-donor liver transplant. Duct-to-duct anastomosis has gained widespread acceptance as the procedure of choice for biliary reconstruction after living-donor liver transplant (1-8).

Biliary complications were encountered in 29.1% of our patients. This is comparable to published data regarding the frequency of biliary complications in living-donor liver transplant, which varies anywhere between 12.5% and 60% (1-8). Significantly lower rates of biliary complications have been achieved since the introduction of newer techniques for biliary reconstruction in living-donor liver transplant (9, 10). We found that the presence of more than 1 bile duct in the graft was associated with a higher frequency of biliary complications: In our study, 63% of grafts with more than 1 bile duct had biliary complications, and only 23% of those with a single duct had biliary complications ($P = .03$). While the frequency was also higher when more than 1 biliary anastomosis was performed (27% for a single anastomosis and 50% for more than 1 anastomosis), there was no statistically significant difference ($P > .05$). We also found that recipient age, liver lobe used, type of biliary anastomosis, and diameter of the bile ducts (4 mm or

less) have no effect on the frequency of biliary complications.

Other investigators have reported additional risk factors including bile duct diameter less than 4 mm (3), duct-to-duct anastomosis (1, 3, 5), and the use of neoadjuvant chemotherapy (11). Cytomegalovirus infection, ABO incompatibility, and a hepatic artery thrombosis also have been described as risk factors (1). In fact, we encountered 1 case of biliary stricture related to a hepatic artery thrombosis, which we treated with the insertion of a metallic stent (because the conventional stents failed), with resolution of the biliary strictures at 2-year follow-up.

Although the effect of the liver lobe used on the frequency of biliary complications was not statistically significant in this study, we believe that right lobe grafts tend to have a more-complex biliary anatomy than do left lobe grafts, which may result in a higher frequency of biliary complications in right lobe grafts. Hwang and associates (3) reported a higher frequency of biliary strictures in right lobe grafts.

In our experience, 2 patients had biliary strictures more than 2 years after implantation. This points to the importance of long-term follow-up to establish the true frequency of biliary complications after living-donor liver transplant. Because of the development of "late-onset biliary strictures," Hwang and colleagues (3) suggest 3 years as a minimum follow-up.

We believe that some of the differences between our results and those previously published are related to the relatively smaller size sample that we analyzed.

In conclusion, biliary complications remain a major concern in living-donor liver transplant despite the tremendous efforts to decrease their frequency. Multiple bile ducts in the graft are associated with a higher frequency of biliary complications. According to our and published data, doing more than 1 biliary

anastomosis also may be associated with a higher frequency of biliary complications. Other factors including recipient age and type of anastomosis have no effect on the frequency of biliary complications. The duct-to-duct technique is the preferred method of biliary reconstruction in living-donor liver transplant. A minimum of 3 years follow-up may be needed to establish the true frequency of biliary complications after living-donor liver transplant.

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