Endoscopic treatment of biliary complications in donors after living donor liver transplantation in a high volume transplant center

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ABSTRACT

Background/Aims: Although living donor liver transplantation (LDLT) has been accepted as a primary treatment for adults with end-stage liver disease, concerns about donor health have emerged. As LDLT is technically complex, it creates perioperative morbidity and mortality risk in donors. Biliary complications such as stricture and leakage are seen most frequently in donors after liver transplantation. While some of these complications get treated with a conservative approach, endoscopic, surgical, and percutaneous interventions may be required in some others. We aimed to present endoscopic retrograde cholangiopancreatography (ERCP) results in donors who developed biliary complications after LDLT.

Materials and Methods: Between June 2010 and January 2018, a total of 1521 donors (1291 right lobe grafts, 230 left lobe grafts) who underwent LDLT were retrospectively reviewed. Sixty-three donors who underwent ERCP due to biliary complication were included in the study.

Results: Biliary stricture was found in 1.6% (25/1521), biliary leakage in 2.1% (33/1521), and stricture and leakage together in 0.3% (5/1521) donors. Our endoscopic success rates in patients with biliary leakage, biliary stricture, and stricture and leakage were 85% (28/33), 92% (23/25), and 80% (4/5), respectively. Surgical treatment was performed on 12.6% (8/63) donors who failed ERCP.

Conclusion: We found that ERCP is a successful treatment for post-LDLT donors who have biliary complications.

Keywords: Living donors, liver transplantation, cholangiopancreatography, endoscopic retrograde, bile duct

INTRODUCTION

The cadaveric liver transplantation due to organ donation is the first priority in the Western countries, whereas living donor liver transplantation (LDLT) is preferred in majority of Asian countries (1). Despite the fact that the left lobe was used extensively in the pediatric patient group in the initial years, with an increased number of patients waiting for transplantation, improved surgical techniques, and reduced donor mortality, right lobe liver transplantation had begun to be applied (2, 3). With an increased number of directly supplied organs, provided elective conditions for the recipient and shortened duration of cold ischemia, LDLT is superior in many ways than liver transplants made from cadaveric donors. Despite these advantages, LDLT donor safety continues to be an area of concern (4, 5). Post-LDLT donor mortality being the most important complication, is usually less than 1%. The most common complication is biliary complication, which is usually seen between 6% and 9.3%. Biliary leakage and stricture are the most frequently seen complications among the biliary complications. Most of the biliary complications are mild and recover with a conservative approach. Unresolved cases may require endoscopic, surgical, and percutaneous intervention (4, 6, 7). In most publications related to donors, the results of all complications have been reported. There are few publications regarding biliary complications and their treatment in donors after LDLT.

In this study, we aimed to present biliary complications and our endoscopic treatment results in the management of these complications in post-LDLT donors.

MATERIALS AND METHODS

A total of 1521 donors, who underwent LDLT between June 2010 and January 2018, were retrospectively reviewed. Sixty-three donors, who underwent endoscopic retrograde cholangiopancreatography (ERCP) due to biliary complications, were included in the study. The study

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was approved by the ethics committee of our university (decision number 20018/18-19) and written informed consents for reaching medical histories and interventions were obtained from all patients.

The demographic characteristics of the donors, ERCP indications (stricture and/or leakage), time past until first ERCP after transplantation, number of ERCP sessions, type of treatment applied, the number and diameter of inserted stents, result of the treatment, and whether or not percutaneous intervention was performed, were reviewed and noted. In all donors who developed biliary complications, the ERCP decision was made by a multidisciplinary committee that included gastroenterologists, transplant surgeons, and radiologists.

When the drainage of 100 mL per day of the bile content from the inserted tube during the surgery of the donor does not stop for almost 7–10 days after the surgery or the appearance of the bile content on intra-abdominal needle aspiration, this complication is defined as biliary leakage. ERCP was performed when bile leakage continued from the drains despite the symptomatic care. Computed tomography or magnetic resonance imaging was performed in donors who had cholangitis or abnormal liver tests. When there were findings of a biliary stricture in these image studies, ERCP was preferred. The ERCP process was performed using a video duodenoscope (TJF 160, Olympus Optical Co., Ltd., Tokyo, Japan) after a 6–8-h fasting. The leakage or stricture region was confirmed by cholangiography using contrast medium during ERCP. All donors were subjected to endoscopic sphincterotomy (EST) during ERCP. For those who had biliary leakage, endobiliary stents were placed across the leakage region via a 0.025- or 0.035-inch guide wire (Jagwire, Boston Scientific, Natick, MA, USA).

MAIN POINTS

- *The primary concern in LDLT is donor safety.*
- *The most common complication in donors after LDLT is biliary complication.*
- *Radiological and surgical interventions are more invasive procedures compared to endoscopic procedures and carry the risk of increasing donor morbidity and mortality.*
- *We found that ERCP is a successful treatment for post-LDLT donors who have biliary complications.*
- *To share data of one of the centers with the highest LDLT count on the world scale may make an important contribution to the literature in managing donor hepatectomy complications.*

In the cases where biliary strictures were detected, the stricture region was passed using a guide wire during ERCP. Depending on the severity of the stricture, a direct stent was inserted to the mild stricture, and when the stricture was severe, a biliary balloon (4, 6, or 8 mm, Hurricane RX, Boston Scientific, Marlborough, MA, USA) and/or bougie (7 and 10 French [Fr], Wilson-Cook Medical GI Endoscopy, Winston Salem, NC, USA) were used to dilate the stricture and endobiliary stents (Amsterdam-type biliary stents, 7 and 10 Fr, 9–18 cm long, Boston Scientific, Marlborough, MA, USA) were placed across the stricture.

The mean stent revision time in our center is 3–6 months. However, control ERCP was performed in the patients whose leakages were stopped after an average of 1–3 months from the first ERCP. The duration of stenting was determined based on the complete recovery of the biliary leakage and stricture. When biliary complication persisted, restenting and/or redilatation were performed endoscopically. When the donors who were followed up without stents were normal clinically, laboratorily, and radiologically, ERCP was considered successful.

In the cases in which ERCP failed (persistent biliary complication despite dilatation and stent placement), our multidisciplinary team determined whether percutaneous transhepatic biliary intervention (PTBI) and/or surgical treatment was indicated. When endoscopic and percutaneous treatments were unsuccessful, surgical treatment was considered as the last option. In this study, ERCP was considered successful when donors included in the study did not have PTBI, surgery, or death due to biliary complication at any time during follow-up after first ERCP.

Statistical Analysis

The data were analyzed using the Statistical Packages for the Social Sciences (SPSS) version 16.0 (SPSS Inc., Chicago, IL, USA) after being entered manually.

RESULTS

A total of 1521 (1291 right lobe grafts, 230 left lobe grafts) liver donors were retrospectively reviewed. The LDLT donor biliary complication rate was 4.1% (63/1521). It was observed to be 4% (52/1291) in right lobe donors and 4.7% (11/230) in left lobe donors. Biliary stricture, leakage, and stricture and leakage frequencies in all donors were 1.6%, 2.1%, and 0.3%, respectively. Our study included 63 (4.1%) donors who underwent ERCP and had developed biliary complications. Of these donors, 17 (26.9%) were female, and the median age was 30 (20–51). Biliary stricture, leakage, and stricture and leakage

Table 1. Biliary complication frequency of donors who underwent ERCP.

Biliary complication type	Biliary stricture (39.6%, n=25)	Biliary leakage (52.4%, n=33)	Biliary stricture and leakage (8%, n=5)	Total (100%, n=63)
Age (median)	30 (20–51)	29 (21–45)	30 (22–40)	30 (20–51)
Sex (female, %)	7 (28)	9 (27.2)	1 (20)	17 (26.9)
Lobe type (right/left, %)	20 (80)/5 (20)	27 (81.8)/6 (12.2)	5 (100)/0 (0)	52 (82.5)/11 (17.5)

Table 2. ERCP results in donors who developed biliary complication.

Biliary complication type	Median of time to first ERCP (week)	Median of ERCP procedure number	Endoscopic treatment	Stent diameter (Fr)	Outcome	Mean follow-up duration (months)
Biliary stricture (n=25)	7 (2–24)	2 (1–6)	ST (56%, n=14), BD/ST (24%,n=6), BD (12%, n=3), only EST (8%, n=2)	7 Fr (68%, n=17) 7 Fr and 10 Fr, respectively (12%,n=3)	WS and SFr (76%, n=19), SG (4%, n=1), PTBI+SG (4%, n=1), WS (4%, n=1), FW* (12%, n=3)	WS and SFr: 6 (2–48) and 22 (1–56) respectively, WS:6, FW*: 28 (24–45)
Biliary leakage (n=33)	2 (1–24)	2 (1–5)	ST (81.8%, n=27), only EST (12.8%, n=6)	7 Fr (72.7%, n=24), 10 Fr (9.1%, n=3)	WS and SFr (66.6%, n=22), SG (15.1%, n=5), FW* (18.3%, n=6)	WS and SFr: 3 (1–28) and 26 (3–98) FW*: 64 (33–90)
Biliary stricture and leakage (n=5)	3 (2–6)	2 (1–4)	ST (80%, n=4)	7 Fr (80%, n=4)	WS and SFr (40%, n=2), PTBI+SG (20%, n=1), WS (40%, n=2)	WS and SFr: 8–12 and 3–12, respectively, WS: 2–14

*Only patients who underwent EST and/or BD.
ST: stent; BD: biliary dilatation; EST: endoscopic sphincterotomy; WS: with stent; SFr: stent-free; SG: surgery; PTBI: percutaneous transhepatic biliary interventions; FW: follow-up.

frequencies were 39.6%, 52.4%, and 8%, respectively, in the donors who underwent ERCP (Table 1).

Stricture was detected in 20 of the right lobe donors and 5 of the left lobe donors. ERCP was successfully applied on 23 (92%) donors who had stricture (Table 2). In two donors, the stricture could not be treated with ERCP. One of these patients underwent PTBI after ERCP. Stenting could not be performed on this donor due to tight stricture. So, the stricture was dilated only. Later, when the stricture did not heal with PTBI treatment, surgery was performed. In the other donor, surgical treatment was performed directly because of tight stricture (Figure 1). In donors with stricture, the median time till the first ERCP after transplant was 7 (2–24) weeks. The median number of ERCP processes in donors with stricture was 2 (1–6). In two donors, only EST was performed. Only biliary stent was applied to 14 donors. In 6 donors, stenting was performed after biliary dilatation. Only biliary dilatation was applied on 3 donors who developed stricture (Table 2). Median stenting period of 20 stented patients who had stricture was 6 (2–48) months. All donors are being followed up without stents except one. The median stent-free follow-up period of these patients is 22 (1–56) months. No recurrence was observed in any patient without stents. In 15 of the patients with stricture, the stentless follow-up period was 12 months or more. In 4 patients, the follow-up period was shorter than 12 months. In the first ERCP session, the 7-Fr stent was inserted in all donors with stricture. In the subsequent ERCP sessions for stent revision, a stent revision was done with 10-Fr stents in 3 cases and two 7-Fr stents in 2 cases because

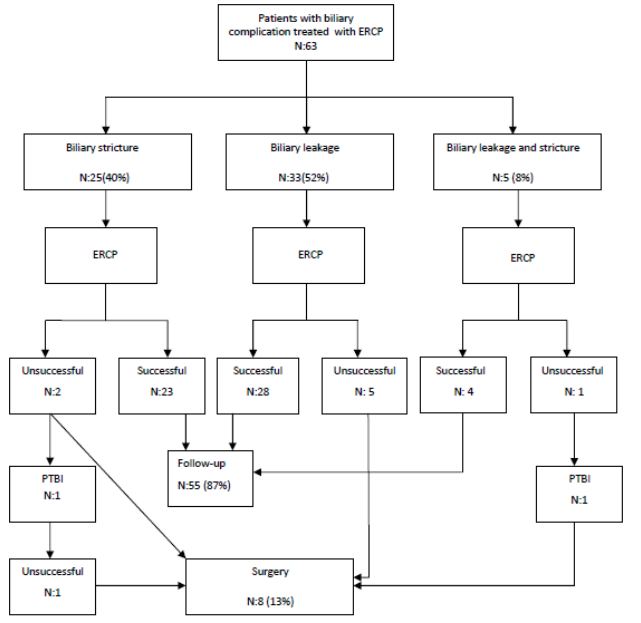

Figure 1. The treatment diagram that we applied to donors who had biliary complications.
ERCP: endoscopic retrograde cholangiopancreatography; PTBI: percutaneous transhepatic biliary interventions

one 7-Fr stent did not fix the stricture. Stent revision continued with one 7-Fr stent in all remaining donors till the stricture was treated (Table 2).

Leakage was observed in 27 of the right lobe donors and in 6 of the left lobe donors (Table 1). ERCP was successfully applied on 28 donors (85%) due to biliary leakage. Surgical treatment was performed on 5 (15%) donors whose leakage problem could not be treated with ERCP (Figure 1 and Table 2). The time till the first ERCP after transplantation was two weeks (1–24 weeks) in donors with leakage. The median number of ERCP processes in donors with leakage was 2 (1–5). In 6 donors with biliary leakage and who only underwent EST, all donors recovered with this treatment (Table 2). The median duration of follow-up after first ERCP in these donors was 64 (33–90) months. In three donors, stricture developed after leakage and stenting continued till the stricture was treated. All 22 donors, whose leakages were successfully treated with ERCP by stenting, are being followed up without stents. In 16 of these patients, the stentless follow-up period was 12 months and more, whereas, in 6 of these patients, the stentless follow-up period was below 12 months. The median stented and stent-free period of these patients are 3 (1–28) months and 26 (3-98) months, respectively. 10-Fr stents were inserted in 3 donors with leakage. A 7-Fr stent was performed in all remaining donors (Table 2).

Leakage and stricture together were observed in 5 donors, and all were right lobe donors (Table 1). ERCP was successfully applied on 4 (80%) cases, but only two patients were followed up without stents. ERCP was unsuccessful on 1 donor. Later on, PTBI and surgery were performed, respectively (Figure 1). The period till the first ERCP after transplantation was 3 weeks (2-6 weeks) in donors with leakage and stricture. The median number of ERCP processes in donors with leakage and stricture was 2 (1–4). Stenting was performed on 4 patients. Two of these donors are still being stented, and the follow-up period of these 2 donors is 14 and 2 months, respectively. Two patients were followed up without stents, and the follow-up period of these donors was 3 and 12 months, respectively. 7-Fr stents were used in all cases (Table 2). Eight patients had pancreatitis and three patients had bleeding at the EST site. All patients recovered with medical treatment. Endoscopic and/or surgical intervention were not needed in any complicated cases.

DISCUSSION

In this study, in donors who developed biliary complications after LDLT, biliary stricture was found in 25 donors, biliary leakage in 33 donors, and stricture and leakage in 5 donors. ERCP was successfully applied on 23 (92%) cases due to biliary stricture, 28 (85%) cases due to biliary leakage, and 4 (80%) cases due to biliary stricture and leakage together. Surgical treatment was performed on 2 (8%) patients with biliary stricture, 5 patients (15%) with biliary leakage, and 1 patient (20%) with both biliary leakage and stricture. Donors with stricture, who did not have surgery, are being followed up without stents except one. The median stent-free follow-up period of these patients was 22 months. All donors with leakage, who did not have surgery, are being followed up without stents. In 16 of these patients, the stentless follow-up period was 12 months and more, whereas, in 6 of these patients, the stentless follow-up period was below 12 months. The median stent-free period of these patients was 26 months. Two donors with stricture and leakage, who did not have surgery, are being followed up without stents. The stent-free follow-up period of these donors was 3 and 12 months, respectively.

Although LDLT has been accepted as a primary treatment for adults with end-stage liver disease, concerns about donor health have emerged. Although many different complications may be seen, the most common complication is

biliary problem. New large-scaled and multicenter studies reported that new techniques have reduced complications in donor hepatectomies (8,9). To share data of one of the centers with the highest LDLT count on the world scale may make an important contribution to the literature in managing donor hepatectomy complications.

LDLT is technically complex. It poses risks for donors because of perioperative morbidity and mortality (5). As surgical techniques may vary, in some centers, 60% of the right lobe is taken, while in some others, 70% of the right lobe is taken. This lack of surgical standardization, such as the lack of consensus on the amount of liver tissue to be resected, and the surgeons' experience, significantly affect morbidity (10,11).

The complication rates in the right lobe liver donors are determined to be significantly higher than those in the left lobe grafts. The right lobe donor morbidity rates range from 0% to 67%; the probable cause of this being in such a wide range is the fact that the definition of complication is different among centers (3,10). In our current study, the LDLT donor biliary complication rate has been detected as 4.1%; it was observed to be 4% in right lobe donors and 4.7% in left lobe donors. Lo et al. have found that the rate of biliary complication in the study was 5.4% (12). Hwang et al. found the rate of biliary complication as 0.8% in a study involving 1162 cases (13). In a meta-analysis by Yuan et al., it was reported that the mean complication rate of 11 studies was 5% (14). Our findings are consistent with the rates in the literature. Biliary complications of right lobe liver donors are observed at higher rates than left lobe donors. In a study including 731 donors, the leakage was observed to be 9.9% and 1.7% in right lobe donors and left lobe donors, respectively (15). In a study involving 69 right and 137 left lobe donors performed by Taketomi and his colleagues, biliary complication was observed in 11 (5.3%) cases. This ratio was 10% in the right lobe donors, while it was 2.9% in the left lobe donors (16). High right lobe LDLT experience in our center may explain our low biliary complication rate in the right lobe donors.

Biliary leakage in donors is seen more commonly than biliary tract strictures. Biliary leakage has an average between 2.4% and 6.6%, while the biliary tract stricture is observed between 1.6% and 2.9% (15,16). In our study, stricture was 1.6%, while biliary leakage was 2.3%. The results of our study were consistent with the literature. Biliary leakage and/or stricture can be seen after ductal resection in donors undergoing hepatectomy. Conservative, endoscopic, and radiologic methods are often used in the management of biliary complications. If the biliary problems do not recover with these methods, surgery is needed (17). Radiological and surgical interventions are more invasive procedures compared to endoscopic procedures and carry the risk of increasing donor morbidity and mortality. In biliary leakage, endoscopic treatment can reduce the bile duct–duodenal pressure gradient and can prevent leakage of bile by placing a stent to bypass the leakage site. Endoscopic treatment is safe for patients with postsurgical biliary leakage. Sphincterotomy with biliary stent or biliary stent alone can be used in this treatment (18). The first treatment method in donor biliary complication is ERCP, and its success rate is significantly high. In a study by Shio et al, 19 of 24 donors (79.1%) with biliary leakage and 4 of 7 donors (57.1%) with biliary stricture were successfully treated with ERCP (15). In another study involving 337 patients, ERCP was successfully applied on 9 (81%) of 11 cases with strictures and 5 (100%) of 5 cases with biliary leakage (6). In our study, ERCP was performed successfully on 23 (92%) cases with biliary stricture. ERCP was successfully applied on 28 (85%) donors who had biliary leakage. ERCP was successfully applied on 4 (80%) cases with stricture and leakage together, but only two patients were followed up without stent. The number of patients in our study is more than those in these studies. Our ERCP success rates in patients with stricture and leak are higher than the rates found in these studies. Our findings suggest that endoscopic treatment is effective in the treatment of biliary complications in donors.

The ERCP success rate in biliary strictures in recipients after LDLT varies between 42.4% and 75% (19,20), and it varies between 34% and 82% in patients with leakage (21,22). In our study, the success rate of ERCP, after LDLT, was 65.1% in patients with strictures and 55% in patients with leakage (23). Publications related to ERCP results in donors are not as many as that for recipients. According to these data, ERCP success rates in donors are higher than the recipients. This difference can be explained by reasons specific to the recipient operation, such as single or multiple anastomoses in the recipient biliary reconstruction and mismatch of the recipient and donor biliary duct diameters (24).

We usually start stenting with a 7-Fr stent in biliary complications such as biliary stricture and/or leakage. Often a 7-Fr stent is sufficient for biliary leakage. However, in some biliary stricture cases, the 7-Fr stent may be insufficient to treat the stricture. In such cases, the diameter of the stent can be increased to 10 Fr. In cases in which a

10-Fr stent is insufficient, the 7- and/or 10-Fr stent can be applied more (15). Woo and colleagues used a 10-Fr stent in biliary stricture and a 7-Fr stent in biliary leakage (6). In our cases, we started by using 7-Fr stent in donors having biliary stricture. In later sessions, the 10-Fr stent was used in 3 cases and two 7-Fr stents were used in 2 donors. We continued with the 7-Fr stent in all the remaining donors. We followed up 3 donors with the 10-Fr stent and the remaining donors with biliary leakage with 7-Fr stent. 7-Fr stents were placed in all the cases with both biliary leakage and stricture.

In our study, we detected that high success was achieved with ERCP in treatment of biliary complications developed in donors after LDLT, and no recurrence was seen in long-term follow-ups of these donors. Our results suggest that ERCP increases donor safety in terms of biliary complications.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İnönü University (decision number 20018/18-19).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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