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ORIGINAL ARTICLE

Removable intraductal stenting in duct-to-duct biliary reconstruction in liver transplantation

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Summary

Biliary reconstruction during liver transplantation (LT) is most oftenly performed by duct-to-duct biliary anastomosis. We hypothesized that the internal stenting might diminish the incidence and severity of biliary complications in patients receiving small duct size donor grafts. The purpose of this study was to report a technique of biliary reconstruction, including intraductal stent tube (IST) placement followed by postoperative endoscopic removal. A custom-made segment of a T-tube was placed into the bile in 20 patients in whom the diameter of the graft bile duct was smaller than 5 mm. The tube was removed endoscopically 4–8 months after LT, or in case of IST-related adverse events. After a median follow-up of 15.2 (range 2.5–27.5) months, endoscopic removal of the IST was performed in 17 patients. No technical failure and no procedure-related complications were recorded during drain removal. Biliary complications occurred in four patients, including one cholangitis, one hemobilia, one asymptomatic biliary leakage, and one anastomotic stricture. No biliary complication occurred in the group of patients who underwent deceased donor whole graft LT. IST is technically feasible and safe, and may help to prevent severe biliary complication when duct-to-duct biliary anastomosis is performed on small size bile ducts.

Introduction

In liver transplantation (LT), biliary tract reconstruction is the final step of the surgical procedure and requires good technical skills. It can be performed either by an end-to-end [1] or a side-to-side [2] ductal anastomosis. When a duct-to-duct anastomosis is not feasible for anatomical reasons or because of an underlying biliary disease, the biliary reconstruction is performed by hepaticojejunostomy [3]. At the end of a difficult procedure, the biliary anastomosis is inappropriately viewed as the easy step of the operation; however, biliary complications are severe events which may eventually compromise outcomes of LT. Despite technical progress in the field of LT, incidence of biliary complications remains high, ranging from 10% to 50% in large clinical series [1,4–8].

Biliary complications are significant causes of post-transplantation morbidity and graft loss. Early complications are mostly represented by bile leaks whereas strictures and their consequences are described as late complications [9]. Technically, the end-to-end choledocho-choledocostomy is the most widely accepted technique for biliary reconstruction. The usefulness of a T-tube placement in whole graft deceased LT has been debated in the literature [1,10].

Our group has published the first randomized study demonstrating that biliary reconstruction may preferentially be performed without a T-tube [1]. In this

multicentric randomized trial, 60% of the overall biliary complications tube following LT were related to the use of the T-tube itself and included mostly bile leaks around the T-tube and cholangitis. Finally, the use of a T-tube had no impact on the rate of biliary strictures but T-tubes were usually removed early, within 3 months following LT. Based on these results, we do not use external biliary drain in LT.

On the other end, endoscopic series have highlighted the efficiency of a prolonged stenting to treat for the treatment of biliary stenosis [11,12]. Given the potential benefit of a prolonged stenting and the reported side effects of an external biliary drainage, we sought to develop a new technique of intraoperative intraductal stent tube (IST) placement followed by its endoscopic stent removal in the postoperative period. We hypothesized that a prolonged and exclusive internal stenting of the duct-to-duct biliary anastomosis may decrease the incidence and severity of both early and late biliary complications while avoiding the drawbacks of a T-tube placement in patients who receive small duct liver grafts. The primary goal of the study was to evaluate the feasibility and safety of this new IST technique. The second endpoint was to assess the ability of the IST technique to prevent the occurrence of biliary complications, especially in the case of small bile ducts reconstruction, which carry a high risk of stenosis.

Methods

Study population

From February 2007 to May 2009, 119 adult LT were performed in our department. Among this population, 20 patients underwent an elective deceased donor LT with the IST technique and were followed prospectively. Demographic characteristics and indications for LT are depicted in Table 1.

Table 1. Demographic characteristics and surgical indications of patients undergoing transplantation.

Patients	20
Gender (M/F)	15/5
Age (year), mean ± SD (range)	49.2 ± 13 (15–65)
Body mass index (kg/m^2), mean ± SD (range)	23.5 ± 4.3 (16.4–35.9)
Previous abdominal surgery, *n* (%)	10 (50)
Indication for liver transplantation	
HCC, *n* (%)	7 (35)
Posthepatitis C cirrhosis, *n* (%)	4 (20)
Posthepatitis B cirrhosis, *n* (%)	1 (5)
Alcoholic cirrhosis, *n* (%)	3 (15)
Polycystic liver disease, *n* (%)	2 (10)
Cystic fibrosis, *n* (%)	2 (10)
Overlap syndrome, *n* (%)	1 (5)
Cirrhosis, *n* (%)	17 (85)
Child (A/B/C)	5/5/7
MELD score, mean ± SD (range)	15.5 ± 6.4 (6–26)

HCC, hepatocellular carcinoma; SD, standard deviation.

Surgical technique and outcomes monitoring

Liver recovery was performed using standard techniques, and University of Wisconsin solution was used for organ preservation. Bile ducts were systematically washed with preservation fluid during organ procurement. Indication for an IST placement at the time of LT was a diameter of the donor bile duct of 5 mm or less. Duct-to-duct biliary reconstruction was always performed via a hepaticocholedocostomy using interrupted polydioxanone .00000 sutures. The connective tissue surrounding bile ducts of the donor and the recipient bile ducts were systematically preserved to ensure a good periductal vascularization. A custom-made segment (2 cm) of a 8 French T-tube was used for the confection of the IST (Fig. 1). No side holes were created. The stent was inserted in the biliary duct without suture fixation. The endoscopic procedure for IST removal was scheduled 4–8 months following LT. Immediate removal was performed in case of IST-related adverse events, such as: abnormal liver function tests (cholestasis or transient hepatocellular dysfunction), fever or intrahepatic bile duct dilatation of more than 2 mm on ultrasound, computed tomography scan or magnetic resonance cholangiography (MRC). IST extraction was performed using a Dormia basket or an endoscopic staple extractor (Fig. 2). The endoscopic IST removal procedure was performed by the same endoscopist (FP), highly experienced with endobiliary maneuvers [13,14].

Operative mortality and morbidity were recorded prospectively for both the LT and endoscopic retrograde cholangiopancreatography (ERCP) procedures. For ERCP,

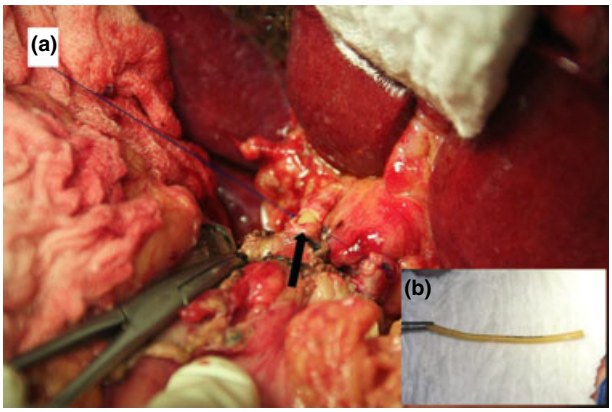

Figure 1 The biliary duct-to-duct anastomosis is performed (a, black arrow) with interrupted sutures, using a custom-made IST (b).

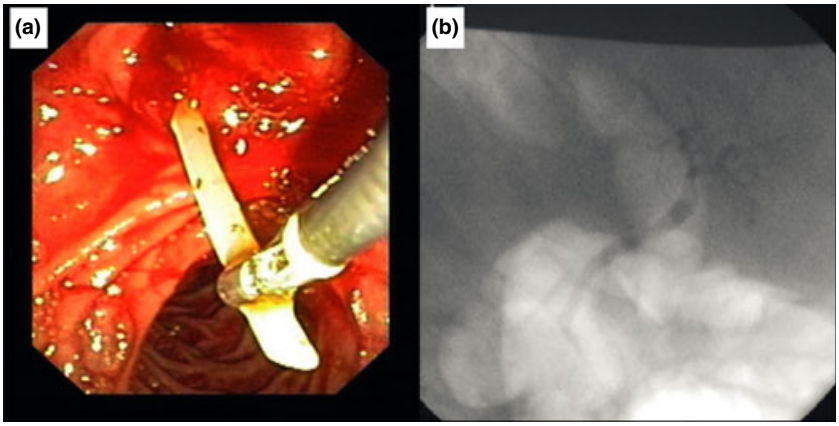

Figure 2 Endoscopic removal of the stent (a) and post-ERCP cholangiography (b).

the rate of pancreatitis, bleeding, duodenal perforations, and failure to remove the IST were specifically monitored. Evaluation of postoperative biliary complications was the second endpoint of the study. All deaths, operative complications [before postoperative day (POD) 90], and late complications (>POD 90) were recorded; complication severity was stratified according to the modified Clavien classification [15].

Statistical analysis

Categorical data were analyzed after setting up multiple 2×2 contingency tables using the chi-squared test or Fisher exact test when appropriate. Because of the small sample size, continuous data were analyzed using the Mann–Whitney *U*-test and expressed as mean ± standard deviation and (range), or median and (range). Cumulative overall survival was computed according to the Kaplan–Meier method. Statistical analysis was made using SPSS 16.0 (Chicago, IL, USA) for Windows software.

Results

Among the 20 patients who underwent IST, 16 patients received a whole liver graft (including one domino), three patients received a split graft (full right graft: segments V-VI-VII-VIII), and one patient received a reduced graft (full left graft: segments II-III-IV). The donor common bile duct was always conserved in partial grafts; thus, hepaticocholedocostomy could be undertaken in these patients as previously described. A combined liver and kidney transplantation was performed in two patients. Intraoperative data of patients who underwent LT and IST are depicted in Table 2. No patient died postoperatively. Postoperative morbidity was 50%. One-year overall survival was 95% (Fig. 3). After a median follow-up of 12.7 (range 3.5–28.5) months, one patient died from a hepatitis C virus recurrence 16 months after LT and another one died from a pulmonary embolism 1 year after LT.

Feasibility and safety of IST

The IST was successfully inserted in all the patients during LT. Eighteen patients underwent a pre-ERCP imaging prior to stent removal: 12 MRC and six ultrasounds after a median of 15 (range 7–180) days following LT. After a median follow-up of 12.7 (range 3.5–28.5) months, endoscopic removal of the IST was successfully performed in 17 patients (85%). One patient died from a pulmonary embolism and two others were lost to follow-up before stent ablation. The median delay between LT and IST

Table 2. Intraoperative data of patients undergoing transplantation.

Type of graft	
Whole deceased donor, *n* (%)	15 (75)
Split (full right graft: V-VI-VII-VIII), *n* (%)	3 (15)
Reduced (full left graft: II-III-IV), *n* (%)	1 (5)
Domino, *n* (%)	1 (5)
Graft weight (g), mean ± SD (range)	1234 ± 311 (580–1700)
Graft steatosis (>10%/10–1%/<1%)	1/2/17
Donor age (year), mean ± SD (range)	48 ± 11.2 (60–25)
Cold ischemia time (hour), mean ± SD (range)	9.7 ± 2.4 (3.5–13)
Warm ischemia time (min), mean ± SD (range)	64 ± 20.9 (40–120)
Piggyback implantation of the liver graft	16
Vena cava replacement	4
Intraoperative transfusion, *n* (%)	5 (25)
Packed red cell units ± SD	4.6 ± 3.9
Donor bile duct size (3 mm/4 mm/5 mm)	4/6/10

SD, standard deviation.

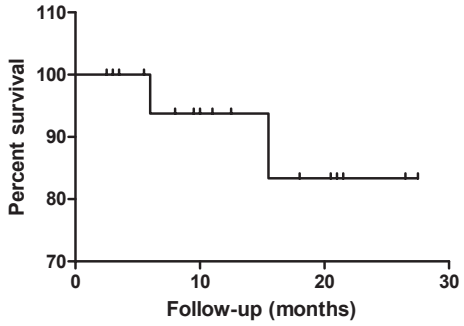

Figure 3 Overall survival.

removal was 26.5 (range 4–72) weeks. During ERCP, a limited sphincterotomy (infundibulotomy) was necessary for IST removals in 15 (88.2%) patients. IST extraction was performed using a Dormia basket in five patients (29.4%) or using an endoscopic staple extractor in 11 patients (64.7%). No technical failure was recorded during drain removal. In one patient, imaging showed 5 months after LT that the drain had spontaneously migrated into the duodenum. It was confirmed during ERCP. A minor and transient elevation of serum amylase level with no clinical symptoms was the only event recorded in one patient after drain removal (Table 3). The stent removal procedure and post-ERCP cholangiography are illustrated in Fig. 2.

Impact of IST placement on biliary complications

Biliary complications occurred in four patients during follow-up. One cholangitis (Clavien II) was successfully treated with antibiotics and drain removal. However, the stent culture did not demonstrated infection. This event was suspected to be related to the migration of the distal part of the drain through the sphincter of Oddi, causing a reflux of digestive contents along the drain into the common bile duct. One patient who underwent combined liver–kidney transplantation developed a hemobilia (Clavien IVa) related to a bilioportal fistula, and was reoperated on POD 30. The IST was removed at the time of reoperation; external T-tube biliary drainage and suture of the portal vein were undertaken in this patient. Eventually, his postoperative course was uneventful. In another patient, asymptomatic biliary leakage (Clavien IIIb) was diagnosed at the time of endoscopic IST removal and was treated successfully by immediate positioning of a covered stent. An anastomotic stricture (Clavien IIIb) occurred 12 months after LT in one patient and was successfully treated by an endoscopic dilatation and stenting. No biliary complication was recorded in the group of patients who underwent a whole graft LT with IST placement. During the same period, biliary strictures occurred in 15 patients (15.1%) among the group of patients who underwent LT without IST placement.

Table 3. Data of patients undergoing intraductal stent tube ablation.

Ablation, *n* (%)	18 (90)
ERCP	17 (94.4)
Surgery*	1 (5.6)
Delay between LT and IST removal (weeks), median (range)	12.7 (3.5–28.5)
Endoscopic infundibulotomy, *n* (%)	15 (88.2)
IST extraction, *n* (%)	
Dormia basket	5 (29.4)
Endoscopic staple extractor	11 (64.7)
Spontaneous migration	1 (5.9)
Technical failure, *n*	0
Procedure-related complication rate, *n*	0

ERCP, endoscopic retrograde cholangiopancreatography; IST, intraductal stent tube.

*One patient who underwent combined liver–kidney transplantation developed bilioportal fistula requiring reoperation on POD 30 and stent removal.

Discussion

Decreasing the rates of biliary complications following LT remains a crucial goal for transplant surgeons and technical refinements are sought actively. To allow tissue healing and to prevent biliary complications, external diversion of the bile flow has been repeatedly advocated in the past. Eventually, reports from several transplant groups worldwide have shown that T-tube diversion of the biliary flow during LT did not prevent from bile leaks or ductal stenosis. Moreover, T-tube insertion itself was associated with an increased morbidity, mainly related to bile leaks at the site of drain insertion. Although others have recently reported opposite results for side-to-side anastomosis [10], we believe that an external biliary drainage in LT is not a valuable option and we do not use T-tubes anymore because of an increased morbidity related the drain placement itself [1,16].

Moreover, T-tubes have been hypothesized to prevent from late complications [17]. However, such assumptions are not supported by clinical reports as T-tubes are often removed early, within the initial three postoperative months, and this delay is probably too short to prevent from the development of biliary stricture. With the present study, we sought to develop a new technique to palliate these shortcomings of external biliary T-tube diversion. In patients with small size biliary duct-to-duct anastomosis, who are at high risk of biliary complication, the IST technique has two potential benefits: (i) protect the biliary anastomosis during tissue healing and (ii) prevent late stricture formation as a result of longer duration

of stenting. These assumptions are supported by the fact that endoscopic maneuvers, to treat biliary complications, have been widely used and the efficacy of endobiliary stents in treatment and prevention purpose is commonly accepted in the transplant community [11,12]. To our knowledge, internal stenting of the biliary anastomosis followed by delayed endoscopic stent removal with the aim to reduce the incidence and the severity of biliary complications after LT has not been previously reported. The present results show that IST placement in patients with high risk biliary reconstruction (duct size ≤5 mm) followed by endoscopic removal is technically feasible, safe, and seems to ameliorate early and late biliary outcomes after LT. No biliary complication occurred in the group of patients who underwent deceased donor whole graft transplantation with small bile ducts. Overall, most complications that occurred in our cohort of patients were successfully treated with a conservative treatment.

The first main finding of our study was that no technical failures were recorded during stent removal. The only procedure-related complication was a minor (<3N) and transitory elevation of serum amylase level without clinical consequences following stent ablation. A single expert operator performed all the ERCPs. The IST was removed using a Dormia basket or an endoscopic staple extractor. In one case, a spontaneous migration was diagnosed during endoscopy. The tube was evacuated through the natural way without incident. A short endoscopic sphincterotomy (infundibulotomy) was most of the time required but none were associated with complications. Interestingly enough, although the median delay between LT and IST removal was 26.5 (range 4–72) weeks, no difficulties were recorded during IST ablation because of stent incrustation. This may be explained by the fact that no side holes were created when the custom-made segment of a 8 French T-tube was used for the confection of the IST. The technical skills of the endoscopist and the limited sphincterotomy may highly contribute to the very low rate of post-ERCP morbidity, which fully support our strategy of intraoperative endobiliary stenting in selected patients with high risk biliary anastomosis.

The second finding of this study was a very low biliary morbidity rate, especially in the group of patients who received a whole graft. There was no complication directly associated with the use of the IST in this group, even if the IST was removed after a median delay of 26.5 (4–72) weeks. We have previously reported overall biliary complications rate among whole graft transplanted patients who underwent a biliary reconstruction with or without a T-tube of 33.3% and 15.5%, respectively [1]. Although not significantly relevant, it was interesting to note that the majority of complications occurred in the group of patient who received reduced size grafts. This finding is in accordance with data in the literature showing higher rates of biliary complications after living donor or split LT [18]. A multicentric prospective comparative study would be required to determine whether IST could improve biliary outcomes in this subset of patients.

The rate of complications after endoscopic ERCP reaches 4% [19]. Despite the low rate of endoscopic complication during IST removal in the present study, it is obvious that introduction of this technique in the current practice would lead to a nonzero, ERCP-related morbidity. Surgical placement of a biodegradable stent might palliate this shortcoming by avoiding further endobiliary maneuvers. Synthetic bioabsorbable stents have been successfully used in animal models for treatment of cystic duct leakage, hepaticojejunal anastomosis, and duct-to-duct biliary reconstruction [20–24]. Although use of biodegradable stents has not yet been reported in clinical LT, this might represent an interesting perspective and a rewarding field of research.

In conclusion, IST is technically feasible and safe, and seems to prevent from severe biliary complication in transplantation of whole liver grafts and small size bile duct. A large prospective study should be performed to confirm the results of this preliminary study.

Authorship

HT: collected data, analyzed data and wrote the paper. SZ: wrote the paper. AS: collected data. MC: performed study. FP: performed study. OS: designed study and performed study, OS: designed study, performed study and analyzed data.

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