Endoscopic Therapy of Posttransplant Biliary Stenoses After Right-Sided Adult Living Donor Liver Transplantation

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Background & Aims: **Endoscopic treatment of biliary strictures after liver transplantation is a therapeutic challenge. In particular, outcomes of endoscopic therapy of biliary complications in the case of duct-to-duct anastomosis after living related liver transplantation are limited. The aim of this study was to evaluate the feasibility and success of an endoscopic treatment approach to posttransplant biliary strictures (PTBS) after right-sided living donor liver transplantation (RLDLT) with duct-to-duct anastomosis.** ***Methods:*** **Ninety patients who received adult-to-adult RLDLT in our center were screened retrospectively with respect to endoscopic treatment of PTBS. Therapy was judged as successful when cholestasis parameters returned to normal and bile duct narrowing was reduced significantly after the completion of therapy.** ***Results:*** **Forty of 90 RLDLT patients received duct-to-duct anastomosis, 12 (30%) showed PTBS. Seven of 12 patients were treated successfully by endoscopy; the remaining 5 patients were treated primarily by surgery. Most patients were treated by balloon dilatation followed by insertion of endoprostheses. A median of 2.5 dilatation sessions were necessary and the median treatment duration was 8 months. One patient developed endoscopy-treatable recurrent stenosis, no surgical intervention was necessary. Mild pancreatitis occurred in 7.9% and cholangitis in 5.3% of the procedures. One minor bleeding episode occurred during sphincterotomy. Bleeding was managed endoscopically.** ***Conclusions:*** **Endoscopic therapy of adult-to-adult right living related liver transplantation with duct-to-duct anastomosis is feasible and frequently is successful. The duct-to-duct anastomosis offers the possibility of endoscopic treatment. Endoscopic treatment of posttransplant biliary strictures is safe, with a low specific complication rate.**

Adult-to-adult right living donor liver transplantation (RLDLT) is used increasingly because of a persistent shortage of cadaveric organs for orthotopic liver transplantation.[1] The adaption and reconstruction of the bile ducts and the technique of biliary anastomosis in RLDLT is a critical aspect of the procedure. The prevalence of biliary complications in LDLT is higher than in orthotopic liver transplantation, with a frequency of up to 40%.[1,2] Biliary complications are a common cause of graft malfunction and are related to a great proportion of posttransplant recipient mortality.[3] The high incidence of stenoses and leaks of the biliary anastomosis in right liver grafting seems to be caused by poorer vascularization of the isolated right biliary tree.[4]

In most centers, anastomoses in RLDLT are fashioned as a cholangiojejunostomy for drainage of more than 1 duct. Potential advantages of a duct-to-duct anastomosis are a more physiologic reconstruction, the avoidance of bowel manipulation, a shorter duration of surgical intervention, and easy access and imaging via endoscopic retrograde cholangiography (ERC) both in the early and especially in the late postoperative period, with the possibility of endoscopic management of bile duct complications. Potential disadvantages are a more laborious dissection of the recipient bile duct and some technical difficulty in accommodating size-mismatched bile ducts, which is specific to the end-to-end technique. Recently our group described the feasibility of duct-to-duct anastomoses independent of the presence of 1 or more graft bile ducts.[4]

Despite several reports of successful endoscopic therapy of PTBS after orthotopic liver transplantation in small patient series, this therapy option remains controversial.[5–16] Success rates of endoscopic therapy of PTBS are reported as 27%–100%. In a recent study, endoscopic/radiologic therapy of 16 patients after LDLT with PTBS achieved a success rate of around 67%. Most of them were treated by percutaneous transhepatic cholangiography.[16] Experience in transpapillary endoscopic therapy

Abbreviations used in this paper: ERC, endoscopic retrograde cholangiography; ITBL, ischemic-type biliary lesion; PTBS, posttransplant biliary strictures; RLDLT, right-sided living donor liver transplantation.

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after RLDLT is limited. Therefore, the aim of our study was to evaluate the effectiveness of endoscopic therapy of biliary strictures after RLDLT.

Patients and Methods

Ninety patients receiving RLDLT between August 1998 and September 2003 were analyzed for the presence of bile duct strictures. In all patients, liver biopsy specimens were obtained before ERC to exclude graft rejection, recurrent hepatitis C infection, or chronic graft pathology.

Biochemical cholestasis parameters such as serum bilirubin levels, alkaline phosphatase levels, and γ-glutamyl transferase levels were noted at the time of indication for ERC. Biochemical cholestasis parameters and ERC reports were entered into a computer database (Access 2000, Microsoft Duetschland, GmbH, Unterschleissheim, Germany) for analysis.

With respect to the results of the ERC, patients were divided into 2 groups: group A with anastomotic stricture; and group B with non-anastomotic strictures of the biliary tract classified as ischemic-type biliary lesions (ITBLs). Depending on the localization of the stenoses, ITBL was subdivided further into 3 groups according to Hintze et al[9]: type I, extrahepatic lesions; type II, intrahepatic lesions; type III, extrahepatic and intrahepatic lesions.

Before endoscopic therapy an endoscopic sphincterotomy was performed. Endoscopic therapy consisted either of balloon dilatation (6-mm MaxForce Balloon; Boston Scientific, Ratingen, Germany) or balloon dilatation combined with the insertion of plastic endoprostheses of an appropriate diameter (7F, 10F, 11.5F Flexima endoprostheses; Boston Scientific) and increasing the diameter size and number when possible. Ischemic-type biliary lesions were treated solely by balloon dilatation (Figures 1 and 2).

Endoscopic therapy was judged as successful when the bilirubin level decreased to a value of 1.5 mg/dL or less and/or there was radiomorphologic resolution of the stricture after completion of the therapy and without inserted endoprostheses. During further follow-up evaluation, patients presented routinely every 2 months in our interdisciplinary transplantation ambulance where abdominal ultrasound and liver function tests were performed.

Statistical analysis was performed with SPSS for Windows release 11.0.1 (SPSS Inc., Chicago, IL). For statistical analysis of paired continuous variables we used the Wilcoxon test; for unpaired continuous variables we used the Mann–Whitney test. To compare unpaired distinct variables a cross-table with a χ^2 test was used. The Pearson correlation procedure also was used. The significance level was a P value of .05 or less.

Results

Of the 90 patients receiving adult RLDLT between August 1998 and September 2003 there were 40 duct-to-duct biliary anastomoses performed. Seven of the 50 (15%) patients who received hepaticojejunostomy developed PTBS. All of them underwent relaparotomy, and re-hepaticojejunostomy was required in most cases. Twelve of the 40 patients (30%) with duct-to-duct anastomosis developed PTBS. Five of these patients were treated primarily by surgery, based on the judgment of our surgeons, without receiving ERC. The remaining 7 patients received endoscopic therapy of their strictures. The median age of patients with strictures was 55 years (range, 45–65 y) compared with 53.5 years (range, 12–65 y) without strictures ($P = .61$). In the stricture group, 4 were women and 8 were men compared with 10 women and 18 men in the nonstricture group ($P = .591$).

In the stricture group 3 of 12 (25%) grafts were stored in University of Wisconsin solution and 9 of 12 (75%) grafts were stored in histidine-tryptophan-ketoglutarate solution compared with 10 of 28 (35.7%) stored in University of Wisconsin solution and 18 of 28 (64.3%) stored in histidine-tryptophan-ketoglutarate in the nonstricture group ($P = .716$) for organ preservation before transplantation. Median cold ischemic time in the stricture group was 209 minutes (range, 124–265 min) compared with 204 minutes (range, 59–403 min) in the nonstricture group ($P = .948$). However, there was a significant difference in median warm ischemic time between both groups with 48 minutes (range, 30–76 min) for the nonstricture and 56 minutes (range, 37–76 min) for the stricture group ($P = .019$).[17–19]

The Pearson correlation model showed a significant correlation between warm ischemic time and PTBS (correlation coefficient [r], .372; significance [P], .025).

ERC showed anastomotic stricture in 5 of 7 and ITBL showed anatomic stricture in 2 of 7 patients (1 patient had ITBL type III and 1 patient had ITBL type I). The median time interval between liver transplantation and first ERC was 4 months (range, 1–10 mo) (Table 1).

All fashioned duct-to-duct anastomoses could be visualized by ERC. The 7 patients received a total of 38 ERC procedures; the median was 3.5 procedures per patient (range, 1–11 procedures). The median time interval between the procedures was 8 weeks (range, 1–32 wk). All patients received standard sphincterotomy via guidewire before endoscopic treatment. Five of 8 patients were treated with balloon dilatation followed by insertion of endoprostheses. Two patients received isolated balloon dilatation and 1 patient received isolated endoprosthetic treatment. A median of 2.5 balloon dilatations (range, 0–6) were performed per patient. We administered a median of 2.5 endoprostheses (range, 3–19) per patient, which provided each patient with two (double-sided) endoprotheses in 17 treatment sessions. The median maximum total endoprosthetic diameter was 14F