

BILIARY COMPLICATIONS AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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SUMMARY:

Biliary complications after liver transplantation occurred as frequent cause of morbidity and mortality after liver transplantation. They are considerate as the technical "Achilles heel"(1).

In this article we have described and analyzed the frequency and the characteristics of the most common biliary complications after liver transplantation based on our experience in University Hospital in Lausanne, Switzerland.

Over a 15-year period from December 1988 to March 2003, 185 orthotopic transplantations were performed on 168 patients. Of the all patient 103 patients were males and 65 females. The average age for males was 51 and for women were 49. End-to-end choledochocholedochostomie with tutor (CC-T) or without (CC) was the first choice method of biliary reconstruction and he was performed on the 168 patients. In 17 causes patients received choledochojejunostomies (CJ) with a long Roux-Y-loop. Biliary complications were identified in 30 (16%) of the 185 OLT. The percent of the early deaths (after detection and treatment the complications) were 0%. The most common biliary complication was bile duct strictures (anastomotic or nonanastomotic), bile leaks and biliary stones.

The biliary complications remain an important cause of surgical morbidity but rarely associated cause of dead. Diagnosis relies on laboratory analysis, abdominal imaging and cholangiographic studies. Management of the detected biliary complications includes nonsurgical and surgical methods. Nonoperative interventions have an increasing role in the treatment. Biliary complications were identified in these series are representatives when the results observed by the other medical centers the Liver Transplantation.

Key words: Orthotopic liver transplantation; Biliary complications; Management of biliary problems after liver transplantation

INTRODUCTION

Since the first experimental liver transplantation in humans by Starzl in 1963 this method was become the choice of treatment for patient with irreversible hepatic diseases. A significant incidence of morbidity and mortality

after liver transplantation has been attributed to biliary tract complications. The improved patient survival of 70 % to 85% is attributable to advances in preoperative patient selection, organ procurement, surgical technique and intraoperative management, immunosuppressive protocols. Major risk factors for biliary complications are bile duct resulting from nonanastomotic techniques of procurement, prolonged cold ischemia time and use of organs from ABO incompatible donors.

The present paper present a retrospective analysis of the biliary complications observed for 15 years experience in orthotopic liver transplantation. Bile duct stricture, leak and obstructions are most frequent complications. Improved surgical techniques, new endoscopic and radiologic methods significantly reduce the incidence.

MATERIALS AND METHODS

Characteristic of the patients

Between December 1988 and March 2003, 185 orthotopic liver transplantation were performed on the 168 patients at the department of the general surgery at the CHUV-University Hospital Lausanne, Switzerland. Of the all 103 patients were in sex male and 65 female. The average age for males was 51 years (between 22 and 68 years) and for women-49(between 12 and 71 years). Of the all 165 patients, 12 received second transplant and 2 patients received a third transplant.

2. The indications for liver transplantations included

Fulminant hepatic failure	- 18 cases
Cholestatic disease	- 13
Congenital disease	- 2
Cirrhosis	- 124
Liver cancer	- 8
Neuroendocrine metastases	- 2
Other	- 7
Retransplantations	- 16

The cirrhosis group includes:

58 alcoholic cirrhosis / 9 cases with hepatocellular carcinoma /

6 autoimmune cirrhosis

11 cirrhosis related virus hepatit B / 2 cases with hepatocellular carcinoma/

32 cirrhotics related virus hepatitis C / 5 cases with hepatocellular carcinoma/

8 cirrhotics related virus hepatitis BD et BCD

3 cirrhotics related virus BC

9 cryptogenic cirrhosis

The indications for retransplantation were:

Acute rejection	1
Chronic rejection	6
Hepatic artery thrombosis	3
Primary non-functioning graft	5
Other	1

Technical characteristics of the Transplantation

In general the surgical technique of the donor and recipient procedure was similar to those described by Starzl et al (2). Monitoring, catheter type Swan-Ganz for hemodynamic parameters and other catheter intra-arterial to continuous observation was performed. The ABO was the first condition for starting the preceding.

Vascular reconstruction

Three vascular anastomoses were performed:

- 1) Venovenous anastomosis :
 - vein cave donor interposition after vein cave recipient resection
 - Or cavo-cave said to said anastomosis
- 2) porto-porto end to end anastomosis
- 3) arterial anastomosis - function of the anatomy to the two patients (3).

Biliary reconstruction:

1) End-to-end choledochocholedochostomy was the first choice method of biliary restoration and he was performed in 168 OLT (4, 5, and 7):

- With T tube in 126 OLT
- Without a T tube in 42 OLT

2) Donor or recipient bile duct of insufficient length or in case the reoperations before postoperative ischemic strictures received choledochojunostomies with a long Roux-Y-loop- 17 case OLT(8)

- With T tube in 7 cases
- Without T tube in 10 cases

- a) In 2 cases we use the tube by the Voelker
- b) In 7 cases - internal stent
- c) in one case tube type d'Escat by the orifice of the cystic duct

The gallbladder and the biliary tree were irrigated with cold saline and the first-routine cholangiography was performed intraoperatively to control the position of the T tube and anastomosis.(9).

Postoperative management

All the patients received standard drug combination

by the protocol of immunosuppression : Cyclosporin or Prograf with corticosteroids. Biopsy-proven steroid rejection was treated with the monoclonal antibody OKT3 or antilymphocyte serum (ATG) or Azathioprine (10, 11).

Routine cholangiography was usually performed at the 10 day under antibiotic prophylaxis to check for leak and patency. In most cases T tube was removed electively after 3 months after control cholangiography.

Liver biopsies were not performed routinely, only when clinically indicated.

RESULTS

- 46 (27,7%) patients died in different periods after TH :

- 1 (2,2%) patient died during the operation
- 9 (19,5%) died during the early post-operative time (0-7days)
- 5 (10,9%) died during the late post-operative time (8-31 days)
- 19 (41,3%) died between the 1st and 12th month
- 12 (26,1%) died after the first year.

Survival and death

The actuarial survival was calculated with Kaplan - Meier method and for 3, 5 and 10 years were respectively 85%, 76% and 73 %.

Biliary complications have developed in 30 (16.7%) of the 185 cases the OLT performed in CHUV

The overall biliary complication rate was 28 (93.3%) in the biliary reconstruction type CC anastomosis, as 14 (50%) with the T- tube and 14 (50%) without T-tube.

- 2 (6.7%) complications were observed after choledochojunostomy.

Biliary complications were diagnosed biochemically, clinically or radiologically.

Ultrasonography was the first choice radiological method, followed by cholangiography, CT and biopsy.

The most common biliary complications observed in our series were:

Biliary strictures

They occurred in 16 (53%) of the cases and they are two types

Anastomotic strictures-number of 10(33.3%)

- 2 cases appeared in the first post-operative month, which we explain with technical causes. When donor and recipient duct are unsatisfactory caliber and was use plastic reconstruction under pressure; in this case controlled ERCP mean inflammation of the surgical line (12).

The other 8 cases were observed between the 2nd and 8th month postoperatively.

- In 5 cases, the cold ischemia time was more than 7 hours.

- In 1 case, the patient was with diagnosis Primary Sclerosing cholangitis, disease known for predisposition for stricture.

- In 4 cases, there was a discrepancy in size between donor and recipient ducts.

- in 4 cases, liver biopsy was significant for chronic liver graft rejection and 1 case lesion by the mixed type-rejection and ischemia, combined with 60 % stricture of the hepatic artery (13, 14, 15).

- In 4 cases, no reasons were found for the complications.

NONANASTOMOTIC STRICTURE

They were 6 (20%) cases. The arterial supply of the biliary tree is essential to the integrity of biliary drainage of the graft, and the intrahepatic biliary tree of the transplanted liver is critically dependent on the patency of the hepatic artery.

In 3 cases they were obstructed during the first postoperative days 3-6. The diagnosis of hepatic artery thrombosis was made by sudden and sharp rise of the liver function. Tests showed changes similar to those in the rejection, confirmation by US (intrahepatic biliary dilation) and directly by reoperation and desobstruction (1 case). Fine needle biopsy performed before, was present massive ischemic hepatic necrosis and ductal strictures.

We found :

- Ischemic necrosis of the end of the donor bile duct (1-1.5cm necrosis distal of the anastomosis), partial disruption of the biliary anastomosis, biliary leaks with bilioperitonitis

- Ischemic-type intrahepatic biliary tree strictures-involving variable sites and segments

- 2 abscess (in 1 case)

- 1 biliary leak

In the other three cases, involved were intrahepatic biliary tree strictures secondary complicated with microstones, micro abscess and biliary leaks by peripheral biliary ducts.

Biliary leak

In our series leaks were present in 6 (20%). There were:

- 2 anastomotic leaks

- 2 leaks of the T tube exit site after program removal of the T tubes

- 1 leak from the donor cystic duct (used for tube drain)

- 1 disruption of the biliary anastomosis with biliary peritonitis

In this series 3 leaks were localized (de novo) biliary anastomotic in the first (in the first two weeks) 2 two postoperative weeks:

- incomplete obstruction of the biliary duct by the

silicon transanastomotic internal drain a straight tube stent could not be passed through the papilla of Vater. The tube remained within the bile duct and caused incomplete obstruction with increased pressure and significant anastomotic leak.

- No significant leak detected by cholangiogram of control

- complete anastomotic obstruction after insertion of T tube in cases when there was technically unsatisfactory anastomosis (different size of diameters)

The three most important biliary leaks were observed after program removal of the T-tube. Usually, this procedure was performed in the 3rd of 4th month after the operation. In two patients we observed the clinic of biliary peritonitis the first day after removal of the T-tube who necessitated reoperation and plastic of the bile duct defect. Secondary complication was anastomotic stricture treated successfully endoscopically with stent for 1 month. In one case we drained biliary tree with transcystic external drain, which was incidentally removed by the patient after 13 postoperative days. US and clinically he presented local peritonitis. Three times endoscope stents placement was ineffective and reoperation with T-tube insertion for 1 month was successful.

Other cause of biliary complications

Biliary stones and sludge

Was observed only one case (3,3%). The patient presented epigastric pain for 3 months with chronic intermittent cholestasis. Ultrasound and ERCP showed dilation of the main bile duct to 1.5 cm in diameter and a stone size of 0.6 cm x 0.8 cm, localized in the inferior portion of the main bile duct with incomplete obstruction. The first selected treatment that was performed was papillosphincterotomy and tentative for extraction- unsuccessful. The second time we performed transhepatic destruction of the stone, ringage and transpapillary extraction.

Development of neoplasia of the biliary anastomosis

In our series we have only one patient with biliary obstruction caused by appearance of new neoplasia 7 months after liver transplantation. The patient developed abdominal pain and clinical findings of obstructive jaundice, loss of weight and appetite. Performed laboratory test and abdominal CT show a tumor mass in size of 7 cm arising in the periportal lymph nodes and compressed the main bile duct. Biopsy confirmed a malignant large-cell lymphoma. The neoplastic cell demonstrated Epstein-Barr virus DNA. This case suggests that the biliary anastomosis is the selective place of appearance of a posttransplant lymphoproliferative disorder – malignant large lymphoma. The treatment was progressive stop of immunosuppressive drugs and regression of the tumor mass with chemotherapy. Two months later, (9 months postoperative) patient died.

CONCLUSION:

1. The percentage of biliary complications by the serie (16.7%) is comparable with the mean for similar observations published in various research magazines.

2. Appearance of the biliary complications is dependent upon the primary indications for liver transplantation.

3. Statistical analysis confirmed when the biliary structure occur the first place. In the early postoperative period the anastomotic type is prevalent. The cause is that the donor and recipient duct are unsatisfactory caliber and may be ischemia of the wall of donor common bile duct when the T-tube protection in the first 3-4 weeks to prevent clinical appearance. In the late postoperative period non anastomotic structures are present. Blood supply disruptions lead to structure of the biliary tree in different levels.

4. Biliary leak remains the major cause for special surgical reintervention in early postoperative stage. Except

for the hepatic artery thrombosis, surgical intraoperative technique is the main source: disruption of the anastomosis or around the T-tube and T-tube exit site after program removes the T-tubes.

5. The diagnostic of the biliary sludge and stones, results from disruption of the epithelium of the biliary tree (Vanishing bile syndrome) are treated successfully endoscopic.

6. The treatment of the most common biliary complications was done endoscopically. Imaging study with US, CT, ERCP may confirm appearance of biliary complications. Percutaneous and endoscopic techniques with papillosphincterotomy long-term stent offer significant, long term, and favorable outcomes.

7. The endoscopic treatment of non anastomotic structure requires multiples interventions over a longer time without satisfactory results. These intrahepatic absces and biloms were treated surgically.

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