Original Articles

Chirurgia (2014) 109: 15-19
No. 1, January - February
Copyright© Celsius

Technical Aspects of Biliary Reconstruction Correlated with Biliary Complications in 46 Consecutive Right Lobe Liver Transplantations from Living Donors

V. Brașoveanu[1], C. Anghel[1], N. Bacalbașa[1], M.I. Ionescu[1], E. Matei[1], I. Barbu[1], M. Grasu[2], D. Tomescu[3], I. Popescu[1]

[1]"Dan Setlacec" Center for General Surgery and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania
[2]Department of Radiology, Medical Imaging and Interventional Radiology, Fundeni Clinical Institute, Bucharest, Romania
[3]Department of Anesthesiology and Intensive Care, Fundeni Clinical Institute, Bucharest, Romania

Rezumat

Aspecte tehnice privind reconstrucția biliară corelat cu complicațiile biliare în 46 cazuri de transplant cu hemificat drept de la donator viu

Introducere: Complicațiile biliare reprezintă o proporție importantă de morbiditate în transplantul cu hemificat drept de la donator viu. Studiul nostru își propune o analiză retrospectivă a tehnicilor de anastomoză biliară corelate cu complicații biliare în cadrul unui lot de pacienți transplantați cu hemificat drept într-un singur centru.
Pacienți și metodă: În perioada 2009-2013, la 46 de pacienți transplantați cu hemificat drept (23 de bărbați și 23 de femei, cu vârste între 19-63 de ani), anastomozele biliare au fost fie: canale biliare sectoriale donator – cale biliară principală receptor termino-terminală (n=24), fie colangio-jejunoanastomoză pe ansă în Y tip Roux, cu sau fără protezare cu stent exteriorizat transcoledocian/transjejunal.
Rezultate: Rata complicațiilor biliare (fistule biliare 15,21%, stenoze biliare 4,34%, totală 17,39 %) nu a fost influențată din punct de vedere al analizei statistice de factorii demografici, de etiologia afecțiunii hepatice sau de diferitele tehnici de anastomoză alese; singurul factor de risc corelat cu probabilitatea de apariție a complicațiilor biliare a fost MELD ridicat (p=0.04).
Concluzii: Alegerea tipului și a tehnicii de anastomoză biliară trebuie adaptată la profilul clinico-biologic al receptorului și la anatomia arborelui biliar al donatorului și receptorului, astfel încât să se mențină o rată cât mai mică de complicații biliare.

Cuvinte cheie: transplant cu hemificat drept de la donator viu, complicații biliare, scor MELD

Abstract

Introduction: Biliary complications contribute to a high morbidity rate in patients with right lobe liver transplant from a living donor. We retrospectively evaluated biliary reconstructions and complications in a number of recipients with liver transplant from a living donor, in a single center.
Patients and Methods: A number of 46 patients (23 males and 23 females aged 9-63) received a right lobe liver graft between 2009 and 2013, with the following types of biliary reconstruction: duct-to-duct choledochocholedochal anastomosis (n=24) or Roux-en-Y hepaticojejunoanastomosis, with or without an external transanastomotic biliary stent.
Results: The rate of biliary complications (leakage 15.21%, anastomotic stenosis 4.34%, overall 17.39%) was not statistically significantly influenced by the demographics of the

Corresponding author: Vladislav Brașoveanu, MD
"Dan Setlacec" Center for General Surgery and Liver Transplantation
Fundeni Clinical Institute, Bucharest, Romania
E-mail: brasoveanuvlad@yahoo.com

studied lot, by the etiology of the liver disease or by the characteristics of the biliary reconstruction; the only risk factor which showed a statistically significant influence in terms of biliary complications was MELD.
Conclusion: The type and technique of the biliary reconstruction in LDLT should be adapted depending on the anatomy of the biliary tree of both the donor and recipient, as well as the clinical and laboratory findings of the recipient.

Key words: right lobe living donor, liver transplant, biliary complications, Model for End Stage Liver Disease (MELD)

Introduction

Although the outcome of right lobe liver transplantation from living donors (R-LDLT) has significantly improved in recent years due to a significant progress in the surgical technique, in the postoperative management and the immunosuppression, biliary complications still remain a major concern, with a morbidity ranging between 20-42.1% (1,2). Several factors influencing the incidence of the biliary complications after R-LDLT, defined as either biliary leakage or biliary stricture, have been identified: MELD score (3), CMV infection prior to transplantation and hepatic artery thrombosis (HAT) (4), type of immunosuppressive regimen (5), learning curve and number of biliary duct openings in the donor graft (6), technical aspects of anastomosis [duct-to-duct choledocho-choledochal/Roux-en-Y hepaticojejunostomy (7), whether external stenting of the anastomosis was used or not (4)] and preservation of the recipient's choledochal blood supply by high hilar plate dissection (8). However, to date, there is no prospective randomized trial correlating different technical approaches of the biliary anastomoses to postoperative biliary leakage or stricture.

Patients and Method

The present study is a retrospective analysis of 46 adults R-LDLT. Our aim is to describe the surgical technique of the different biliary anastomoses techniques and to assess subsequent biliary complications.

The first R-LDLT was performed in our center in February 2003. 19 patients received a right hemi-liver graft between 2003 and 2008, yet overall results were suboptimal. Subsequently, the operating team benefited from training in Asian Medical Center in Seoul (South Korea). The technique of reconstructing venous outflow tributaries and the use of an external stent for the biliary anastomosis were adopted, with improved subsequent results (9).

The inclusion criteria fulfilled by the 46 adult patients in the study was right hemiliver transplantation from a AB0-group compatible living donor, in a single center (General Surgery and Liver Transplantion, Fundeni Clinical Institute, Bucharest, Romania) from November 2009 to December 2013; one patient only underwent a dual-graft liver transplantation (right hemi-liver + left lateral liver segments) (10), and this case was excluded from our study. The median follow up time was 515 days (range 12-1475). The underlying liver diseases requiring transplant were: liver cirrhosis (n=29), hepatocellular carcinoma (n=15) and fulminant liver failure (n=2). Their age ranged from 19 to 63 years old; gender distribution was balanced between males (n=23) and females (n=23). The graft-to-recipient weight ratio (GRWR) varied between 0.92 and 2.07 (median value 1.29) and the median MELD score was 17 (range 6-35). The anatomy of the biliary tree in the donor was assessed preoperatively by magnetic resonance cholangiography (MRCP).

Surgical technique

The donor operation consisted in the removal of the right hemi-liver with a CT-estimated volume of 63.81±5.88 (range 41.03-75.73%); all grafts were perfused with HTK (Histidine-Tryptophan-Ketogluatarate) solution on the back-table. After the completion of the vascular anastomoses, donor's bile ducts were anastomosed to the recipient's common bile duct in 24 patients (*Fig. 1*), whereas in 22 patients the biliary reconstruction consisted in a Roux-en-Y hepaticojejunostomy (RYHJ) (*Fig. 2*). The choice between the two anastomotic designs depended on various factors: the number of bile duct openings in the graft, risk of tension in the anastomosis due to a short recipient main bile duct and the previous experience of the operating team.

Whenever possible, the biliary reconstruction was performed in an end-to-end choledocho-choledochal (DD) fashion, using an external stent (20 out of 24 cases). In the D-D group, 15 donor cases had a single biliary duct anastomosis, whilst in other 9 patients the donor graft had 2 ducts. There are several advantages for the former type of anastomosis that have been previously demonstrated (11), yet the operating team paid special attention not to dissect the donor right hepatic duct too close to its main bile duct, in order to avoid any biliary lesions in the donor operation; therefore, although efforts were made to obtain 1 bile duct

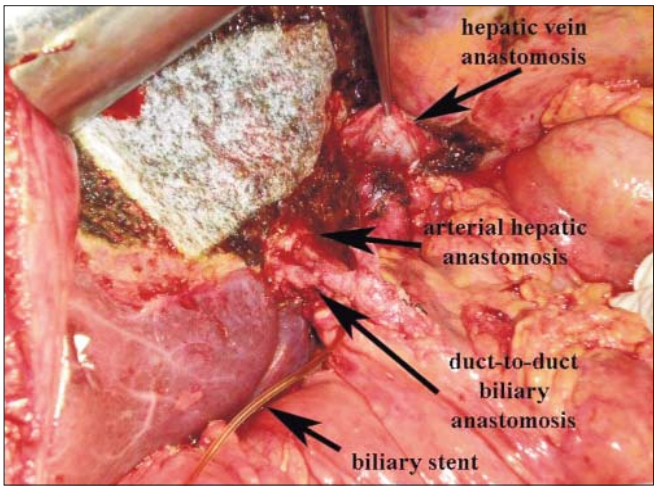


Figure 1. *Intraoperative aspect*

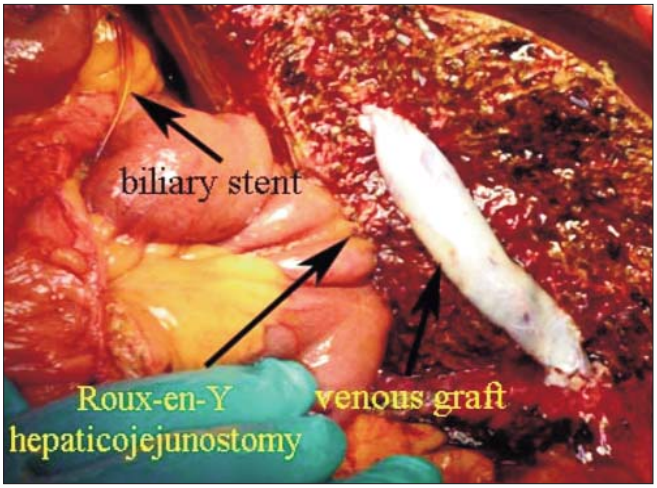


Figure 2. *Intraoperative aspect*

in the liver graft, this came second after donor safety.

Before choosing the type of reconstruction, the operating surgeons made sure there was no potential tension in the anastomosis and that the anastomotic margins received optimal blood flow; if any of the previous seemed deficient, a RYHJ was chosen. External stenting was applied in both groups whenever the diameter of the anastomosis was less than 5 mm in order to avoid the risk of anastomotic stricture and to decrease the pressure inflicted by the biliary flow upon the anastomosis.

In terms of technique, the biliary reconstruction began by placing absorbable PDS 6-0 (polydioxanone suture) stay sutures at 3 o'clock and 9 o'clock, respectively. When 2 openings occurred, a biliary ductoplasty was performed with 6-0 absorbable interrupted sutures, in order to join the two openings. Subsequently, a single biliary opening in the graft was created. Both the posterior and the anterior aspects of the anastomosis were performed with interrupted sutures. The external stent, if used, was anchored with a 6-0 PDS suture. The same technique was employed in the RYHJ cases. After the anastomosis was completed, saline solution was injected through the external stent in order to identify potential biliary leaks. A cholangiography was performed on the external biliary stent on POD 15-30, and if a normal aspect was demonstrated, the tube was closed and removed after approximately one year.

The immunosuppressive protocol was based on daclizumab as initiating therapy, and tacrolimus and mycophenolate as maintenance therapy up until October 2010. Henceforth, the standard regimen consists in initiation with basiliximab, administered in two doses: intraoperatively and in POD 4, while tacrolimus and mycophenolate are added in POD 4.

The statistical analysis was performed using the SPSS software, version 19.00. Comparison of categorical variables was performed using the Chi-square test or Fisher's exact test where appropriate. Non-parametric continuous variables were compared by the independent samples t-test and presented as mean ± standard deviation. P values of less than 0.05 were regarded as statistically significant. All p values were two-tailed.

Results

In terms of defining the biliary complications, a patient was considered to have biliary leak if there was bile drainage into intraoperatively placed drains or if a postoperative computed tomography (CT) scan showed a bile collection or biloma that needed drainage; a biliary stricture was defined as the narrowing of the biliary anastomosis on cholangiography or bile duct dilatation on CT that required interventional treatment.

During the follow-up period (median of 17 months), biliary leakage occurred in 7 patients and biliary anastomotic stenosis in two patients (1 patient developed biliary leakage in the first month post transplantation and anastomotic stenosis after more than one year). The overall survival was 76.08 %; early postoperative mortality (< POD 30) occurred in 6 cases due to either vascular complications as hepatic artery thrombosis (n=2 – both cases occurred before the microscopical arterial anastomoses in our clinic), and portal vein thrombosis (n=1), or primary graft non-function (n=1), uncontrolled sepsis by postoperative bronchopneumonia (n=1) or cerebral edema with brain herniation in one patient.

Risk factor analysis for bile leakage

In this group, one patient with portal vein thrombosis and intestinal fistula from the entero-enteral anastomosis of the Roux-en-Y limb of the hepaticojejunostomy was intra-operatively diagnosed with an anastomotic leakage, which was sutured. Late mortality in 5 cases, with survivals ranging from 72 to 399 days, was caused by: HAT which required liver retransplantation, with subsequent repeated HAT (n=1), liver failure due to reactivation of VHC (n=1), HCC recurrence after liver transplantation (n=1), renal failure in a patient with pretransplant renal dysfunction and ischemic stroke (n=1).

Three other cases required laparotomy with anastomotic suturing, with subsequent repair of the fistula. One of these patients presented with an anastomotic fistula between the recipient cystic duct and a donor sectorial duct, while another anastomosis performed at the same time in a different patient, between the donor sectorial bile duct and the recipient common bile duct, was intact; ERCP did not solve the bile leakage, therefore a laparotomy and suture of the fistula was necessary.

Conservative treatment was adopted in three other cases of bile leakage, with complete resolution of the biliary drainage and subsequent discharge.

Biliary anastomotic stenosis developed in 2 patients, after more than 3 months postoperatively. Both cases were managed by percutaneous transhepatic biliary drainage (PTBD), and the patients are currently alive, with normal graft function.

Risk analysis for overall biliary complications

The statistical study (*Table 1*) showed no significant difference upon the development of the biliary leakage or overall biliary complications in terms of demographics (recipient or donor

Table 1. *All values are expressed as mean ± standard deviation.*
HCC - hepatocellular carcinoma; HAT - hepatic artery thrombosis; PVT - portal vein thrombosis; CIT - cold ischemia time; WIT - warm ischemia time.

		Biliary leakage		
Risk factors		**Yes=7**	**No=39**	***p***
Donor age (yrs)		31.57±8.44	33±9.01	.63
Recipient age (yrs)		50.14±6.01	45.72±13.86	.41
Gender mismatch (number of cases)		4	22	0.97
Presence of HCC	Yes	4	10	
	No	3	29	.19
MELD		14.14±4.63	17.51±4.99	.104
GRWR		1.44±0.26	1.28±0.23	.105
CIT (min)		168.57±71.88	163.79±42.74	.809
WIT (min)		37.14±26.01	46.59±26.48	.38
Type of anastomosis	DD	4	20	
	RYHJ	3	19	.08
Vascular complications (HAT ± PVT)	Yes	1	6	
	No	6	33	.91
External biliary stent	Yes	7 (100%)	35	.37
	No	0	4	
Number of stented anastomoses < number of biliary anastomoses	Yes	2	1	
	No	5	38	.056
More than one biliary ducts anastomosed	Yes	6	20	
	No	1	19	.11

age, gender mismatch between donor and recipient), GRWR, presence of HCC, or the duration of ischemia (CIT and WIT), yet a higher MELD was identified as a statistically significant risk factor for the occurrence of overall biliary complications ($p < 0.044$) (*Table 2*). In terms of surgical technique, the choice between duct-to-duct choledochocholedochal anastomosis and hepaticojejunostomy, the use of an external biliary stent or the number of donor sectorial ducts anastomosed did not influence the occurrence of biliary leakage; despite the fact that it was not statistically significant, using an external stent for only one of the biliary anastomoses when more than one are performed in a single patient presented a certain trend towards the development of biliary leakage ($p < 0.056$).

Discussion

In our series of patients, biliary leakage, biliary stenosis and overall biliary complications rates were 15.21%, 4.34 % and 17.39 %, respectively. This was in accordance with the rates of overall biliary complications reported by other authors (20-30%), which are much higher than those occurring in DDLT, proving once again that biliary complications remain the

Table 2. *All values are expressed as mean ± standard deviation.*
HCC - hepatocellular carcinoma; HAT - hepatic artery thrombosis; PVT - portal vein thrombosis; CIT - cold ischemia time; WIT - warm ischemia time

		Biliary complications		
Risk factors		**Yes=8**	**No=38**	***p***
Donor age (yrs)		31.00±7.98	33.50±9.07	.448
Recipient age (yrs)		50.63±5.73	45.50±13.98	.103
Gender mismatch (%)		50 %	57.89%	.71
Presence of HCC	Yes	4	10	
	No	3	29	.092
MELD		14.63±4.53	17.71±4.90	.044
GRWR		1.42±0.25	1.28±0.23	.19
CIT (min)		176.88±70.57	161.92±41.66	.579
WIT (min)		40±22.78	46.24±26.75	.509
Type of anastomosis	DD	4	20	
	RYHJ	4	18	.70
Vascular complications (HAT ±PVT)	Yes	1	6	
	No	7	32	.96
External biliary stent	Yes	8 (100%)	34	
	No	0	4	.58
Number of stented anastomoses < number of biliary anastomoses	Yes	2	1	
	No	6	36	.074
More than one biliary ducts anastomosed	Yes	7	19	
	No	1	19	.43

Achille's heel of LDLT (12). A review of the literature (13) shows that in the early postoperative period leaks tend to occur more frequently than strictures, while after more than 3 months following the operation, the biliary strictures tend to outnumber leaks. If biliary anastomotic strictures occur, they should be treated by interventional radiology means (14).

Kobayashi et al. reported a significantly lower rate of biliary leakage when using a duct-to-duct biliary reconstruction with a T-tube (15). However, our study showed no significant outcome in terms of biliary complications depending on the design of the anastomosis. When choosing the type of the anastomosis (DD/RYHJ) one should take into consideration several factors. Performing a Roux-en-Y hepaticojejunostomy is advantageous if surgical procedures have been performed on the biliary tree (16) and some reports suggest that there is a higher rate of anastomotic strictures in the DD group (1,2,13), yet there are several pitfalls in choosing the RYHJ technique: longer operation time (17), potential contamination from the opened loop of jejunum, delayed return of gastrointestinal function, the impossibility of performing ERCP postoperatively, and the fact that the reestablished bilioenteric connection in RYHJ is not physiological. Moreover, if a DD anastomosis is performed, there is no intestinal manipulation and therefore the risk of intraabdominal contamination decreases.

Using an external stent in the biliary reconstruction allows an easy access to the biliary tree, with the possibility of performing a quick and noninvasive tube-cholangiography and obtaining bile cultures; it also protects the anastomosis from leakage by lowering biliary pressure (4,18); however, our study did not show a significant association between the use of an external biliary stent and a lower rate of biliary complications. There were no biliary fistulas provoked by either accidental displacement of the tube or at the time of its removal (one year postoperatively); if a late biliary stricture is suspected, MRCP is the preferred diagnostic means, after the removal of the external stent renders a tube cholangiography impossible (19).

Although in our series of patients serious vascular complications (HAT, PVT) had no significant association with biliary complications, it is well known that these conditions have a strongly negative influence on the outcome of the biliary anastomosis due to the severe ischemic effect on the anastomosis, especially in HAT (16). In this case there is a dramatic increase in the mortality of LDLT patients.

Conclusion

In conclusion, we recommend that a choledochocholedochal anastomosis using an external biliary stent should be performed for the biliary reconstruction after LDLT if there is no previous surgery on the extrahepatic biliary tree, if there is no potential tension in the anastomosis and if there is a satisfactory blood flow in both the recipient and the donor biliary tree. The hepaticojejunostomy is an alternative for the remaining cases. Further studies on larger series of patients may show significant associations between the several techniques of biliary anastomoses and the postoperative biliary complications.

References

1. Marsh JW, Gray E, Ness R, Starzl TE. Complications of right lobe living donor liver transplantation. J Hepatol. 2009;51(4): 715-24.
2. Kim BW, Bae BK, Lee JM, Won JH, Park YK, Xu WG, et al. Duct-to-duct biliary reconstructions and complications in 100 living donor liver transplantations. Transplant Proc. 2009; 41(5): 1749-55.
3. Liu CL, Lo CM, Chan SC, Fan ST. Safety of duct-to-duct biliary reconstruction in right-lobe live-donor liver transplantation without biliary drainage. Transplantation. 2004;77(5):726-32.
4. Kasahara M, Egawa H, Takada Y, Oike F, Sakamoto S, Kiuchi T, et al. Biliary reconstruction in right lobe living donor liver transplantation: comparison of different techniques in 321 recipients. Ann Surg. 2006;243(4):559-66.
5. Tashiro H, Itamoto T, Sasaki T, Ohdan H, Fudaba Y, Amano H, et al. Biliary complications after duct-to-duct biliary reconstruction in living-donor liver transplantation: causes and treatment. World J Surg. 2007;31(11):2222-9.
6. Ramacciato G, Varotti G, Quintini C, Masetti M, Di Benedetto F, Grazi GL et al. Impact of biliary complications in right lobe living donor liver transplantation. Transpl Int. 2006;19(2):122-7.
7. Yazumi S, Chiba T. Biliary complications after a right-lobe living donor liver transplantation. J Gastroenterol. 2005; 40(9):861-5.
8. Soejima Y, Fukuhara T, Morita K, Yoshizumi T, Ikegami T, Yamashita Y, et al. A simple hilar dissection technique preserving maximum blood supply to the bile duct in living donor liver transplantation. Transplantation. 2008;86(10): 1468-9.
9. Braşoveanu V, David L, Matei E, Anghel C, Popescu I. The role of the middle hepatic vein in the living donor liver transplantation with right hemiliver. Chirurgia (Bucur). 2012; 107(2):158-61.
10. Botea F, Braşoveanu V, Constantinescu A, Ionescu M, Matei E, Popescu I. Living donor liver transplantation with dual grafts - a case report. Chirurgia (Bucur). 2013;108(4):547-52.
11. Yamamoto S, Sato Y, Oya H, Nakatsuka H, Kobayashi T, Hara Y, et al, Hatakeyama K. Risk factors and prevention of biliary anastomotic complications in adult living donor liver transplantation. World J Gastroenterol. 2007;13(31):4236-41.
12. Todo S, Furukawa H, Kamiyama T. How to prevent and manage biliary complications in living donor liver transplantation? J Hepatol. 2005;43(1):22-7.
13. Yi NJ, Suh KS, Cho JY, Kwon CH, Lee KU. In adult-to-adult living donor liver transplantation hepaticojejunostomy shows a better long-term outcome than duct-to-duct anastomosis. Transpl Int. 2005;18(11):1240-7.
14. Hwang S, Lee SG, Sung KB, Park KM, Kim KH, Ahn CS, et al. Long-term incidence, risk factors, and management of biliary complications after adult living donor liver transplantation. Liver Transpl. 2006;12(5):831-8.
15. Kobayashi T, Sato Y, Yamamoto S, Oya H, Hara Y, Watanabe T, et al. Long-term follow-up study of biliary reconstructions and complications after adult living donor liver transplantation: feasibility of duct-to-duct reconstruction with a T-tube stent. Transplant Proc. 2009;41(1):265-7.
16. Kumar A, Wadhawan M, Taneja S, Shandil R. Biliary complications after liver transplantation. Apollo Medicine. 2012;9:32–37.
17. Duailibi DF, Ribeiro MA Jr. Biliary complications following deceased and living donor liver transplantation: a review. Transplant Proc. 2010;42(2):517-20.
18. Kirimlioglu V, Tatli F, Ince V, Aydin C, Ersan V, Ara C, et al. Biliary complications in 106 consecutive duct-to-duct biliary reconstruction in right-lobe living donor liver transplantation performed in 1 year in a single center: a new surgical technique. Transplant Proc. 2011;43(3):917-20.
19. Fulcher AS, Turner MA. Orthotopic liver transplantation: evaluation with MR cholangiography. Radiology. 1999;211(3): 715-22.