Life Science Journal

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Stentless Duct to Duct Biliary Anastomosis in LDLT Recipients with en Bloc High Hilar Dissection: Outcomes and Complications

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Abstract: Introduction: Biliary reconstruction of living donor grafts was done either by Roux-en-Y enteric anastomosis or duct to duct anastomosis duct-to-duct biliary anastomosis is considered nowadays the preferred procedure with many advantages over the Roux-en-Y hepatico-jejunostomy including, 1) avoiding the reflux of enteric contents into the biliary tree with decreasing the incidence of cholangitis; 2) faster and easier technique; and 3) maintaining the continuity of the bile duct which enables endoscopic access post operatively if needed. This study sought to compare the incidence of occurrence of biliary complications between two groups of recipients; group (A) high hilar dissection with (DDS), group (B) high hilar dissection with (DDD) as regard early bile leak or fistula and late bile duct strictures and cholangitis .Patient and method: Between February 2017 and February 2019 a total of 125 LDLT cases were transplanted in Ain Shams University Specialized Hospital and Wadi-Elnile hospital by the same surgical team, 25 cases were excluded due to different causes and the remaining 100 cases were randomly divided in to two groups according to their biliary anastomosis into 2 groups, Group (A) duct to duct anastomosis with intraductal trans-anastomotic external biliary stent (DDS) and Group (B) direct duct to duct anastomosis without stent (DDD). We compared the results of both methods of biliary reconstruction as regards the biliary complications namely bile leaks or fistula, anastomotic biliary strictures, and ascending cholangitis. Results: The incidence of bile leakage and biliary stricture were higher in group B (DDD) (10%) and (14%) than in group A (DDS) (6%) and (8%) respectively, however this was statistically insignificant, In both groups bile leakage was managed conservatively, while Biliary strictures were managed by ERCP with balloon dilation and plastic stent insertion. The incidence of cholangitis is lower in DDD occurred only in 3, while occurred in 6 patients in DDS group which also, statistically insignificant. Conclusion: Stentless duct to duct biliary anastomosis in LDLT with en bloc high hilar dissection in both donor and recipient seems to be better choice after adding isolated stent morbidity with comparable incidence of postoperative biliary complications.

[Mohamed Ahmed Rady, Ahmed Adel Abbas Abdelshafy, Mohamed Abdelsattar Abdelhamid, Rasha O. Refaie, MD and Dalia Fahmy Emam. **Stentless Duct to Duct Biliary Anastomosis in LDLT Recipients with en Bloc High Hilar Dissection: Outcomes and Complications.** *Life Sci J* 2020;17(1):29-36]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 5. doi:10.7537/marslsj170120.05.

Keywords: Duct to duct anastomosis, LDLT, stricture, leak.

1. Introduction

Living donor liver transplantation (LDLT) is one of the main management options for end-stage liver disease (ESLD). Biliary reconstruction of living donor grafts was done either by Roux-en-Y enteric anastomosis or duct to duct anastomosis. (1)

Recently, duct-to-duct biliary anastomosis is considered the procedure of choice with many privileges over the Roux-en-Y hepatico-jejunostomy including, 1) avoiding the reflux of GIT contents into the biliary tree with lowering the incidence of cholangitis; 2) faster and easier technique; and 3) maintaining the continuity of the bile duct which enables endoscopic access post operatively if needed.(2)

However, biliary complications still one of the most life threatening morbidities following LDLT, with reported complication rates as high as 20–34% for right lobe LDLT(3).The high incidence of biliary complications can be attributed to many reasons, the most important is affecting the blood supply of both the donor and recipient bile ducts.(4)

The high hilar dissection technique used during the recipient hepatectomy and donor graft dissection in LDLT was described aiming the preservation of the bile duct vascular supply in both the donor and the

recipient by preserving the right hepatic artery in continuity with the common bile duct during the dissection. [5]

Also, controversy between duct-to-duct anastomosis with stent (DDS) using external biliary stenting versus direct duct-to-duct anastomosis without stent (DDD) was reported in different studies as regard the incidence of bile leak, fistula, late strictures and cholangitis. [6,7]

This study sought to compare the incidence of occurrence of biliary complications between two groups of recipients; group (A) high hilar dissection with (DDS), group (B) high hilar dissection with (DDD) as regard early bile leak or fistula and late bile duct strictures and cholangitis.

2. Patients and Methods:

A prospective study was conducted on 125 LDLT Recipients cases were transplanted in Ain Shams University Specialized Hospital and Wadi-Elnile hospital by the same surgical team between February 2017 and February 2019.

25 cases were excluded due to in hospital mortality (n=11), pediatric cases (n=3), hepaticojejunostomy anastomosis due to underlying recipient bile duct disease (sclerosing cholangitis) (n=2), technical issues with devascularized recipient hepatic ducts (n=2), donor to recipient number of ducts mismatch (n=2) and hepatic artery thrombosis (HAT)(n=5). The in hospital mortality was due to bacterial or fungal chest infection (n=4), small for size syndrome (n=2), bleeding and disseminated intravascular coagulopathy (DIC) (n=2), hepatic artery thrombosis with failure of redo of the hepatic artery anastomosis (n=1), acute myocardial infarction (n=1), and Cerebrovascular stroke (n=1).

The remaining LDLT 100 cases were randomly divided according to their biliary anastomosis into 2 groups, Group (A) (n=50) duct to duct anastomosis with intraductal trans-anastomotic external biliary stent (DDS) and Group (B) (n=50) direct duct to duct anastomosis without stent (DDD). We compared the results of both methods of biliary reconstruction as regards the biliary complications namely bile leaks or fistula, anastomotic biliary strictures, and ascending cholangitis.

Bile leak or fistula was defined as persistent bilious drainage from drains or wound more than one-week post-transplant or peri-anastomotic collection on imaging that proves to be bile by Ultrasound guided aspiration and/or bilirubin level from drains or aspirate more than 3 times patient's serum bilirubin. Biliary stricture was defined as intrahepatic duct dilatation of >3 mm with narrowing of the biliary tree, which was identified either by Magnetic Resonance Cholangio-Pancreatography (MRCP) or Ultrasonography, with cholestatic pattern of liver function tests (elevated Total and Direct Bilirubin and/or Alkaline Phosphatase and Gamma Glutamyl Transferase GGT) with or with-out symptoms of biliary obstruction in the form of jaundice and cholangitis. Also the external biliary stent complications were recorded in group (A) as regard stent slippage, cholangitis due to the stent that resolved after stent removal, positive bacterial culture and sensitivity from the stent and patient compliance to the stent and requirements of daily dressing and care for the stent till its removal after 3 months after stent cholangiogram. The median follows up period was 16 months (9-23 months).

Surgical Strategy:

Donor operation

All donors were right lobe grafts. We started by a hockey stick incision with retraction of the costal margins with self-retaining retractor followed by mobilization of the right lobe after division of its ligamentous attachments. Then piggyback technique to isolate the right lobe of the liver from the retro-hepatic Vena Cava till the right hepatic vein was reached and isolated. Cholecystectomy and intraoperative cholangiogram via the cystic duct using 4 Fr silicon tube was done to identify the biliary anatomy (1 or 2 right ducts). This was followed by donor vascular pedicle dissection namely the right hepatic artery and the right portal vein without any trial to dissect the peri-ductal tissue around the right hepatic duct to preserve its blood supply which is an essential step in donor hepatectomy to decrease the incidence of postoperative biliary strictures and avoid thinning of the right duct wall by excessive dissection allowing it to hold the stitches well in the recipient biliary reconstruction step, also allowing easy closure of the donor duct stump after completion of resection. After those preparatory steps, formal right lobe resection using CUSA (Cavitron Ultrasonic Surgical Aspirator), bipolar cautery and monopolar spray cautery. CUSA was essential during liver resection to identify the veins draining segments 5 and 8 to be reconstructed in the recipient if they were large enough to avoid graft congestion, dysfunction and small for size syndrome. After completion of resection the right duct is divided after marking the line of division by metal clips at the edge of the right duct and repeating cholangiogram to accurately divide the right duct to avoid injury or stenosis of the donor remnant duct and avoid unnecessary increase of the number of right ducts to be reconstructed in the recipient Fig (1). Right lobe was then harvested after vascular control of the arterial and portal inflow and venous outflow. The graft was sent to the back table with flushing of the graft with preservative solution

HTK (Histidine tryptophan ketoglutarate), with possible ductoplasty if there were multiple ducts that can be approximated without tension and twist with 6/0 PDS.

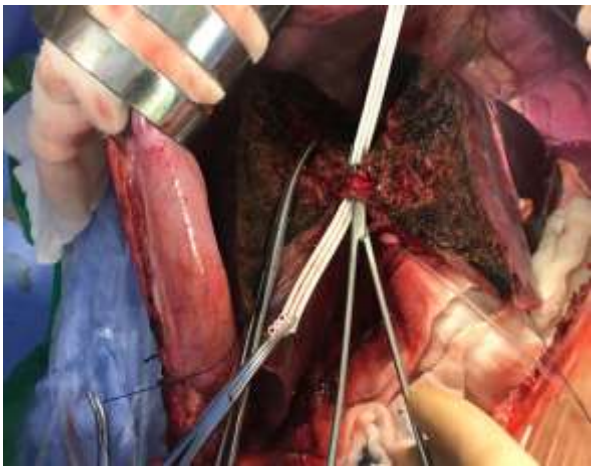

Fig (1): Marking the line of division of right hepatic duct with metal clips after completion of resection.

Recipient operation

All patients received a right lobe graft with a minimum Graft Weight Recipient Ratio (GRWR)>= (0.8). We started by a hockey stick incision with retraction of the costal margins with self-retaining retractor followed by mobilization of the right lobe and left lobe after division of its ligamentous attachments. Then piggyback technique to isolate the right lobe of the liver from the retro-hepatic Vena Cava till the right hepatic vein was reached and isolated. Then careful pedicle dissection starting with left hepatic artery from below upwards as high as possible till its branches to ensure good length of artery as in our technique the left artery was our first choice of arterial graft reconstruction. This was followed by left portal vein dissection then we shifted to dissection of the right portal vein then dissection of the common portal vein downwards. The right hepatic artery as well as the right hepatic duct were divided en bloc as high as possible to preserve the blood supply of the bile duct from minute twigs from the right hepatic artery.

Biliary reconstruction; the technique of biliary anastomosis in both groups was the same (Duct to Duct anastomosis), whether one or two anastomoses. Two corner stitches with double armed 6/0 PDS on either side of the graft duct were inserted with another stitch at the middle of the anterior wall of the graft duct (hang up stitch) to expose the posterior wall of the graft duct to facilitate the anastomosis. This was followed by insertion of interrupted stitches to the posterior wall of the graft and the recipient ducts with the stitches tied outside. In the stent group, a 5-Fr. plastic stent is inserted via a puncture on the anterior wall of the recipient common bile duct to be passed inside the donor duct, then fixed to the anterior wall of the anastomosis using one of the corner stitches. The anterior wall of the anastomosis was continued in both groups in an interrupted fashion with the sutures being tied after completion of the whole anterior wall to facilitate the anastomosis and avoid accidental incorporation of the posterior wall by stitches leading to narrowing of the anastomosis.

In the DDS group cold saline was injected through the stent to check for possible leakage while in the DDD group leakage was tested via a temporary stent inserted in the recipient cystic duct Fig (2). In both groups an intraoperative cholangiogram was done to confirm the anastomotic patency and absence of leakage. The external biliary drain was fixed to the skin in an S shaped manner by 5 or 6 stitches prolene 4/0 to avoid slippage and decrease tension on the stent. The external biliary drain was left to drain freely to urinal bag until normalization of liver enzymes then closed until its removal after 3 months after doing stent cholangiogram to check for biliary anastomotic patency and absence of leakage.

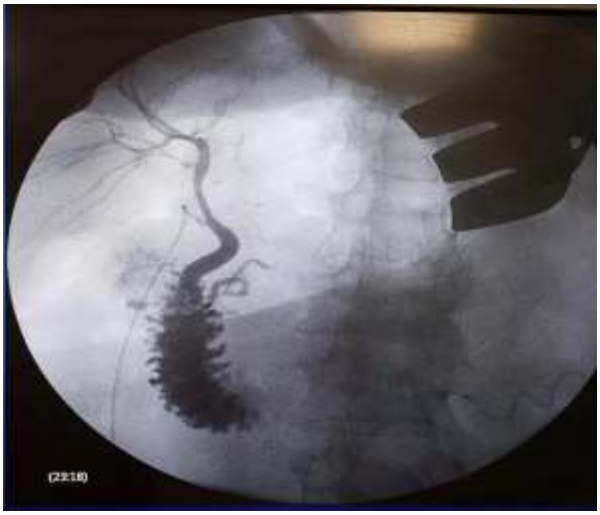

Fig (2): Intraoperative cholangiogram from temporary stent in the recipient cystic duct (DDD group)

Statistical Analysis:

Descriptive and inferential statistics of patient and operative characteristics were performed with t tests for continuous variables and chi-square for categorical variables. A multivariable logistic regression model was constructed to study the association between patient and operative characteristics and biliary complications. P value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 20 statistical software (SPSS).

3. Results

Between February 2017 and February 2019, a total of 100 LDLT cases were enrolled in this study. There was no significant statistical difference in both groups as regards age, sex, underlying liver disease, MELD score, Child classification, and presence or absence of HCC. These demographic data are summarized in table (1).

Table (1): Study group demographic data:

		Group A	Group B	P-value	Sig.
		No. = 50	No. = 50		
Age	Mean±SD	52.94 ± 6.72	50.42 ± 8.46	0.102	NS
	Range	39 – 65	34 – 65		
Sex	Females	14 (28.0%)	9 (18.0%)	0.235	NS
	Males	36 (72.0%)	41 (82.0%)		
Hepato-pathy	HCV	43 (86.0%)	37 (74.0%)	0.373	NS
	HBV	3 (6.0%)	7 (14.0%)		
	Autoimmune hepatitis	2 (4.0%)	3 (6.0%)		
	Cryptogenic	1 (2.0%)	3 (6.0%)		
	Wilson	1 (2.0%)	0 (0.0%)		
MELD	Mean±SD	18.08 ± 4.91	18.10 ± 5.43	0.985	NS
	Range	8 – 30	8 – 30		
HCC	No	36 (72.0%)	38 (76.0%)	0.648	NS
	Yes	14 (28.0%)	12 (24.0%)		
Child	A	5 (10.0%)	4 (8.0%)	0.836	NS
	B	3 (6.0%)	2 (4.0%)		
	C	42 (84.0%)	44 (88.0%)		

There was no significant difference as regard the bile ducts number of donor in both groups as well the number of biliary anastomosis in both groups as well table (2).

Table (2): Summary of donor number of bile ducts and number of bile duct anastomosis.

No. of bile duct	Group A (DDS)	Group B (DDD)	P- value	Significance
Single	22 (44%)	24 (48%)	0.834	NS
Double	28 (56%)	26 (52%)	0.923	NS
Ductoplasty	10 (20%)	11(22%)	1.2	NS
total single anastomosis	32(64%)	35(70%)	0.912	NS
total double anastomosis	18(36%)	15 (30%)	0.876	NS

The incidence of bile leakage and biliary stricture were higher in group B (DDD) (10%) and (14%) than in group A (DDS) (6%) and (8%) respectively, however this was not statistically significant, In both groups' bile leakage was managed conservatively as most of those patients the drain stopped to drain bile spontaneously with only 3 patients required ultrasound guided aspiration and pig tail insertion. Biliary strictures were managed by ERCP with balloon dilation and plastic stent insertion.

The incidence of cholangitis is lower in DDD occurred in 3 patients only and are directly related to anastomotic biliary strictures occurred in those 3 patients. Cholangitis in the DDS occurred in 6 patients, 2 out of the 6 patients were also related to the development of anastomotic biliary strictures, the remaining 4 patients with cholangitis were due to ascending infection through the external biliary drain with +ve bacterial cultures from the external biliary drain, 2 out of those 4 patients, cholangitis occurred after the routine cholangiogram after 3 months post transplantation. Cholangitis required hospital readmission and administration of antibiotics which was a financial and psychological burden on the patients.

However, the incidence of cholangitis in both groups was not statistically significant. The biliary complications were summarized in table (3).

Table (3): Biliary complications:

	Group A(DDS)	Group B (DDD)	p value	significance
Leak	3 (6.0%)	5 (10.0%)	0.538	NS
Stricture	4 (8%)	7 (14.0%)	0.401	NS
Cholangitis	6 (12.0%)	3 (6.0%)	0.110	NS

The incidence rate of biliary complications in DDS group was 26% compared to 30% in the DDD group which was statistically insignificant. The overall incidence of bile leak and biliary stricture in both groups were 8% and 11% respectively. The incidence rate of biliary complications was 28% in both groups.

Isolated stent morbidity:

Apart from cholangitis in the DDS group caused by the external biliary drain, the presence of the external biliary drain requires more care for the patients in the form of daily dressing and care to avoid slippage. Also, the stent holding stitches were painful to some patients. One patient in the DDS group developed bile leakage and biloma due to accidental slippage of the stent one-month post-transplant. This patient was managed by U/S guided aspiration of the biloma and drain insertion (pig tail) till resolution of the bile leakage.

Another problem due to the presence of the stent that occurred in 10 patients was the plastic tip of the stent being broken before stent closure making its connection it to the urinal bag more difficult which required more frequent visits to the outpatient clinic to fix the problem.

An unusual intraoperative morbidity occurred in DDS group during stent insertion was accidental injury to the right hepatic artery at the site of puncture of the common bile duct due to abnormal position of the Rt hepatic artery with intraoperative bleeding till compete isolation of the right hepatic artery from the bile duct to control bleeding with subsequent devascularization of the bile duct and development of biliary stricture 3 months later. Hypersensitivity to the contrast dye injected through stent cholangiogram was recorded in 6 patients that required day case admission and medical treatment of the condition.

All the postoperative care and stent morbidity were avoided in the DDD group making the postoperative care and patient satisfaction after transplantation much better.

4. Discussion

LDLT is an important source of liver grafts for patients with end stage liver disease or hepatocellular carcinoma in absence of cadaveric organ transplantation in Egypt. However biliary complications remain the most frequent early complication. Duct to duct anastomosis remains the preferable method of biliary reconstruction. It carries many advantages on Roux-en-y hepaticojejenostomy including shorter operative time, no enteric anastomosis, preservation of the physiological sphincter of oddi, easy access to the biliary tree through endoscope for detection and management of biliary complications. [1, 2].

The blood supply of the bile duct anastomosis plays a crucial role in duct to duct biliary reconstruction. Biliary ischemia is incriminated in

post transplantation biliary complications and poor long-term graft prognosis. A delicate arterial plexus surrounding the biliary tract is one of the most important sources of this blood supply. [8]

Moreover, an arterial network that is bilaterally fed by the plexus from branches of both the right and left hepatic artery is considered the vascular supply for both hepatic ducts. During the donor operation, dissection along the bile duct should be done so carefully and away from the bile duct wall to avoid any injury to this fine arterial plexus. As a result of the tenuous blood supply from the graft side and the pathologic changes in the biliary tree are mainly localized proximal to the anastomotic site, microcirculatory problems are of greater importance for the donor bile duct. [9]

For the recipient operation, the common hepatic duct for the anastomosis should be dissected with maintaining an adequate blood supply from the ascending axial vessels, that's why minimal dissection should be done around bile duct. A free anastomosis within the wall of the bile duct is formed by multiple arteriolar branches coming from the 3 o'clock, 9 o'clock, and retro portal arteries. [4]

Vellar reported that the arterial plexus on the wall of bile duct is usually supplied from below from the posterior superior pancreaticoduodenal artery by its ascending marginl arteries. Additionally, the marginal arteries form an anastomosis within the mucosa of the bile duct which also contributes to the blood supply for the anastomosis. [10]

The high hilar dissection techniques in both donor and recipient operations of the periductal soft tissue including the peri-choledochal vasculature are currently universally performed for LDLT. Those techniques have led to decrease the incidence rate of biliary complications in our center from 41% to 30%.

In a study by *Abu-Gazala et al*, en bloc hilar dissection was accompanied with minimal rates of biliary complications after controlling of patients and operative characteristics [8]. In particular, biliary strictures were less common. The lower rate of biliary stricture found in this study are similar to what *Soejima et al*, reported when they applied high hilar dissection. [9]

The use of external biliary stent in duct to duct biliary reconstruction in LDLT facilitate access to the biliary tract, with the possibility of performing a rapid and noninvasive tube-cholangiography and obtaining bile cultures; it also protects the anastomosis from leakage by lowering biliary pressure [11, 12]. A study by *Popescu et al*., did not show a significant association between the use of an external biliary stent and a lower rate of biliary complications [13]. A study by *hong et al.*, reported that a thick and tight duct to duct anastomosis using a 6-0 suture could reduce bile leaks without an external biliary drain, but that it would increase biliary strictures after LDLTs [14]. *Liu et al*. found that the bile leak did not increase without use of an external biliary stent in LDLTs, but that the incidence of biliary strictures was as high as 24% for a short median follow-up period of 13 months1. [15]

Temporary biliary stent is a point of controversy with many studies advocating its advantages and disadvantages. A study by *Vivek et al.,* defy the need of biliary stenting. [16] While another two studies demonstrated that the external stent markedly decrease the incidence of biliary stricture. [17, 18]

In our study the overall incidence of biliary complications was 28% in both groups and the overall incidence of bile leak and biliary stricture in both groups were 8% and 11% respectively. *Akamatsu et al*., in a systematic review of biliary complications in 2812 LDLT patients, reported a 19% incidence of biliary strictures and a 9.5% incidence of bile leak [19].

Our results are comparable to the recorded worldwide results of biliary complications. In our study there were statistically no significant difference as regard the rate of biliary complications between DDS and DDD groups though the rate of bile leak and stricture was slightly higher in the DDD group and incidence of cholangitis was higher in the DDS group. An added value of stentless duct to duct anastomosis is the absence of the isolated external biliary stent morbidity decreasing the frequent outpatient clinic visits, more patient's compliance and satisfaction and no stent cholangiogram after 3 months before removal of the stent with its hazards of cholangitis and hypersensitivity to the contrast injected. In absence of stent postoperative biliary tree imaging can be accurately assessed via MRCP abolishing need for any postoperative cholangiograms.

Conclusion

Duct-to-duct biliary reconstruction in right lobe LDLT is a good option with better endoscopic access for treating biliary stricture. Stentless duct to duct biliary anastomosis in LDLT with en bloc high hilar dissection in both donor and recipient seems to be better choice after adding isolated stent morbidity with comparable incidence of postoperative biliary complications. Long term observation may be required to collect adequet data for this treatment modality to become more popular. It is hoped that increased experience and continuing refinements of the technique will lead to improved outcomes in right lobe LDLT.

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1/8/2020