

Management of Early Post-Operative Biliary Complications Recipient of Adult Living Donor Liver Transplantation

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ABSTRACT

Background: Living donor liver transplantation (LDLT) has become a well-recognized treatment option for patients with end-stage liver disease due to the scarcity of deceased donor organs. While there have been significant advancements in graft preservation technologies, immunosuppressive medications, and surgical technique for this operation, the primary cause of patient morbidity, graft loss, and death after LDLT continues to be biliary problems.

Aim and objectives: to highlight different early post-operative biliary complication in recipients of adult living donor liver transplantation and their different management modalities and their outcomes.

Subjects and methods: this study conducted at Ain shams university hospitals from March 2018 to January 2020. This study was conducted on 100 patients.

Result; Regarding age Mean $\pm$ SD was 48.65 $\pm$ 11.67 and sex male was more prominent 78.0%. There was highly statistically significant difference between Biliary Complication and management lines as p value <0.001*. There was no statistically significant difference between Biliary Complication and age, sex, HCC and Past history. MELD score was 16 %, Child score as C10 was the highly percent was 24%. Operative time) MEAN $\pm$ SD) was 506.57 $\pm$ 89.94, Cold ischemia Median was 50 and Warm ischemia Median was 45.

Conclusion: biliary complications remain a common source of morbidity, which requires further technical refinement and established management strategy.

Keywords: early post-operative biliary complications, recipient of adult living donor liver transplantation.

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This is a Retrospective study. This study was conducted in Ain Shams University Hospitals. From March 2018 to January 2020.

Study population

Inclusion criteria: Adult older than 18 years and eligible for living donor liver transplantation.

Exclusion criteria: Pediatric patient.

Sampling Method: according to the inclusion and exclusion criteria.

Sample Size: 100 patients.

Method:

Pre-operative work up:

Clinical assessment: General examination (Abdominal Examination) and Investigational Studies (Routine laboratory investigations and Radiological investigation), Endoscopy, Medical Consultations and Calculation of MELD score and CHILD classification.

Ethical Consideration: Official permissions were obtained from Hepato-pancreatico-biliary Unit, Surgery Department, Faculty of Medicine, Ain Shams University, Scientific ethical committee of patients was respected, The study group was informed about the nature and the purpose of the study and a signed consent was taken from the patients, after they are given a full explanation of the study before interview, The study group weren't exposed to any harm and Ensuring confidentiality.

Statistical Analysis: The data were collected tabulated and statistically analyzed using IBM SPSS software (statistical program for social science version 21). Description of quantitative variables were done as mean and standard deviation, and qualitative data as frequency. Chi square test was used to compare the groups as regard qualitative variable. Student t-test was used to compare two groups as regard quantitative variable in parametric data.

The comparison was done using: The student "t" test, Mann Whitney test, Chi- square test (X²), Z-test for percentage and Odds ratio (OR).

INTRODUCTION

Living donor liver transplantation (LDLT) has become a well-recognized treatment option for patients with end-stage liver disease due to the scarcity of deceased donor organs. Though there have been significant advancements in graft preservation technologies, immunosuppressive treatments, and surgical technique for this operation, the primary cause of patient morbidity, graft loss, and death after LDLT remains biliary problems (1).

Regardless of the kind of graft, biliary strictures have been documented to occur in 18%-32% of LDLT patients. While a stricture may appear at any point following transplantation, a median of 5.9 months passed between LDLT and the beginning of biliary stricture. After a year of LDLT, between 70% and 87% of biliary strictures develop (2).

One possible source of bile leakage is the anastomotic location. cystic duct stump remnant. tract of T tubes. The graft's surface is cut. or a bile duct accessory that is injured. similar to restrictions. Anastomotic leaking is frequently caused by ischemia damage or vascular insufficiency. Between 5% and 18% of patients experience bile leakage following LDLT (3).

One of the most common complications in the early post-LDLT period is bile leakage, which is discovered during the first month following LDLT in 70% of instances (4).

Sometimes, biliary problems following a transplant result in graft failure or recurrent hospital stays. Which need a second transplant? which raise the price of medical care (5).

Despite the fact that no precise treatment algorithm has been developed. Treatment options for biliary problems are many and well-developed. encompassing endoscopic methods. Transhepatic percutaneous intervention. as well as surgical treatments (6). Endoscopic treatment is considered to the preferred first-line modality for patients that have previously undergone duct-to-duct biliary as it is less invasive. Safe. Effective. More easily accessible. And more convenient for the patient. Percutaneous therapy is then subsequently considered in cases where the endoscopic approach has failed (7).

This study aimed to highlight different early post-operative biliary complication in recipients of adult living donor liver transplantation. That occurred in Ain shams university hospitals and their different management modalities and their outcomes.

PATIENTS AND METHODS

Chi ld sco re						
A5	4(6.1)	2(50)	0	0	0	Mc=7.43
A6	5(7.6)	)	2.2)	7)	0	P<0.001*
B7	0	0	3(3	0.0)	0	
B8	6(9.1)	0	3.3)	1(6.7)	3(5.0)	
B9	8(1	2(	3.3)	3(2	3(5	
C1	2.1)	50	1(11	0.0)	0.0)	
0	16(	)	.1)	2(1	0	
C1	24.2	0	0	3.3)	0	
1	)	0	0	0	0	
C1	16(	0	0	0		
2	24.2	0	0	5(3		
C1	)			3.3)		
3	7(1			0		
C1	0.6)					
4	3(4.5)					
	1(1.5)					

MC: Monte Carlo Test, KW:Kruskal Wallis test *statistically significant

Biloma, Leak +biloma

This table showed that there was a statistically significant difference between the studied groups as regard MELD score. There was no statistically significant difference between the studied groups as regard relation between MELD score, child score and types of biliary complications.

Table (3): relation between operative characters and types of biliary complications

Biliary Complication						Test of significance
	no	Leak	Structure	Leak + structure	Others #	
Operative (time minutes) Median (min-max)	510 (162-720)	660 (450-720)	540 (480-630)	480 (480-720)	520 (480-540)	Kw=6.72 P=0.151
Cold ischemia Median (min-max)	45 (20-140)	60 (45-75)	48 (45-70)	56 (30-150)	32.5 (20-45)	Kw=10.16 P=0.038*
Warm	45 (20-150)	105 (30-)	45 (35-90)	50 (30-55)	42.5 (30-)	Kw=5.31 P=0.

RESULTS

Table (1): relation between demographic, past history and types of biliary complications

Biliary Complication						Test of significance
	no	Leak	Stricture	Leak + stricture	Others#	
Age/years	47.7 3±1 3.09	57. 50± 4.7 3	50. 56± 7.3 7	47. 60± 9.3 2	52. 67± 4.8 0	F=0. 943 P=0. 443
Sex Male Female	52(7 8.8) 14(2 1.2)	3(7 5.0) 1(2 5.0)	9(1 00) 0	11(73. 3) 4(2 6.7)	3(5 0.0) 3(5 0.0)	Mc= 5.52 P=0. 238
HC C-ve +ve	39(5 9.1) 27(4 0.9)	2(5 0.0) 2(5 0.0)	5(5 5.6) 4(4 4.4)	12(80. 0) 3(2 0.0)	4(6 6.7) 2(3 3.3)	Mc= 2.76 P=0. 599
Past history -ve +ve	30(4 5.5) 36(5 4.5)	1(2 5.0) 3(7 5.0)	5(5 5.6) 4(4 4.4)	10(66. 7) 5(3 3.3)	2(3 3.3) 4(6 6.7)	Mc= 3.84 P=0. 429

MC: Monte Carlo test, *statistically significant

Biloma, Leak +biloma

This table showed that there was no statistically significant difference between the studied groups as regard relation between demographic, past history and types of biliary complications.

Table (2): relation between MELD score, Child score and types of biliary complications

Biliary Complication						Test of significance
	no	Leak	Stricture	Leak + stricture	Others#	
<u>M</u> <u>EL</u> <u>D</u> <u>scores</u> Median (min-max)	16(6-35)	15(7-18)	13(8-18)	16(8-23)	17(12-22)	Kw=6.76 P=0.149

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C13 C14	1(1.5)	0	
A	9(13.6)	5(14.7)	$\chi^2=3.67$
B	14(21.2)	13(38.2)	P=0.159
C	43(65.2)	16(47.1)	

Z: Mann Whitney U test, χ^2 =Chi-Square test, MC: Monte Carlo test

This table showed that there was no statistically significant difference between the studied groups as regard relation between MELD score, child score and Prevalence of biliary complications.

Table (29): Outcome in donors.

	N=100	%
Cell saver		
Mean± SD (min-max)	481.5±271.7 (140.0-1200.0)	
ICU stay (days)		
Mean± SD (min-max)	2.49±0.58 (2.0-4.0)	
Hospital stay (days)		
Mean± SD (min-max)	10.41±2.99 (5.0-20.0)	
Complications		
No	97	97.0
Yes	3	3.0
Management		
Conservative	97	97.0
Conservative with pigtail	1	1.0
Pigtail	2	2.0

This table showed that there was no Complications by percent 97 %. Conservative Management percent was 97%.

DISCUSSION

Liver transplantation is currently considered worldwide a definite therapy for end-stage liver disease. Vascular complications in liver transplantation are one of the most serious complications that can affect graft viability; therefore, early recognition is critical for proper management. Insufficient liver blood supply can lead to early graft failure; therefore, intraoperative and early postoperative diagnosis is crucial for graft survival (8).

In current study, regarding age Mean ±SD was 48.65±11.67 and sex male was more prominent 78.0%. Presence HCC was 38%, Primary diagnosis including Hepatitis C virus-associated liver cirrhosis was 72.0%, Hepatitis B virus-associated liver cirrhosis was 3%, autoimmune hepatitis was 11.0%, Primary biliary cirrhosis was 1%, Budd Cairri was 2%, Fulminant hepatic failure was 1%, Cryptogenic cirrhosis was 5%, Bilharziasis was 4% and Primary sclerosing cholangitis was 1%.

Our results agreement with Aal et al. who found that the median age was 47 years (range,

ische mia	)	120			50)	257
Medi an		)				
(min-max)						

KW:Kruskal Wallis test , *statistically significant

Biloma, Leak +biloma

This table showed that there was a statistically significant difference between the studied groups as regard Cold ischemia. There was no statistically significant difference between the studied groups as regard Operative time and Warm ischemia.

Table (4): relation between bile duct number and anastomosis and types of biliary complications

	no	Leak	Stricture	Leak + stricture	Others#	Test of significance
Bile duct NO	1(1-4)	2(1-2)	1(1-2)	2(1-3)	2(1-3)	Kw=7.64 P=0.106
Bile duct anastomosis No	43(65.2) 23(34.8)	2(50.0) 2(50.0)	8(88.9) 1(11.1)	8(53.3) 7(46.7)	4(66.7) 2(33.3)	Mc=4.17 P=0.842
Bile duct anastomosis type	57(86.4) 4(6.1) 2(3.0) 3(4.5)	4(100.0) 0 0 0	7(77.8) 2(22.2) 0 0	9(60.0) 5(33.3) 0 1(6.7)	6(100) 0 0 0	Mc=13.93 P=0.305
• duct-to-duct anastomosis.						
• approx. of 2 ducts into one						
• Roux En Y						
• duct-to-duct anastomosis + approx. of 2 ducts into one						

MC: Monte Carlo Test, KW:Kruskal Wallis test *statistically significant

Biloma, Leak+ biloma

This table showed that there was no statistically significant difference between the studied groups as regard relation between bile duct number and anastomosis and types of biliary complications.

Table (5): relation between MELD score, child score and Prevalence of biliary complications

	Biliary Complication		Test of significance
	no n=66(%)	yes n=34(%)	
MELD score.			
Median (min-max)	16(6-35)	14(7-23)	Z =1.34 P=0.181
Child score			
A5	4(6.1)	2(5.9)	Mc=16.35 P=0.06
A6	5(7.6)	3(8.8)	
A7	0	3(8.8)	
B7	6(9.1)	4(11.8)	
B8	8(12.1)	6(17.6)	
B9	16(24.2)	8(23.5)	
C10	16(24.2)	3(8.8)	
C11	7(10.6)	0	
C12	3(4.5)	5(14.7)	

HCC, past history. There was no statistically significant difference between primary diagnosis and Prevalence of biliary complications.

Our results agreement with Dabbous et al. who found that the mean age, sex distribution, the median degree of steatosis, the number of biliary ducts, and biliary anastomosis were similar in both groups ($p > 0.05$) (12).

In current study, there was no statistically significant between MELD score, child score and Prevalence of biliary complications. There was statistically significant difference between operative time and Prevalence of biliary complications. There was no statistically significant difference between Cold ischemia, Warm ischemia and Prevalence of biliary complications.

In current study, there was no statistically significant difference between bile duct number, anastomosis and Prevalence of biliary complications.

Our results disagreement with Arianet al. who found that duct-to-duct anastomosis was the mostly commonly performed technique in group single bile duct, whereas double duct-to-duct and duct-to-sheath were significantly higher in group multiple bile duct (13).

Operating time was quite high in group B compared to group single bile duct (438 ± 72 minutes vs 420 ± 61 minutes, respectively; $P = .05$). Regarding biliary complications ($n = 40$, 23.2%), the rates of biliary leakage ($n = 17$, 9.9%) and strictures ($n = 25$, 14.5%) were similar in both groups ($P = .164$ and $.773$, respectively). CPS was positively correlated (for Child B and C, odds ratio [OR]: 10.669 and 17.866, respectively).

In current study, there was no statistically significant difference between Stent uses, IOC, HA anastomosis and Prevalence of biliary complications but there was statistically significant difference between HARI and Prevalence of biliary complications. There was no statistically significant difference between vascular complications and Prevalence of biliary complications.

Hepatic arterial stenosis (HAS) was detected in four (3.3%) of the cases with vascular complications. It was usually localized at the site of anastomosis. Management of the cases by the means of interventional radiology in the form percutaneous transluminal angioplasty, balloon dilatation, and stent insertion was done (9).

Biliary complications among studied cases as HARI were no statistically significant differences. Operative time was more statistically significant difference. Regarding Age/years (Mean $\pm$ SD) was 29.73 ± 7.43 ,

17–68 years). The median body weight was 81.3 kg (range, 50–170 kg). The median BMI was 27.05 kg/m^2 (range, 17–44 kg/m^2). The donor was related to the recipient in 60.9% of cases and not related in 39.1% of cases. Primary diagnosis including Hepatitis C virus-associated liver cirrhosis was 32.5.0%, Hepatitis B virus-associated liver cirrhosis was 2.8%, and autoimmune hepatitis was 3.5%, Primary biliary cirrhosis was 1%, Budd Cairri was 2%, Fulminant hepatic failure was 1%, cryptogenic cirrhosis was 5.9%, Bilharziasis was 4% (9).

The most frequent original liver diseases were hepatitis C virus (HCV) (51.8%), hepatocellular carcinoma (HCC) (31.8%) and cryptogenic liver cirrhosis (5.3%) (10).

In current study, MELD score was 16 %, Child score as C10 was the highly percent was 24%.

Operative time (MEAN $\pm$ SD) was 506.57 ± 89.94 , Cold ischemia Median was 50 and Warm ischemia Median was 45.

The median cold ischemia (CIT), warm ischemia (WIT), and HA anastomotic times were 60 (range; 20–340) mins, 50 (range; 25–120) mins and 60 (range; 11–290) mins respectively. This reported by % (10).

In current study, there was no statistically significant difference between operative time and types of biliary complications. There was no statistically significant difference between Warm ischemia and types of biliary complications. There was statistically significant difference between Cold ischemia and types of biliary complications.

Our results disagreement with Nakamura et al. who found that There were no differences in recipient and donor age, model for end-stage liver disease (MELD) score, amount of blood loss, operative time, or cold and warm ischemia time between two groups (11).

Our results showed that there was no statistically significant difference relation between stent uses, IOC, HA anastomosis and types of biliary complications but there was statistically significant difference between Biliary Complication and HARI. There was no statistically significant difference between vascular complications and types of biliary complications.

Assessment with early and regular postoperative follow-up imaging and careful surgical dissection allows identification and performance of satisfactorily vascular anastomosis, which significantly reduces vascular complications (9).

Our results showed that there was no statistically significant difference among prevalence of biliary complications and demographic characters as Age/years, Sex,

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regarding sex male was 76%, left Dominant hand was 52%, Blood group O+ was 47, Unrelated Relations was 52%, Weight/Kg (Mean $\pm$ SD) was 75.02 $\pm$ 11.36, BMI (Kg/m²) Mean $\pm$ SD was 24.29 $\pm$ 3.01.

our results showed that Presence Previous surgical operation was 24%, Rt. Inferior hepatic vein was represent 8.0% Bifurcated was 96.0%, arise Celiac trunk was 98%, Dominant right Hepatic vein 98%, no Ligated 75%, Single right duct was 44%, RLV Mean $\pm$ SD was (528.92 $\pm$ 123.5), MHV Mean $\pm$ SD was (528.92 $\pm$ 123.5), Actual weight Mean $\pm$ SD was (853.88 $\pm$ 191.5), Diff. Mean $\pm$ SD was (70.05 $\pm$ 132.7) normal Mutation was 90%, Operative time/hrs. (Mean $\pm$ SD) was 6.54 $\pm$ 1.1 and Abnormal Liver biopsy was 58.

In current study, Cell saver (Mean $\pm$ SD) was 481.5 $\pm$ 271.7, ICU stay (Mean $\pm$ SD) was 2.49 $\pm$ 0.58, Hospital stay (Mean $\pm$ SD) was 10.41 $\pm$ 2.99, and absence of Complications 97%, Conservative Management was 97%.

In a study by Aal et al. Who found that Left lobe liver transplantation was performed in 17 cases, and right lobe liver transplantation was performed in 983 cases. The operation was done electively in 937 (93.7%) cases and as emergency in 63 (6.3%) cases. The median operative time was 10.83 h (range, 5.47–17.25 h). The median blood loss was 1750 ml (range, 120–19 000). The median hospital stay for the patients was 23 days (range, 14–171 days). This results proposed with our results (9).

Our results in line with Koksai et al. anastomotic stricture and leakage contribute significantly to morbidity after liver transplantation; but with advances in both operative and therapeutic modalities, these complications have become better controlled. With the growing number of centers adopting DD biliary reconstruction, endoscopic treatment has become the standard strategy for biliary complications after transplantation with satisfactory results (14).

CONCLUSION

This systematic review revealed that biliary complications remain a common source of morbidity, which requires further technical refinement and established management strategy.

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