SURGICAL MANAGEMENT OF POST LIVING DONOR LIVER TRANSPLANTATION BILIARY COMPLICATIONS

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ABSTRACT

Background: *Biliary tract complications are the most common complications after liver transplantation and it remains a major source of morbidity in liver transplant patients. Non-operative treatment is often successful in early complications. Late complications presenting with leaks and obstruction are often more difficult to treat non-operatively and frequently require surgical treatment or re-transplantation. Some centers are more aggressive with management of biliary strictures and prefer early surgical intervention as opposed to multiple endoscopic dilations.*

Aim of the work: *The aim of this study is to, discuss the surgical management of post-transplant biliary complications and its outcome and rate of success with or without previous non-surgical methods in the postoperative follow up.*

Patients and methods: *This is a combined prospective and retrospective study conducted in DAR EL FOAD hospital, liver transplantation unitduring the period from 2011 till 2020. it included patient with post-transplant biliary complications who underwent surgical intervention with and without prior conservative trials. the study contains 14 patients who had failed non operative management. We discussed the surgical management and its outcome.*

Results: *380 patients underwent liver transplantation during this period. 45 had biliary complications, of them 31 patients were managed by non-surgical measures and those were excluded from our study. 14 patients underwent surgical intervention. we had 4 patients with stricture, 7 patients with leakage and 3 patients with stricture and leakage. two patient had recurrent biliary complications after surgery and there was only one mortality.*

Conclusion: *Non-surgical measures are the primary treatment option for post transplantation biliary complications, but surgical management is the definite management for refractory cases with less hospital stay and recurrent admissions.*

Keywords: *liver transplantation, biliary complication, stricture, leakage*

INTRODUCTION:

Liver transplantation has become a well-established treatment for end stage liver disease. Living donor liver transplant (LDLT) is still the predominant form for trans-plantation in Egypt.[1]

The postoperative course in liver transplantation patients ranges from straight forward to extremely complicated, and the

outcome depends on the status of the recipient, donor organ, and technical issues in the operation. Complications after liver transplantation can have a significant impact on outcomes and costs of the procedure. Timely diagnosis of alterations in the normal postoperative course is the critical factor to minimize morbidity and mortality and to improve outcomes.[2]

Postoperative complications include, vascular complications as hepatic artery or portal vein stenosis or thrombosis, biliary complications as anastomotic stricture or leakage, graft rejections which may be acute or chronic rejections and other complications as bleeding, infection or encephalopathy. [3]

Biliary tract complications are the most common complications after liver transplantation. These complications are encountered more commonly as a result of increased number of liver transplantations and the prolonged survival of transplant patients. [4]

Non-operative treatment is often successful in early complications. Late complications presenting with leaks and obstruction are often more difficult to treat non-operatively and may require surgical treatment or re-transplantation. [5]

Anastomotic bile leaks after liver transplants in both Duct to duct anastomosis (DD) and Roux-en-Y Hepaticoje junostomy (RYHJ) with failed non operative management are managed surgically. Treatment may include the surgical revision of an anastomosis or the conversion of a DD to a RYHJ. Small anastomotic leaks after liver transplants can be managed with endoscopic stenting (DD) and PTC stenting with an internal-to-external drain (RYHJ). [6]

AIM OF THE WORK:

The aim of this study is to, discuss the surgical management of post-transplant biliary complications and its outcome and rate of success with or without previous non-surgical methods in the postoperative follow up.

PATIENTS AND METHODS:

This was a combined prospective and retrospective study conducted in DAR EL FOAD hospital, liver transplantation unit during the period from 2011 till 2020.

Group of patients; patient with post-transplant biliary complications undergoing surgical intervention with and without prior conservative trials.

Inclusion criteria: Adult or pediatric male or female patients. Patients with biliary complications either leakage or stricture post-transplant. Patients with early and late biliary complications. Patient with failed conservative and interventional radiology methods.

Exclusion criteria: Patient refusal. Patients with biliary complications treated with conservative methods.

All patients will be subjected to the following:

Pre transplantation assessment for the Recipient: Full clinical history; personal history, present history, past history of any medical disorder. Full clinical examination; vital signs, body examination. Routine preoperative investigations including, complete blood count, random blood sugar, liver function test, bilirubin level, kidney function test, coagulation profile, blood gases. Pelvis abdominal ultrasound, MRCP and portal vein and hepatic artery duplex. Preoperative co-morbid factors such as hypertension, Diabetes mellitus or electrolyte disturbance, bilirubin nephropathy or encephalopathy will be controlled when possible before surgery

Post transplantation assessment of the Recipient: Patient follow up is done first in

ICU where strict monitoring is done and if he/she is stable vitally and surgically, patient can be discharged from ICU to the transplantation unit where strict monitoring and follow up is done before patient can leave the hospital**.**

Monitoring of patient postoperatively include: -vital signs include pulse, blood pressure and temperature. Complexion of patient including pallor, cyanosis or jaundice. Laboratory follow up including liver functions, kidney functions, bilirubin level, CBC, coagulation profile, blood gases and lactate level. If any abnormalities appear as fever or jaundice or bile in drains or patient become toxic with increase leucocytic count, elevated serum bilirubin or dramatic increase in liver enzymes, so further investigations and imaging should be done as: Pelvi abdominal ultrasound or Pelvi-abdominal CT for any intra-abdominal collections. -MRCP for imaging of biliary tree in case of suspecting biliary complications as leakage or stricture. -Hepatic artery and Portal vien duplex in case of suspecting ischemia or thrombosis. Liver biopsy in case of suspecting graft rejection.

Management of biliary complications: Biliary complications being the most common complications postoperatively after transplantation, are first managed conservatively either by external drainage (pig tail) or internal drainage by ERCP or PTC.

Surgical intervention is considered in: Failure of repeated endoscopic or percutaneous conservative measures. Multiple strictures in biliary tract. Biliary stricture due to ischemia of duct. Secondary biliary cirrhosis.

Surgical intervention in case of post transplantation biliary complication includes: Surgical drainage of intra-abdominal collections that is hard to drained percutaneously. Revision of previous biliary anastomosis. Conversion of duct to duct anastomosis into bilio-enteric anastomosis. Re-transplantation in case of recurrence of sclerosing cholangitis or severe secondary biliary cirrhosis.

Data collection:

Data was collected from patient records, medical files, and interviews.

Statistical analysis:

The data was collected, tabulated and statistically analyzed. Description of quantitative variable was done as mean and standard deviation, and qualitative data as frequency. Fisher exact test was used to compare the groups as regard qualitative variable. One way Anova test was used to compare two groups as regard quantitative variable in parametric data. The results was considered significant(S) with $P<0.05$ & highly significant (HS) with $P<0.01$.$P \geq 0.05$ will be considered non-significant (NS). Analysis of data will be done using IBM SPSS software (statistical program for social science version 21).

RESULTS:

Table 1 Patient demographic data.

Variable	Outcome
Gender	
Male	11(78.6%)
Female	3(21.4%)
Age	
mean±SD	44.93±9.25
Range	28 - 58
BMI	
mean±SD	26.71±3.29
Range	18 - 30
Complication	
Stricture	4 (28.57%)
Leakage	7 (50%)
Stricture+leakage	3 (21.43%)

Total transplanted patients were 380 patients, 45 (11.84%) patients had post-operative biliary complications. 31 (68.9%) patients were managed successfully by nonsurgical techniques and those patients were excluded from our study. 14 (31.1%)

patients were managed surgically and those patients were discussed in our study.

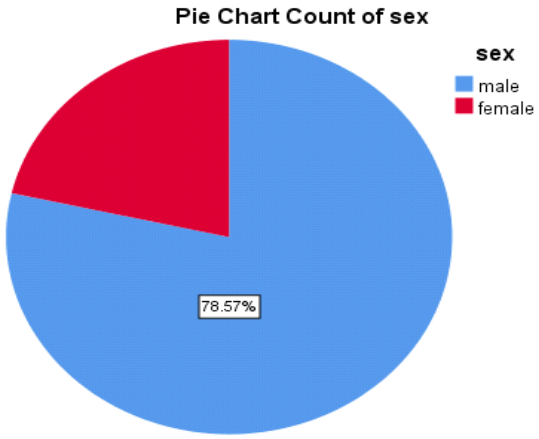

Figure 1 patient's sex

Table 2 Comorbidities

Variable	Outcome
DM	
Yes	3(21.4%)
No	11(78.6%)
Cause of cirrhosis	
HCV	11(78.6%)
HBV	1(7.1%)
Autoimmune	1(7.1%)
Cryptogenic	1(7.1%)

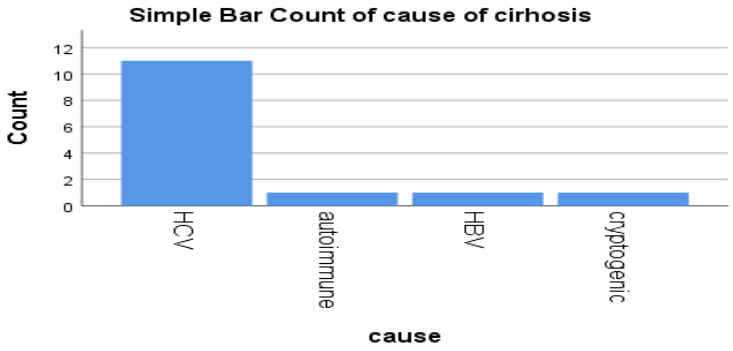

Figure 2 Cause of cirhosis

Table 3 Complications and demographic data

		Stricture (4)	Leakage (7)	Stricture+leakage (3)	P value
Age	mean±SD	42.50±11.39	48.85±7.08	39.00±9.64	0.268
Sex	Male	3(75%)	7(100%)	1(33.3%)	
	Female	1(25%)	0(0%)	2(66.7%)	0.047
DM	Yes	0(0%)	2(28.6%)	1(33.3%)	
	No	4(100%)	5(71.4%)	2(66.7%)	0.538
Cause of cirrhosis	HCV	3(75%)	6(85.7%)	2(66.7%)	
	HBV	0(0%)	1(14.3%)	0(0%)	
	Autoimmune	0(0%)	0(0%)	1(33.3%)	0.500
	Cryptogenic	1(25%)	0(0%)	0(0%)	

Table 3 shows the relation between different biliary complications and patients demographic data and cause of cirrhosis.

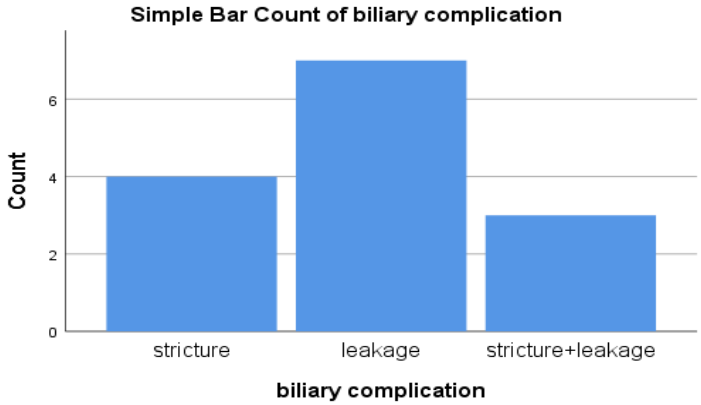

Figure 3 cases in each complication

Table 4 complication and previous transplantation data

		Stricture (4)	Leakage (7)	Stricture+leakage (3)	P value
No of ducts	Single	3(75%)	2(28.6%)	2(66.7%)	0.388
	Multiple	1(25%)	5(71.4%)	1(33.3%)	
Hepatic artery	Patent	3(75%)	4(57.1%)	3(100%)	0.874
	Stenosis	0(0%)	1(14.3%)	0(0%)	
	Thrombosis	1(25%)	2(28.6%)	0(0%)	
Cold ischemia time	mean±SD	57.50±9.57	55.00±5.00	51.67±10.41	0.620
Hot ischemia time	mean±SD	46.25±4.79	47.86±7.56	65.00±27.84	0.169
Time for complication	Early	0(0%)	5(71.4%)	2(66.7%)	0.086
	Delayed	4(100%)	2(28.6%)	1(33.3%)	

Table 4 shows the relation between 1ry transplantation data and complications, it shows that leakage occur more in multiple ducts (5 patients) and stricture occurs more in single duct (3 patients), but these differences were statistically in significant with p value = 0.388. also there was no significant difference in hepatic artery abnormalities, cold and hot ischemia time with p value (0.874, 0.620, 0.169). also we can see that leakage occurred early mainly (in 5 patients) while stricture occurred late (in 4 patients) but these results were statistically insignificant with p value = 0.086.

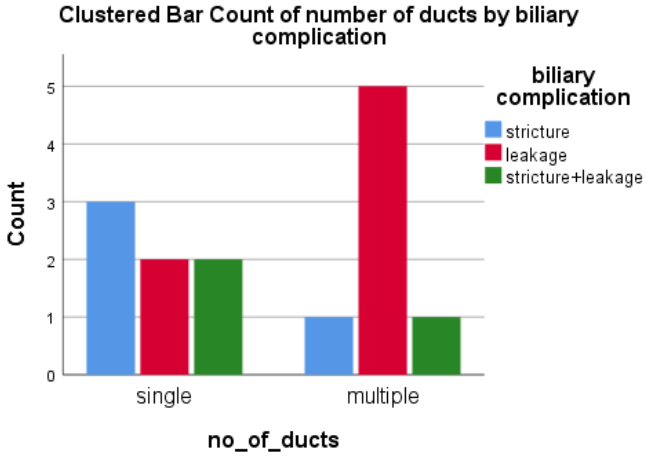

Figure 4 number of ducts in each complication

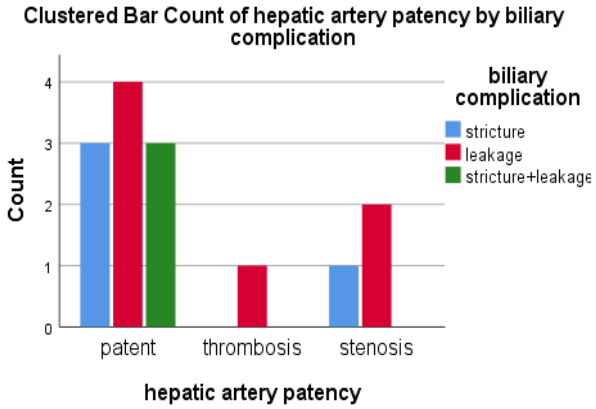

Figure 5 hepatic artery abnormalities in each complication

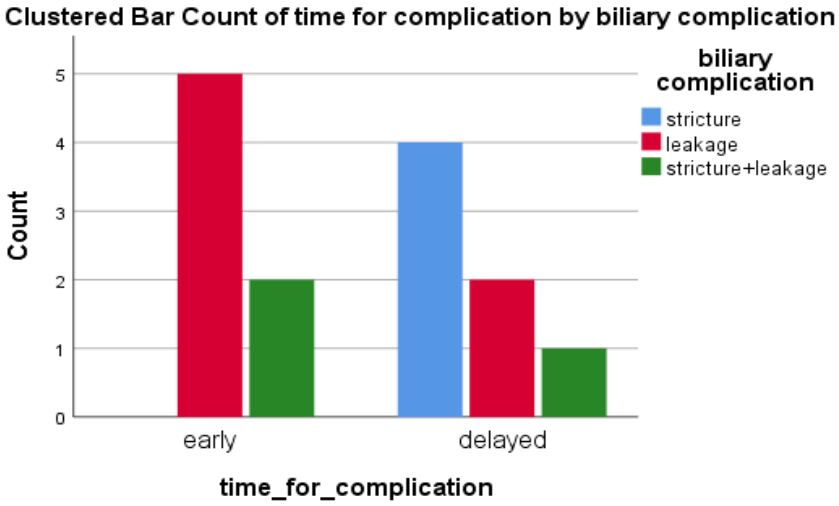

Figure 6 time to develop complication

Table 5 non surgical management

		Stricture (4)	Leakage (7)	Stricture+leakage (3)	P value
Pig tail	Yes	0(0%)	3(42.9%)	0(0%)	0.250
	No	4(100%)	4(57.1%)	3(100%)	
ERCP	Yes	3(75%)	3(42.9%)	3(100%)	0.371
	No	1(25%)	4(57.1%)	0(0%)	
PTC	Yes	0(0%)	1(14.3%)	1(33.3%)	1.000
	No	4(100%)	6(85.7%)	2(66.7%)	

Table 5 shows the previous non-surgical management done in eachcomplication.

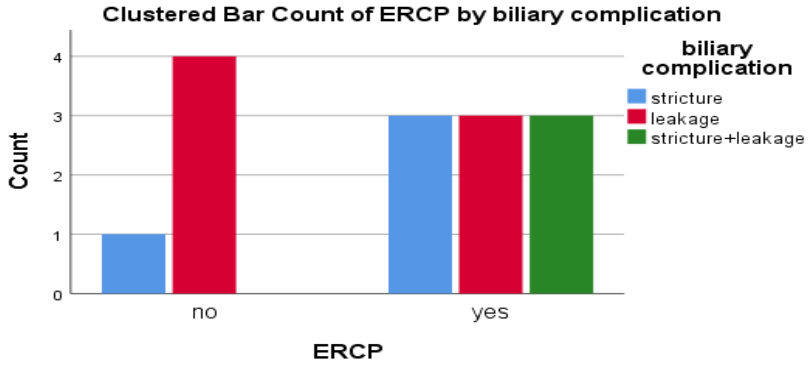

Figure 7 ERCP trial in each complication

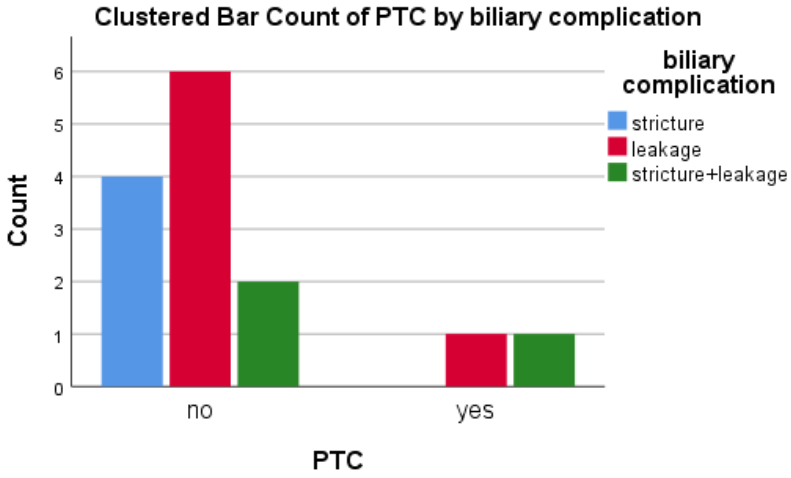

Figure 8 PTC trial in each complication

Table 6 surgical intervention and operative andpost operative data

		stricture	Leakage	Stricture+leakage	P value
Surgical intervention	Drainage	0(0%)	4(57.1)	0(0%)	0.076
	hepaticojejuonstomy	4(100%)	2(28.6%)	3(100%)	
	Repair + stenting	0(0%)	1(14.3%)	0(0%)	
Operative time	mean±SD	141.25±15.48	109.29±19.46	131.67±10.41	0.030
Hospital stay	mean±SD	22±3.74	28±4.83	38.67±28.94	0.282

Table 6 shows the surgical intervention and operative time in biliary complication surgery.

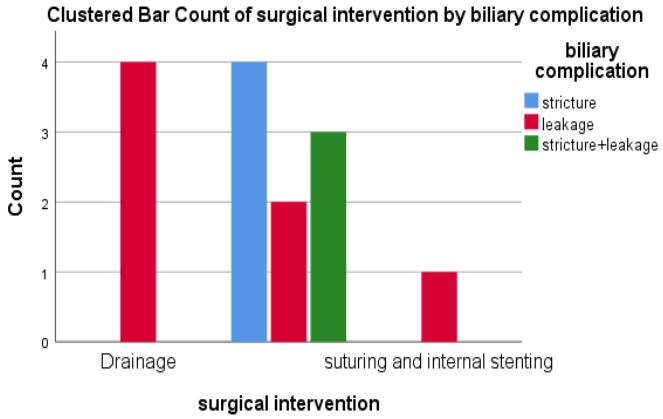

Figure 9 surgical intervention in each complication

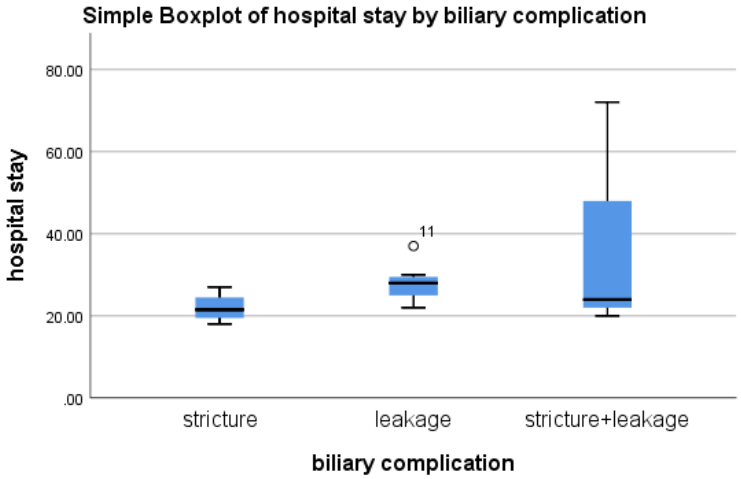

Figure 10 hospital stay in each intervention

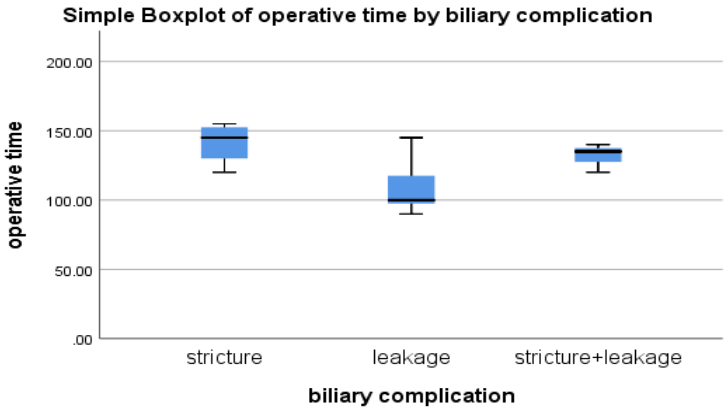

Figure 11 operative time in each complication

Table 7 operative time and hospital stay in each surgical intervention

		Drainage (4)	Hepaticojejuonstomy (9)	Repair + stenting (1)	P value
Operative time	mean±SD	98.75±8.54	136.67±12.75	100	<0.001
Hospital stay	mean±SD	26.5±3.70	28.56±16.61	37	0.809

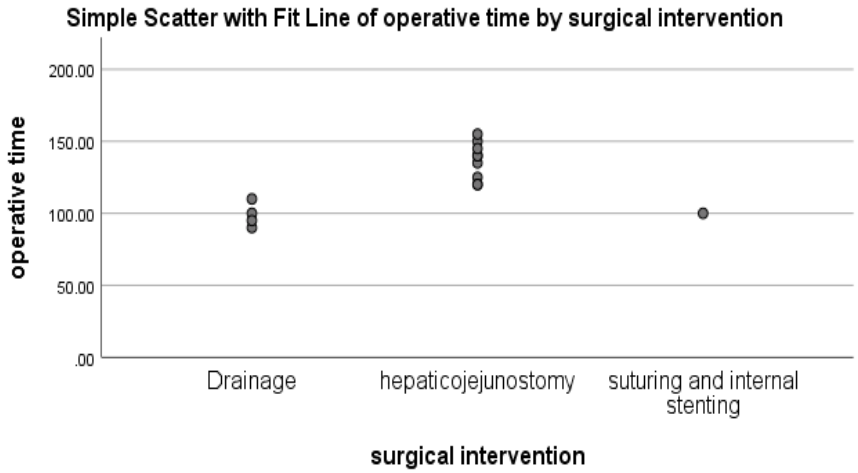

Figure 12 operative time in each surgical intervention

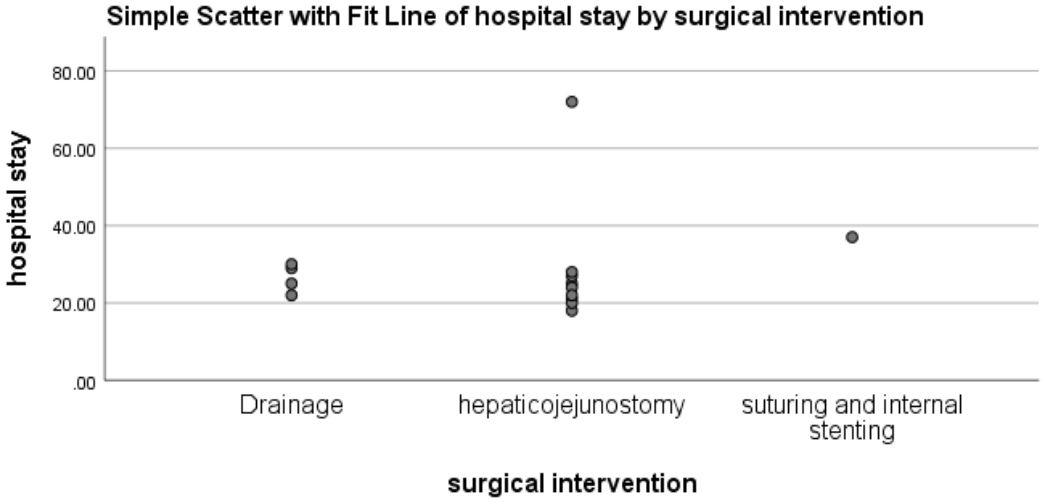

Figure 13 hospital stay in each surgical intervention

Table 8 operative and post operative data

Variable	Outcome
Operative time (min)	
mean±SD	123.21±21.63
Range	90 – 150
Hospital stay (day)	
mean±SD	28.57±13.41
Range	18 - 72
Recurrent biliary complication	
Yes	2 (14.29%)
No	12 (85.71%)
Mortality	
Yes	1 (7.14%)
No	13 (92.86%)

Table 8 shows operative and post-operative data.

DISCUSSION:

In a study by **Hwang S et al** BC have been a major source of morbidity and graft failure with a reported high incidence of (12–40%). Many risk factors have been identified to contribute to such high incidence including multiple duct anastomoses, duct diameter <4 mm, and small unrecognized bile ducts[7]**.** In our center the biliary complications incidence was 11.84%.

The clinical presentation of BC varies from slightly abnormal liver function tests to life-threatening biliary sepsis; however, most patients present with early leaks and/or strictures. The majority of strictures are anastomotic (90%) rather than non-anastomotic strictures**.**[8]

Early diagnosis and appropriate multidisciplinary management approach is crucial to avoid graft dysfunction, life-threatening sepsis, and graft or patient loss. A combination of several diagnostic tools might be necessary to provide accurate assessment of the biliary problem; some investigations are non-invasive as US, CT and MRCP, while others are more invasive like ERCP and PTC. Most centers would usually resort to conservative non-surgical strategy as the first choice in managing BC after LDLT. In a study by **Kato H et al** Non-surgical measures are primarily endoscopic retrograde procedures and percutaneous trans hepatic procedures; the use of endoscopic procedures has shown success rates around (40–70%). In our center the success rate of non-surgical management for biliary complications was 68.9%. [9]

Most centers prefer to use endoscopic retrograde procedures as the first line of management and reserve percutaneous trans-hepatic procedure to those patients who failed endoscopic management or those patients who had Hepaticojejunostomy. [10]

It is important to emphasize that the success rates after endoscopic and percutaneous manipulations vary significantly between different liver transplant programs depending on the institutional field strengths and expertise; some centers report success rates as high as 100% while others, **including our center**, have much inferior success rates with non-surgical approaches. [10]

Surgical reconstruction of BC following LDLT is usually the last resort after the failure of all conservative non-surgical measures. [11]

The reluctance to surgically manage BC followed by LDLT is owed to many predicted technical difficulties such as the presence of dense adhesions around the bare cut surface, small proximal intrahepatic

ducts, which are often difficult to identity, presence of more than one duct with the need for multiple anastomoses, and fear of damage to precious vascular structures. Therefore, because of the above-mentioned reasons, most centers would adopt long-term conservative strategy rather than early consideration of surgical reconstruction for treating such complications; this non-surgical approach usually involves repeated endoscopic and percutaneous procedures necessitating multiple hospital admissions and prolonged hospital stay. Despite this widespread reluctance to perform early surgical revision, there are many reports confirming that surgical revision is feasible in most cases with excellent long-term outcomes.[12]

In our experience, surgical revision was feasible in most of the operated cases and has significantly reduced the need for hospital admissions and invasive procedures. it significantly improved the patient's quality of life by reducing morbidities and hospital admissions. Moreover, both the decrease in hospital admissions and the reduction in the number of invasive procedures are both associated with potential cost savings and reduced resource utilization and saving the graft.

There are few reports in the literature in the setting of OLT. The initial experience by **Davidson et al** reported 20% morbidity and 6% mortality. [13] However, more recent reports by **Langer et al** show less morbidity (16% to 18%), and no mortality. [14] In our study the morbidity was 14.29% and the mortality was 7.14%.

In our study there was 14 patients with biliary complications that was managed surgically. 4 patients with stricture, 7 patients with leakage and 3 patients with stricture and leakage. 3 patients were managed surgically from the start and the other 11 patients had non successful non operative managements.

Nine patients underwent redo hepatico-jejuonstomy, four patients underwent only surgical drainage and one patient underwent primary suturing and internal stenting.

There were only two patients (14.29%) who encountered recurrence of the biliary complications after surgery and one patient (7.14%) who died after surgery by ARDS.

As the surgical management was the last resort in managing biliary complications, our study sample was limited

Conclusion:

Non-surgical measures are the primary treatment option for post transplantation biliary complications, but surgical management is the definite management for refractory cases with less hospital stay and recurrent admissions.

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التعامل الجراحى فى المضاعفات المرارية بعد عملية زراعة الكبد من التبرعين الأحياء

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تعد مضاعفات القناة الصفراوية من أكثر المضاعفات شيوعًا بعد زراعة الكبد ولاتزال مصدرًا رئيسيًا للمرض في مرضى زراعة الكبد. غالبًا مايكون العلاج غير الجراحي ناجحًا في المضاعفات المبكرة وغالبًا مايكون علاج المضاعفات المتأخرة مع التسريب والانسداد أكثر صعوبة في العلاج غيرالجراحي وغالبًا مايتطلب العلاج الجراحي أوإعادة الزرع. تكون بعض المراكز أكثر قوة في التعامل مع ضيق القناه الصفراوية وتفضل التدخل الجراحي المبكر بدلاً من التوسيع بالمنظار.

الهدف من هذه الدراسة هو مناقشة العلاجات الجراحية لمضاعفات مابعد الزرع ونتائجها ومعدل النجاح مع أوبدون تدخلا تغير جراحية سابقة في متابعة مابعد الجراحة.

كانت دراستنا دراسة استباقية واسترجاعية أُجريت في مستشفى دارالفؤاد فى وحدة زراعة الكبد خلال الفترة من ٢٠١١ حتى ٢٠٢٠. شملت المرضى المصابون بمضاعفات ما بعد الزرع وخضعوا لتدخل جراحي مع اوبدون تدخلات غير جراحيه سابقه. تضمنت الدراسة ١٤ مريضاً فشلوا في العلاج غيرالجراحى .وناقشنا التدخلات الجراحية ونتائجها.

وقد وجدنا٣٨٠ مريضا خضعوا لعملية زرع الكبد خلال هذه الفترة. ٤٥ مريضا كان لديهم مضاعفات في القناة الصفراوية، من بينهم ٣١ مريضًا تمت معالجتهم من خلال تدخلات غير جراحية وتم استبعاد هؤلاء من دراستنا. ١٤ مريضا خضعوا لتدخل جراحي. كان لدينا ٤ مرضى مصابون بضيق القناه المرارية ٧ مرضى يعانون من التسريب و ٣ مرضى يعانون من الضيق والتسريب. مريضا نعانوا من مضاعفات متكررة في القناة الصفراوية بعد الجراحة وكان هناك حالة وفاة واحدة فقط.

نستنتج من هذه الدراس m ان التدابيرغيرالجراحية هي خيارالعلاج الأساسي لمضاعفات القناه الصفراويm ما بعد زراعة الكبد،ولكن التدخلات الجراحية هي العلاج الامثل للحالات المستعصيm مع إقامة أقل في المستشفى وحالات دخول متكررة.