Effect of tracing bile duct leaks using intralipid injection through the cystic duct stump versus saline injection followed by cholangiography on posthepatectomy biliary complications

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Background
Bile leakage is a common and serious complication after hepatic resection. It is important to prevent it by early detection and repair of leaking points intraoperatively and hence minimizing postoperative leaks.
In this study, the authors prospectively compared the effect of transcystic intralipid injection versus saline test and then cholangiography on biliary complications in different cases of liver resection.
Patients and methods
This is a prospective randomized clinical trial in which we compared between the use of the White test and the use of saline test followed by cholangiography for the intraoperative detection of bile leakage in patients who underwent liver resection with cholecystectomy. The 52 cases were carried out in the National Liver Institute from May 2019 till March 2021.
Results
The incidence of postoperative bile leakage in both groups was compared. Bile leakage occurred in nine (34.6%) patients in the conventional saline and then cholangiography and in three (11.5%) patients in the White test group; this was statistically significant (P=0.048). In addition, the White test detected intraoperatively a significantly larger number of bile leakage sites (seven cases) compared with the saline and then cholangiography group (two cases).
Conclusion
Based on the results of this study, the authors strongly recommend using the white test to saline test and then cholangiography as the bile leak test of choice in minimizing posthepatectomy bile leak.

Keywords:
bile leakage test, hepatectomy, white test

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Introduction

Many methods have been introduced to prevent bile leakage after hepatic transection, including intraoperative cholangiography [1], using fibrin glue on the transected liver surface [2], assessment of bile duct patency by injecting air under ultrasound monitoring [3], and the bile leakage test. The latter is a common approach to decrease postoperative bile leakage [4]. By using bile leakage test, some studies have identified intraoperatively additional potential bile leakage points in 19.7–80.8% of the included cases. The bile leakage test is proved to be useful for preventing postoperative bile leakage in several studies; however, other studies suggested no advantage of using it [5].

The aim of the bile leakage test is to detect insufficiently closed stumps of bile ducts on the transected liver surface by elevating biliary pressure followed by suturing the leakage site [6].

The White test can be easily repeated a number of times necessary to detect and close all leakage points and also it is available and inexpensive. This technique is easier to perform than fluorescent imaging, and it is more sensitive and more reliable compared with saline bile leakage test used alone [7,8].

Bile leakage test lowered the incidence of postoperative bile leakage and could not increase the incidence of other complications. Moreover, fat emulsion may be the best choice of solution for use in the bile leakage test [5].

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Patients and methods

This is a prospective randomized trial conducted on 52 patients who underwent liver resection for any disease, with postoperative follow-up for at least 4 weeks, in the National Liver Institute, Menoufia, Egypt, from May 2019 till March 2021.

Ethical considerations: patients voluntarily gave informed consent to participate. Participant's confidentiality and data security were guaranteed. Participants were able to withdraw from the research process at any time.

Intervention

After completion of the resection using harmonic scalpel, diathermy, and bipolar coagulation in all cases with added cavitron ultrasonic suction aspiration (CUSA) in all noncirrhotic livers including donors, either transcystic saline injection and then cholangiogram or the White test was then performed.

The White test was performed using 10–20 ml of a 5% sterile fat emulsion (SMOFLipid 20%), slowly injected while occluding the distal common bile duct. The presence of the white fluid was then assessed at bile leakage sites on the transected liver surface. The detected bile leakages were closed with proper prolene sutures. Rinsing and injection were repeated until no leakage was seen. After the test, saline was injected into cystic duct to rinse the fat emulsion from the biliary tract. The number of bile leakage sites found were recorded in each test.

The conventional bile leakage test was done by injecting 10–20 ml of normal saline via the catheter while occluding the distal common bile duct. The transected liver surface was then inspected for leakage followed by a cholangiography with C-arm fluoroscopy to check for biliary leakages and strictures in the remnant bile duct, and then closure of any detected points was done, followed by repetition of the test till no remaining leaking points detected.

Results

A total of 52 different cases of liver resection with cholecystectomy were enrolled in this study.

Saline test followed by cholangiogram was done in 26 patients, and the White test was done in another 26 patients. Intraoperative assessment of leakage points in both tests was calculated, and postoperative follow-up was done.

Comparison between the two studied groups according to clinical data is shown in Tables 1 and 2.

Table 1 Comparison between the two studied groups according to clinical data and operative time

	Bile leak detection test type [*n* (%)]			
Demographic data	Group I: White test (*n*=26)	Group II: Saline then cholangiography test (*n*=26)	*P*	Significance
Sex				
Male	15 (57.7)	17 (65.4)	0.569	NS
Female	11 (42.3)	9 (34.6)		
Age (years)				
Minimum–maximum	7.0–75.0	1.0–62.0	0.611	NS
Mean±SD	42.65±19.90	40.12±15.60		
Type of resection				
Nonanatomical resection	6 (23.1)	6 (23.1)		
Caudate lobectomy	1 (3.8)	1 (3.8)		
Right hepatectomy	16 (61.5)	13 (50.0)	0.863	NS
Left hepatectomy	3 (11.5)	5 (19.2)		
Left lateral resection	0	1 (3.8)		
Operative time (h)				
Minimum–maximum	2.0–8.0	3.0–8.0	0.572	NS
Median (IQR)	4.0 (3.50–5.0)	4.25 (3.50–6.0)		

IQR, interquartile range.

Table 2 The number of cirrhotic and noncirrhotic cases in each group

Condition/ test	White test Total number of cases and their percentage in each group [*n* (%)]	Saline test and then cholangiogram Total number of cases and their percentage in each group [*n* (%)]
Cirrhotic	11 (42.3)	11 (42.3)
Noncirrhotic	15 (57.7)	15 (57.7)

Tables 2–4 show liver condition in each group cases, type – whether benign or malignant, number and percentage of lesions and indication of resection, number and percentage of each indication in both test groups, and type of resection in each case (Tables 5 and 6).

Course and primary outcome

Comparison between the two studied groups regarding postoperative ICU stay, hospital stay, intraoperative detection of bile leak, and number and site of leaking points is shown in Tables 4 and 7. Moreover, Figures 1 and 2 show detected two leaking points after using the White test and then no more intraoperative leaks after prolene sutures in the same case, whereas Fig. 3 shows postresection cholangiography after left hepatectomy with no detected leaking points.

Table 3 The number and percentage of benign and malignant cases in each group

Condition/test	White test Total number of cases and their percentage in each group [*n* (%)]	Saline test and then cholangiogram Total number of cases and their percentage in each group [*n* (%)]
Benign	13 (50)	12 (46.2)
Malignant	13 (50)	14 (53.8)

Postoperative course for all patients

comparison between the two studied groups according to postoperative bile leakage, leak onset, and leak offset is shown in Table 8.

Postoperative clinical course and follow-up

Management of the leak group is shown in Table 9.

Discussion

The purpose of the intraoperative bile leakage test is to identify those hidden leakage points in the hepatic resection plane by injecting a chromogenic agent into

Table 4 Indication of resection and the number and percentage of each indications of liver resection in both test groups

Condition/test	White test Total number of cases and their percentage in each group [*n* (%)]	Saline test and then cholangiogram Total number of cases and their percentage in each group [*n* (%)]
HCC	11 (42.3)	12 (46.2)
Nonanatomical resection	6 (23.1)	5 (19.2)
Anatomical resection	5 (19.2)	7 (26.9)
	2 right hepatectomy	4 right hepatectomy
	1 caudate lobectomy	3 left hepatectomy
	2 left hepatectomy	
Right lobe-MHV donors	5 (19.2)	5 (19.2)
Left lobe donors	1 (3.85)	1 (3.85)
Left lateral lobe donors	–	1 left lateral donor (3.85)
Colorectal liver mets	2 (7.7)	2 (7.7)
	Right hepatectomy	1 (3.85)
		Right hepatectomy
		1 (3.85)
		Nonanatomical segment 7 (3.85)
Huge hemangioma	3 (11.54)	1 (3.85)
		Right hepatectomy
	Right hepatectomy	1 (3.85) caudate lobectomy
		1 (3.85)
		Left hepatectomy
Miscellaneous	1 (3.85) right hepatectomy	1 (3.85) right hepatectomy
Mesenchymal hamartoma	–	1 (3.85) right hepatectomy
Spindle cell tumor	1 (3.85) right hepatectomy	–
Biliary cystadenoma	–	1 (3.85)
Biliary cystadenocarcinoma	1 (3.85)	Extended right hepatectomy
Hydatid cyst	Right hepatectomy	–
Focal nodular hyperplasia	–	1 (3.85) right hepatectomy

HCC, hepatocellular carcinoma; MHV, middle hepatic vein.

Table 5 Comparison between the two studied groups according to estimated blood loss and received packed RBCs units

	Bile leak detection test type			
	Group I: White test (*n*=26)	Group II: saline and then cholangiography test (*n*=26)	*P*	Significance
Estimated blood loss				
Minimum–maximum	100.0–2000.0	100.0–2000.0	0.325	NS
Median (IQR)	600.0 (400.0–800.0)	700.0 (400.0–900.0)		
Received packed RBCs units				
Minimum–maximum	0.00–4.00	0.00–4.00	0.088	NS
Median (IQR)	0.00 (0.0–0.0)	0.00 (0.0–2.0)		

IQR, interquartile range; RBC, red blood cells.

Table 6 Comparison between the two studied groups regarding postoperative ICU stay and hospital stay

	Bile leak detection test type			
	Group I: White test (*n*=26)	Group II: saline and then cholangiography test (*n*=26)	*P*	Significance
Postoperative hospital stay (days)				
Minimum–maximum	3.0–15.0	4.0–23.0	0.509	NS
Median (IQR)	7.0 (6.0–8.0)	7.50 (6.0–8.0)		
ICU stay (days)				
Minimum–maximum	1.0–3.0	1.0–5.0	0.944	NS
Median (IQR)	2.0 (1.0–2.0)	2.0 (2.0–2.0)		

IQR, interquartile range.

Table 7 Comparison between the two studied groups regarding intraoperative detection of bile leak and the number and site of leaking points

	Bile leak detection test type [*n* (%)]			
	Group I: White test (*n*=26)	Group II: conventional test and then cholangiogram (*n*=26)	^{FE}P	Significance
IO detection of bile leakage				
No	19 (73.1)	24 (92.3)	0.140	NS
Yes	7 (26.9)	2 (7.7)		
Number of leaking points				
No	19 (73.1)	24 (92.3)	0.170	NS
Yes	7 (26.9)	2 (7.7)		
Number of detected sites of leakage				
1 site	5 (19.2)	2 (7.7)		
2 sites	2 (7.7)	0		
Site of detected leakage Hilar plate	1 (14.3)	0	1.000	NS
Caudate duct	1 (14.3)	0	1.000	NS
Cut surface	4 (57.1)	1 (50.0)	0.350	NS
Right duct stump	1 (14.3)	1 (50.0)	1.000	NS

FE, Fisher's exact test.

the common bile duct and increasing the pressure of the bile duct [9].

Nowadays, intraoperative bile leakage tests are having more concerns and different application methods.

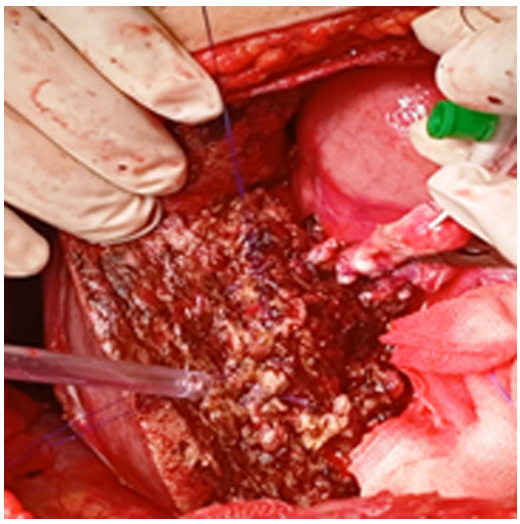
Bile leakage test using only saline injection was investigated in a randomized trial by Ijichi *et al.* [4], concluding no advantage of using this test during hepatic resection. This partially supports the result of group 2 in our study using saline injection and then cholangiography.

In a retrospective study, Nadalin and colleagues reported on a bile leakage test using white fat emulsion after hepatectomy. The incidence of postoperative bile leakage was 5.1%, which was significantly reduced when compared with that (8%) before the use of a bile leakage test [10].

Figure 1

Detected two leaking points after using the White test.

Figure 2



No more intraoperative leaks after prolene sutures.

This supports the result of our study as postoperative biliary leak was significantly less in white test group than the saline test and then cholangiography group.

Li *et al.* [11] concluded that the White test decreased postoperative bile leak after major resection when compared with nonbile leak test (5.3 vs. 22.9%).

Our results go parallel with this result.

In 2012, a randomized controlled trial was carried out by Liu *et al.* [12], for the intraoperative bile leakage test, and its role in preventing bile leakage after hepatic resection intraoperative detection was found in 62.3% (33/53) of the cases and postoperative leakage was encountered in only 3.8% (2/53) of the cases. This also strongly goes with the findings of our study.Aboul Naga and colleagues, in 2018, carried out a study comparing both the White test and the saline test in hepatectomized patients and found that bile leakage was detected in 22 (44%) patients in the conventional

Figure 3

Postresection cholangiography with no detected leaking points.

Table 8 Comparison between the two studied groups according to postoperative bile leakage, leak onset, and leak offset

	Bile leak detection test type [*n* (%)]		*P*	Significance
	Group I: White test (*n*=26)	Group II: conventional test then cholangiogram (*n*=26)		
Postoperative bile leakage				
No	23 (88.5)	17 (65.4)	0.048*	S
Yes	**3** (**11.5**)	**9** (**34.6**)		
Timing of PO detection of bile leakage (leak onset)	*n*=3	*n*=9		
Minimum–maximum	1.0–6.0	1.0–6.0	0.771	NS
Median (IQR)	3.0 (2.0–4.50)	3.0 (2.0–3.0)		
Duration of drainage (leak offset)	*n*=3	*n*=9		
Minimum–maximum	7.0–21.0	3.0–50.0	0.709	NS
Median (IQR)	7.0 (7.0–14.0)	14.0 (7.0–21.0)		

IQR, interquartile range; S, significant. Biliary leaks was more significant in group II.

Table 9 Management of the leak group

	Bile leak detection test type [*n* (%)]		
	Group I: White test (*n*=26)	Group II: conventional test then cholangiogram (*n*=20)	*P*
Postoperative bile leak	3 (11.5)	9 (34.6)	
Surgical drain only	3 (100.0)	6 (66.7)	0.509
Puncture ttt (simple aspiration vs. pigtail)	1 (33.3)	3 (33.3)	1.000
ERCP	1 (33.3)	2 (25.0)	1.000
Surgery if needed	0	0	–

ERCP, endoscopic retrograde cholangiopancreatography.

method group and in four (8%) patients in the White test group. In addition, the White test detected intraoperatively a significantly higher number of bile leakage sites compared with the conventional method [13].

The results of our study are strongly support these results.

Conclusion

Several bile leak tests have been proposed, with none gaining wide acceptance.

After investigating both the saline test followed by cholangiography and the White test, we strongly recommend using white test to detect hidden bile leakage sites after liver resections and hence decreasing postoperative bile leak.

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Conflicts of interest

None declared.

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