White test versus conventional saline test in detecting intraoperative bile leakage in liver resection

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Background
Intraoperative bile leakage testing is an important procedure in liver resection as it helps in detection of bile leaking points on the cut surface, thereby decreases postoperative bile leakage, which is one of the most dreadful complications following liver surgery. In this study, we tried to assess the efficacy of using White test in comparison with conventional saline test in detecting intraoperative bile leakage.
Patients and methods
In this study, we assessed whether the White test is better than the conventional saline test for the intraoperative detection of bile leakage in patients undergoing liver resection. This study included 100 patients who underwent elective liver resection. The conventional saline test (injecting an isotonic sodium chloride solution through the cystic duct) was carried out in 50 patients and the White test (injecting a fat emulsion solution through the cystic duct) was carried out in 50 patients.
Results
Incidence of postoperative bile leakage was compared between the conventional method and the White test. Bile leakage occurred in 22 (44%) patients in the conventional 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. Therefore, the White test seems to be better than the conventional test for the intraoperative detection of bile leakage.
Conclusion
Based on our study, we recommend that surgeons investigating bile leakage sites during liver resections should use the White test instead of the conventional saline test.

Keywords:
bile leakage, hepatectomy, White test

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Introduction

Postoperative bile leakage is one of the commonest causes of sepsis and liver failure after liver resection [1,2]. Various studies have demonstrated that the incidence of postoperative bile leakage after liver resection ranges from 3 to 27% [2–5].

The timely detection and repair of intraoperative bile leakage is extremely important, but small leakage points are often difficult to detect [6]. There are several methods for detecting and/or preventing bile leakage after hepatectomy, including bile leakage tests, which detect open bile duct stumps on the resection surface by increasing fluid pressure within the duct [7].

The conventional intraoperative saline test, which involves injecting an isotonic sodium chloride solution through the cystic duct, has been used for detection of leaking points from the transected liver surface [8]. One of the major problems in using the conventional bile leakage test is that the isotonic sodium chloride solution is a transparent solution. Therefore, it is difficult to detect the point of bile leakage. A previous randomized study indicated that there is no advantage of using the isotonic sodium chloride solution for the bile leakage test during liver resection [8].

Recently, intraoperative application of the White test has been demonstrated to reduce the incidence of postoperative bile leakage [9,10]. In this technique, bile leakage sites on the transected liver surface are identified by injecting a fat emulsion solution through the cystic duct. Some previous prospective observational studies suggested that the fat emulsion solution used in the White test is easily recognized, innocuous to the tissues, and can be easily removed

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without misleading tissue staining [9,10]. Therefore, we designed a prospective study to assess whether the White test is better than the conventional saline test for the intraoperative detection of bile leakage and better prevention of postoperative bile leakage.

Patients and methods

Patients

This prospective randomized study included 100 patients with Child–Pugh A score, who were scheduled for elective liver resection at Al-Demerdash Hospital and Ain Shams University Specialized Hospitals from January 2016 to August 2017, and they were followed up for at least 3 month. Informed consent was obtained from the patients, and this study was approved by Al-Demerdash Hospital ethics committee.

Interventions

Liver tissue was transected using a harmonic scalpel and electrocautery with intermittent occlusion of hepatic inflow if needed. After complete liver resection, bleeding from the liver surface was controlled, and the visible points of bile leakage were secured with interrupted sutures placed with an atraumatic needle. The conventional saline test was applied on 50 cases, and the White test was performed in the other 50 cases.

To perform the tests, a catheter (or cannula) was inserted through the cystic duct into the common bile duct.

For the conventional bile leakage test, 10–20 ml of isotonic sodium chloride solution was injected via the catheter while manually occluding the distal common bile duct. The transected liver surface was then inspected by two surgeons for the leakage of any isotonic sodium chloride solution. After marking the sites of bile leakage, if any, the residual isotonic sodium chloride solution was removed by syringe aspiration via the catheter.

To perform the White test, 10–20 ml of a 5% sterile fat emulsion (SMOFlipid 20%) was slowly injected while manually occluding the distal common bile duct. The presence of the white fluid was then assessed at bile leakage sites on the transected liver surface by two surgeons. The number of bile leakage sites found on the cut surface, transacted stump, or hailer plate was recorded in each test.

After finishing the tests, the detected bile leakage sites were closed with interrupted sutures (5–0 or 6–0 polydioxanone sutures). Drainage of the operative field was performed with a silicone drain connected to a closed drainage system.

Postoperative bile leakage was defined as bilirubin concentration in the drain fluid at least three times the serum bilirubin concentration on or after postoperative day 3 or at the need for radiologic or operative intervention resulting from biliary collections or biliary peritonitis.

Statistical analysis

Data were collected, revised, coded, and entered to the statistical package for the social science (SPSS, version 23, New York, USA). Quantitative data were presented as mean, SDs, and ranges when parametric, and median with interquartile range when nonparametric. Moreover, qualitative data were presented as numbers and percentages. The comparison between the two groups regarding qualitative data was done by using χ^2 test. Moreover, the comparison between two independent groups regarding quantitative data with parametric distribution was done by using Independent t test, whereas for nonparametric data was done using Mann–Whitney test. The confidence interval was set to 95%, and the margin of error accepted was set to 5%. So the P value was considered significant at the level of less than 0.05.

Results

A total of 100 hepatectomized patients were enrolled. The patients studied included 40 patients with benign tumors, five patients with liver metastasis from colorectal cancer, five patients with intrahepatic cholangiocarcinoma, and 50 patients with hepatocellular carcinoma. Overall, 63 patients underwent right hepatectomy and 37 underwent left hepatectomy. The type of hepatectomy was statistically insignificant. The clinical characteristics of the patients are shown in Table 1.

Primary outcome

The primary outcome was intraoperative identification of bile leakage. To determine whether the conventional bile leakage test or the White test is superior for the intraoperative identification of bile leakage. Each test was performed on 50 patients after completing the liver resection, and the leaking points from the cut surface were counted every time, as well as leaking from the stump and the hilar plate. The White test identified a significantly higher number of bile leakage sites from the cut surface than the conventional method, as well as from the hilar plate, but leakage from the stump was statistically insignificant (χ^2 test; P=0.000) (Table 2).

The postoperative course for all patients showed that 22 (44%) patients of the saline test group had bile leakage, which was managed conservatively in all cases, but in the White test group, only four (8%) patients had leakage, where two of them were managed by endoscopic retrograde cholangio-pancreatography (ERCP) and the other two were managed conservatively.

Otherwise, there was no significant difference between both groups regarding other complications, especially postoperative liver affection recorded by liver decompensation in the form of deterioration of the liver synthetic functions to exclude any toxic effect of the White test on the residual liver (Table 3 and Figs 1–6).

Table 1 The clinical characteristics of the patients

	Saline test (*N*=50)	White test (*N*=50)	Test value	*P* value	Significance
Age(years)					
Mean±SD	49.08±17.6	41.64±19.32	2.013[a]	0.047	S
Range	3–68	2–67			
Sex [*n* (%)]					
Female	10 (20.0)	13 (26.0)	0.508[b]	0.476	NS
Male	40 (80.0)	37 (74.0)			
Type of hepatectomy [*n* (%)]					
Right	28 (56.0)	35 (70.0)	2.102[b]	0.147	NS
Left	22 (44.0)	15 (30.0)			

S, significant. [a]Independent *t* test. [b]χ^2 test.

Table 2 Intraoperative data

Operative	Saline test (*N*=50)	White test (*N*=50)	Test value	*P* value	Significance
Duration of surgery (h)					
Mean±SD	6.84±1.92	7.04±2.9	–0.402[a]	0.688	NS
Range	4.4–13.2	4–15.5			
Blood loss (CC)					
Median (IQR)	400 (250–800)	600 (500–800)	–2.958[b]	0.003	HS
Range	127–3500	300–3500			
Number of leakage points from cut surface [*n* (%)]					
1	35 (70.0)	12 (24.0)	22.358[c]	0.000	HS
2	9 (18.0)	16 (32.0)			
≥3	6 (12.0)	22 (44.0)			
Leakage from stump [*n* (%)]					
No	23 (46.0)	18 (36.0)	1.033c	0.309	NS
Yes	27 (54.0)	32 (64.0)			
Leakage from hilar plat [*n* (%)]					
No	30 (60.0)	14 (28.0)	10.390[c]	0.001	HS
Yes	20 (40.0)	36 (72.0)			

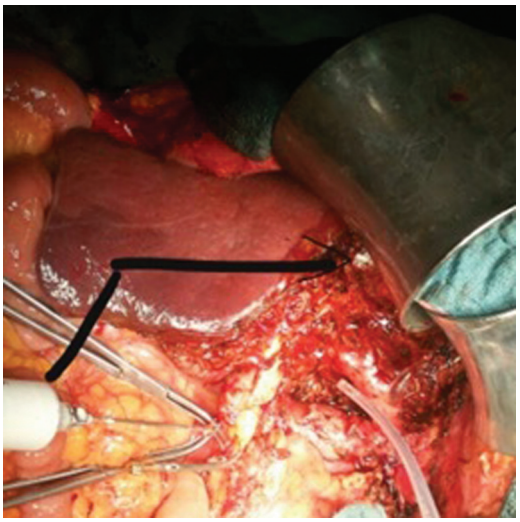
HS, highly significant; IQR, interquartile range; S, significant. [a]Independent *t* test. [b]Mann–Whitney test. [c]χ^2 test.

Table 3 Comparison of postoperative complications

Postoperative	Saline test [*n* (%)]	White test [*n* (%)]	Test value[a]	*P* value	Significance
Bile leakage					
No	28 (56.0)	46 (92.0)	16.840	0.000	HS
Yes	22 (44.0)	4 (8.0)			
Stricture					
No	44 (88.0)	45 (90.0)	0.102	0.749	NS
Yes	6 (12.0)	5 (10.0)			
Abdominal infection					
No	47 (94.0)	45 (90.0)	0.543	0.461	NS
Yes	3 (6.0)	5 (10.0)			
Liver function affection					
No	46 (92.0)	47 (94.0)	0.154	0.695	NS
Yes	4 (8.0)	3 (6.0)			

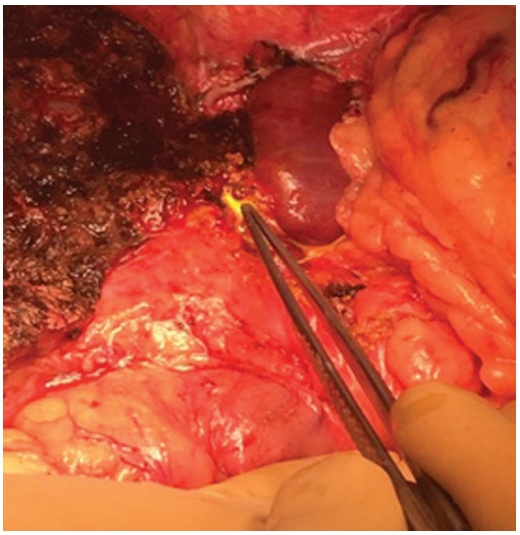
HS, highly significant; S, significant. [a]χ^2 test.

Figure 1



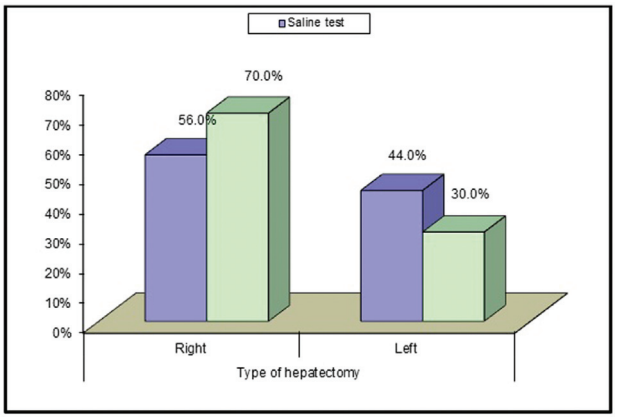
Intraoperative White test shows area of leakage at the cut surface.

Figure 2



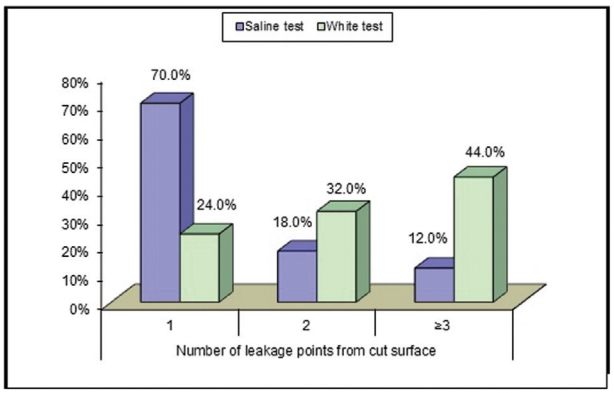
Leakage detected by the White test at the hilar plate after left lateral hepatectomy.

Figure 3



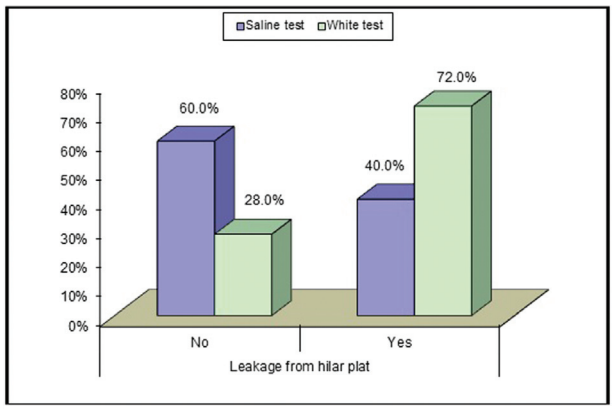
Type of hepatectomy in both groups.

Figure 4



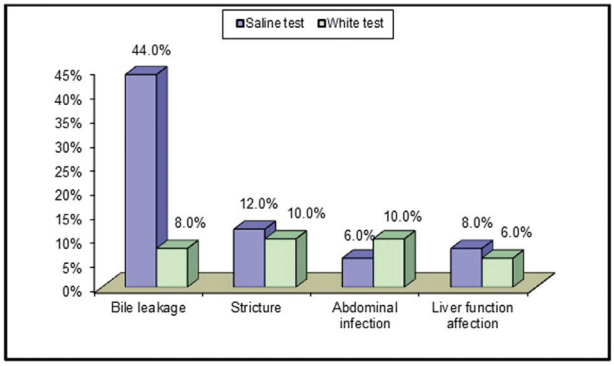
Comparison of number of leaking points from cut surface.

Figure 5



Comparison of number of leaking point from the hilar plate.

Figure 6



Comparison of postoperative complications.

Discussion

One of the previous randomized trials that have investigated the role of the conventional saline test during liver resection reported that bile leakage was demonstrated and repaired by the conventional saline test in 41% of patients. However, the incidence of postoperative bile leakage did not significantly differ

between the group receiving the conventional bile leakage test and the control group. Recent studies have demonstrated that bile leakage test with fluorescent dye solution could detect bile leakage that could not be identified by a conventional bile leak test, yet it is not available all the time [11,12]. Therefore, we hypothesize that the transparent sodium chloride solution used in the conventional saline test is a major problem in detecting bile leakage sites. However, specialist equipment and expertise for performing the bile leakage tests with fluorescent dye solution are not available at every hospital.

The White test uses fat emulsion, which is normally used for parenteral nutrition, for localization of bile leakage [13]. The use of fat emulsion in bile leakage tests does not require special equipment, contaminate the wound, cause allergic reaction or damage the bile duct and surrounding tissues. It can easily be repeated the number of times necessary to detect and close all leakage points, can pinpoint even small leaks and is inexpensive. This technique is easier to perform than fluorescent imaging and is more sensitive and reliable compared with saline bile leakage test used alone [14,15].

A previous prospective study included 74 patients receiving no bile leakage test as a control group and 63 patients undergoing the White test as the study group. Postoperative bile leakage was found in 22.9% patients in the control group and in 5.3% patients in the White test group [9].

The results of the study by Capussotti *et al.* [16] agreed with the previous studies in that a bile leakage test cannot definitely prevent postoperative bile leakage because all of the biliary stumps on the transected liver surface cannot be identified by this technique.

In our study, postoperative bile leakage was found in four (8%) patients in the White test group in comparison with 22 (44%) patients in the other group. All our patients received major hepatectomies, either right or left formal resection. A Previous study indicated that high-risk procedure (hepatectomies in which the cut surface exposed the major Glisson's sheath and included the hepatic hilum) is the independent risk factor for development of bile leakage [17]. The association of liver parenchyma disease and the incidence of bile leakage should be further evaluated.

Conclusion

So finally, we recommend the use of White test by surgeons investigating the presence of bile leakage sites during liver resections instead of the conventional saline test, as it helps in detecting more bile leaking points, thereby decreases the incidence of postoperative bile leak. However, large randomized trials of the White test during major and minor liver resections should be performed before routinely using the test for liver resection procedures.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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