Value of staging laparoscopy for the assessment of operability in periampullary cancer patients: a comparative study versus exploratory laparotomy

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Objectives
The aim of this study was to evaluate the diagnostic yield of staging laparoscopy (SL) for patients with periampullary cancer with no signs of inoperability on computed tomography (CT) imaging.
Patients and methods
Thirty-eight patients with malignant obstructive jaundice were considered for this study. Only patients with no distant metastases and with lesions potentially resectable on CT criteria were included. Patients were randomized to two groups: group A included patients who underwent exploratory laparotomy (EL) based on CT findings, and group B included patients who were subjected to SL and then proceeded to laparotomy according to SL findings. Primary outcomes included the frequency of cancelled laparotomy and the frequency of positive laparoscopy, indicating inoperability or irresectability.
Results
EL confirmed CT findings in eight (42.1%) patients of the EL group. In total, resection was not indicated nor possible in 11 patients of the, Replace:=wdReplaceAll, Format:=True, Forward:=True, MatchWildcards:=False, Wrap:=wdFindStop EL group and were considered as false positive for CT. SL confirmed CT findings in seven (36.8%) patients of the SL group. SL detected signs of inoperability in 12 patients. In total, resection was not indicated nor possible in 13 patients of the SL group and were considered as false positive for CT. Collectively, CT could define operability and lesion resectability with a positive predictive value (PPV) of 36.8% and low specificity. However, preliminary SL could define operability and lesion resectability of patients with free CT with a PPV of 85.7% (95% confidence interval: 47.72–97.53) and specificity rate of 92.3% (95% confidence interval: 63.97–99.81).
Conclusion
Reliance on CT imaging alone for defining operability of patients with periampullary is accompanied by a relatively high unnecessary laparotomy rate. SL should be considered for defining inoperability with high PPV and specificity. SL could spare unnecessary laparotomy in around 50% and allowed shorter theater time and postoperative hospital stay for inoperable patients compared with EL.

Keywords:
malignant obstructive jaundice, periampullary carcinoma, staging laparoscopy

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Introduction

Periampullary cancer includes cancer of the head and neck of the pancreas, cancer of the distal end of the bile duct, cancer of the ampulla of Vater and cancer of the second part of the duodenum [1]. Surgical resection is the only potentially curative treatment for pancreatic and periampullary cancer.

Despite the availability of high-resolution computed tomography (CT) scans, occult distant metastases can still be found in 11% of patients during the operation [2] and a considerable proportion of patients undergo unnecessary laparotomy because of underestimation of the extent of the cancer on CT scanning [3], thus the accurate staging is becoming increasingly important [4].

Laparoscopy can detect metastases not visualized on CT scanning, enabling better assessment of the spread of cancer [3]. In the absence of reliable risk factors to predict distant metastases, staging laparoscopy (SL) should be offered to all patients with radiographic localized disease [2]. Moreover, SL is considered

useful for detecting peritoneal metastasis, a task that is difficult using conventional imaging modalities [5]. Moreover, SL allows avoiding laparotomy with unsuccessful resection, and can lead to rapid induction of chemotherapy for unresectable pancreatobiliary cancers [6].

SL has become routine in certain cancers, especially gastric cancer and hilar cholangiocarcinoma, and may play a role in hepatopancreaticobiliary malignancy; however, with ever improving radiology, its role remains controversial [4]. Thus, the current study aimed to evaluate the diagnostic yield of SL for patients with hepatopancreaticobiliary cancer with no signs of inoperability on CT imaging.

Patients and methods

The current randomized controlled trial was conducted at General Surgery Department, Cairo University Hospitals between January 2014 and July 2016. The study protocol was approved by the local ethical committee and in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. Thirty-eight patients with malignant obstructive jaundice fit to undergo surgery were considered for this study. Only patients with no distant metastases and with lesions potentially resectable on CT criteria were included in this study. All patients underwent routine preoperative workup. Endoscopic Retrograde Cholangiopancreatography (ERCP) was routinely performed preoperatively. Biliary drainage could not be achieved in one patient only due to gastric outlet obstruction.

Using sealed envelopes, patients who agreed to take part in the study were randomized to two groups:

(1) Group A included patients who underwent exploratory laparotomy (EL) based on CT findings.
(2) Group B included patients who were subjected to SL and then proceeded to laparotomy according to SL findings.

SL was performed under general anesthesia using three 10–11-mm umbilical, left and right subcostal cannulas. The abdominal cavity was explored, using a 30° telescope, for ascites and peritoneal, omental and surface hepatic deposits. Ligament of Treitz and transverse mesocolon were visualized to look for peritoneal deposits specifically at these two areas. Any positive finding was confirmed with frozen section. Ascitic fluid, if present, was sent for cytology.

Study outcome

Primary outcome included the following items:

(1) The frequency of cancelled laparotomy.
(2) The frequency of positive laparoscopy, indicating inoperability assured by frozen section.

Secondary outcome

The secondary outcome included influence of adding SL on operative time.

Results

The study included 38 patients eligible for inclusion in the study. All patients presented with malignant obstructive jaundice with other varied manifestations, and their CT imaging assured operability of patients and resectability of the lesion. There was a nonsignificant ($P>0.05$) difference between patients enrolled in both studies as regards age, sex, and frequency of presenting manifestations, as shown in Table 1.

EL confirmed CT findings in eight (42.1%) patients of the EL group and proceeded to Whipple's procedure. These eight cases were considered as true positive for CT.

Three patients had locally advanced disease precluding completion of resection. All three patients had the plastic stents changed to metal stents before referring them to oncology for palliative chemotherapy.

Among the remaining eight patients in the EL group, three patients had small surface liver deposits, four patients had peritoneal nodules, and one patient had omental mass. Frozen section confirmed malignancy.

Table 1 Patients' enrollment data

Data	EL group (n=19)	SL group (n=19)
Age (years)	53.1±14.4	58.1±12
Sex		
Male	12 (63.2)	11 (57.9)
Female	7 (36.8)	8 (42.1)
Clinical manifestations		
Jaundice	19 (100)	19 (100)
Cachexia	11 (57.9)	10 (52.6)
Mass	3 (15.8)	1 (5.3)
Fever	12 (63.2)	11 (57.9)
Vomiting	8 (42.1)	6 (31.6)
Anemia	9 (47.4)	7 (36.8)

Data are presented as mean±SD and numbers. Percentages are given in parentheses. EL, exploratory laparotomy; SL, staging laparoscopy.

In total, resection was not indicated nor possible in 11 patients in the EL group and were considered as false positive for CT.

SL confirmed CT findings in seven (36.8%) patients of the SL group and proceeded to resection through laparotomy. Unfortunately, during laparotomy, one patient was found to have a locally advanced tumor more than that appreciated by laparoscopy. This patient was considered as false positive for both CT and SL. In the remaining six cases, Whipple's procedure was performed uneventfully, and these cases were considered as true positive for both CT and SL.

SL detected signs of inoperability in 12 patients (either peritoneal/omental deposits or surface liver deposits) (Figs 1–5). Laparotomy was cancelled and plastic biliary stents were changed to metal ones postoperatively. Laparoscopic gastrojejunostomy was performed for one patient with gastric outlet obstruction. This patient had a percutaneous transhepatic metallic biliary stent inserted postoperatively.

In total, resection was not indicated nor possible in 13 patients in the SL group and were considered as false positive for CT.

Collectively, CT could define operability and lesion resectability with a positive predictive value (PPV) of 36.8% and low specificity. However, preliminary SL could define operability and lesion resectability of patients with free CT with a PPV of 85.7% [95% confidence interval (CI): 47.72–97.53] and specificity rate of 92.3% (95% CI: 63.97–99.81).

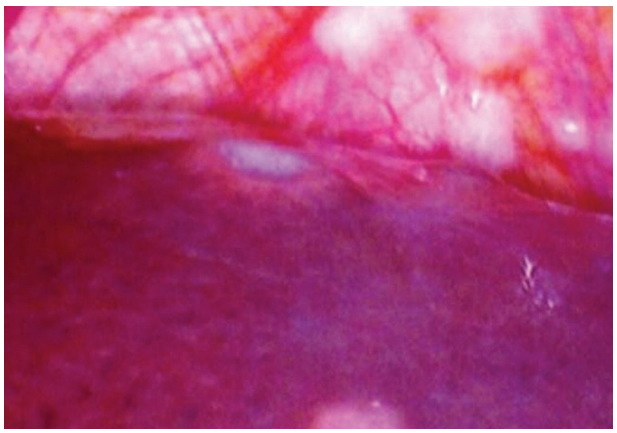
Receiver operating characteristic curve analysis of SL and CT as predictor for operability defined SL as significant predictor with area under the curve (AUC) of 0.897 (95% CI: 0.769–1.005), whereas CT could not be the sole diagnostic modality as it showed an AUC of 0.5 with nonsignificant difference versus the null hypothesis (Fig. 6).

The mean operative time for patients found to be inoperable was significantly (P=0.003) shorter with SL compared with EL. However, mean total theater

Figure 1

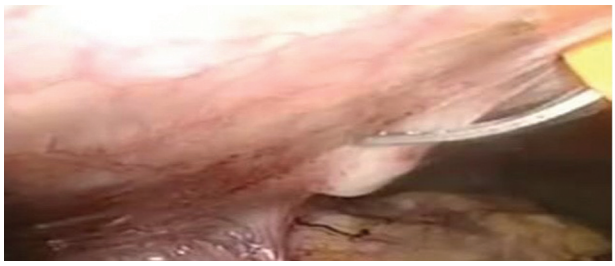
Surface liver deposits Segment V/VIII.

Figure 2



Surface liver deposits Segment II, III and deposits on Falciform ligament.

Figure 3



Peritoneal Nodules.

Table 2 Operative time and duration of hospital stay of patients according to operative approach and performed procedure

Findings	Inoperable patients		Operable patients	
	SL alone	EL alone	SL and completed laparotomy	Exploration and completed laparotomy
Number	12	11	6	8
Operative time (min)	28.3±3	35.7±6.9[a]	252.1±39.7	203.8±44.7[a]

Data are presented as mean±SD. EL, exploratory laparotomy; SL, staging laparoscopy. [a]Indicates significant difference versus counter group.

time for operable patients who were subjected to SL followed by open Whipple procedure was significantly (P=0.046) longer than that for patients who had completed EL (Table 2).

Cumulative 24-h postoperative pain VAS score was significantly (P=0.001) higher in patients who underwent laparotomy (3.4±0.6) compared with scores determined in patients who underwent laparoscopy (2.2 ±0.5). Moreover, patients who underwent laparotomy requested significantly higher rescue analgesia compared with laparoscopy patients (P=0.001). The mean number of times rescue analgesia was requested with laparotomy versus laparoscopy was 2±0.8 vs. 0.6±0.5, respectively.

Discussion

The study included 38 patients with malignant obstructive jaundice diagnosed using CT imaging as operable patients with resectable lesions. However, EL detected inoperability/irresectability of 12 patients (one had SL) and SL defined another 12 inoperable patients. Fourteen patients were considered as true positive for CT imaging that showed a PPV of 42.11% and AUC for predictability of operability of 0.5 with a nonsignificant difference versus area for the null hypothesis. However, SL spared laparotomy in 12 patients, but unfortunately underestimated local extent of the disease in one patient who underwent unnecessary laparotomy. Statistical analyses defined a PPV of 85.7% and specificity rate of 92.3% for SL for the identification of operable patients. Moreover, receiver operating characteristic curve analysis showed that SL is positive significant predictor for operability with AUC of 0.897.

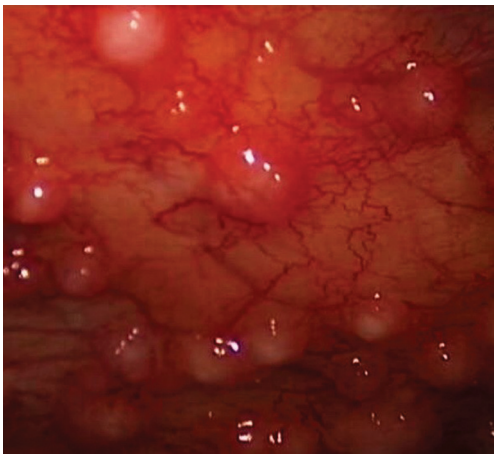
According to our study, 20 (52.6%) patients of 38 (eight in the EL group and 12 in the SL group) with potentially curable disease on CT criteria could potentially be spared a laparotomy.

Many hepatobiliary centers would consider SL as a routine step in the workup of gall bladder cancer (GBC) patients and Klatskin's tumor patients. However, SL is usually performed on selective basis in pancreatic cancer patients.

Zhuang *et al.* [7] found that SL in GBC is sensitive in detecting disseminated disease and increases the curative resection rate, shortens the recovery time, and has no negative implications on overall survival, and Agarwal *et al.* [8] also found that SL identified 94.1% of the detectable lesions, thereby obviated a nontherapeutic laparotomy in 55.9% of patients with unresectable disease and 23.2% of overall GBC patients.

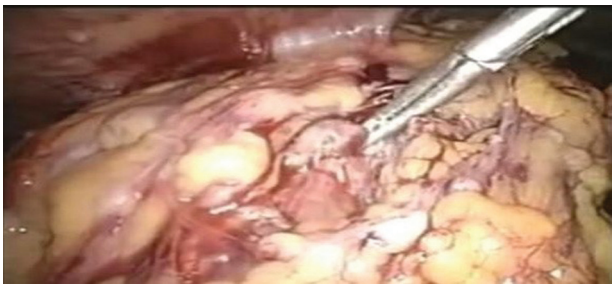
Bird *et al.* [9] reported that the accuracy for all-cause nonresection for SL was 66% with a PPV of progress to resection of 81% and concluded that SL proved useful

Figure 4



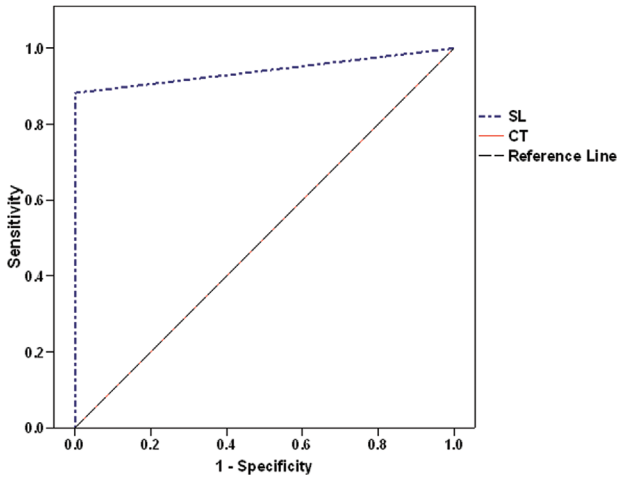
Omental deposits.

Figure 5



Omental mass and nodules.

Figure 6



ROC curve analysis of predictability of SL and CT for operability of patients had malignant obstructive jaundice.

in determining the presence of radiologically occult metastatic disease in perihilar cholangiocarcinoma (PHC). Moreover, Coelen *et al.* [10] found that the sensitivity of SL to detect unresectable disease in potentially resectable PHC patients ranged from 31.6 to 75% and the sensitivity was highest for peritoneal metastases (80.7%, 95% CI: 70.9–88.3). Recently, Tian *et al.* [11] through their meta-analysis including eight studies documented that 32.4% of patients with PHC and 27.6% of patients with GBC may avoid unnecessary laparotomy with the use of SL.

Königsrainer *et al.* [12] documented that in pancreatic cancer patients laparoscopy should be considered as an additional staging tool to rule out peritoneal carcinomatosis, and Sakamoto *et al.* [13] found that laparoscopic biopsy taking is a useful less-invasive procedure that allows obtaining sufficient specimen regardless of the location and size of the tumor and is more reliable compared with imaging-guided biopsy.

Bird *et al.* [9] reported that the sensitivity of SL for the detection of peritoneal disease was 71% in patients with PHC, and Karabicak *et al.* [14] documented that, in patients with radiographically defined locally advanced pancreatic ductal adenocarcinoma, SL detected peritoneal dissemination in 19% and liver metastasis in 15% of patients.

Moreover, cytological examination of peritoneal lavage samples obtained during SL detected malignant cells indicating the presence of metastatic lesion out of reach of SL and reliability of cytology for the diagnosis of inoperability of suspicious cases. Similarly, Karabicak *et al.* [14], in their series of patients with radiographically defined locally advanced pancreatic ductal adenocarcinoma, reported that SL detected positive peritoneal lavage cytology in 23% of patients. As regards operative time and total postoperative hospital stay of studied patients, SL significantly reduced theater time and hospital stay for patients diagnosed as inoperable compared with EL. Similarly, multiple previous studies documented that SL required a shorter operating room time, and a briefer hospital stay [4,7,15–17].

These results indicated the superiority of preliminary SL for defining operable cases and its ability to spare unnecessary laparotomy with its subsequent sequelae. In support of this assumption, Allen *et al.* [3,18] searched the Cochrane Central Register of Controlled Trials to determine the diagnostic accuracy of SL as an add-on test to CT scanning in the assessment of curative resectability in pancreatic and periampullary cancer and documented that SL with biopsy and histopathological confirmation of suspicious lesions before laparotomy would avoid unnecessary laparotomies in 21 [3] and 23% [18] of patients in whom cancer resection was planned.

The lack of consistency in CT reporting in this study may have contributed to the relatively high percentage of inoperable patients considered for surgery and then found to have peritoneal disease. However, this is more in favor of performing SL routinely in our setup.

Conclusion

Reliance on CT imaging alone for defining operability of patients with periampullary is accompanied by a relatively high unnecessary laparotomy rate. SL should be considered for defining inoperability with high PPV and specificity. SL could spare unnecessary laparotomy in around 50% of patients defined as operable using CT imaging. SL allowed shorter theater time and postoperative hospital stay for inoperable patients compared with EL.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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