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STAGING LAPAROSCOPY AND PERITONEAL CYTOLOGY IN THE DEFINITIVE MANAGEMENT OF PATIENTS WITH PERIAMPULLAY AND PANCREATIC BODY AND TAIL TUMOURS.

By
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Aim. *Staging laparoscopy and peritoneal cytology prevents unnecessary exploratory laparotmies among patients with pariampullary and pancreatic body and tail tumors. The study aims at evaluating this hypothesis.*
Patients and methods. *The study was carried out on patients suffering from periampullary or pancreatic body and tail tumours who were scheduled for definitive resectional surgery of their tumours. Preoperative radiological staging was based on CT abdomen findings. Staging laparoscopy and peritoneal cytology were performed under general anaesthesia and the abdomen examined in a standardized sequence of 10 steps and table positions.*
Results. *Staging laparoscopy was successfully performed on 20 patients without any morbidity or mortality, after excluding 18 patients for advanced disease. Staging laparoscopy and peritoneal cytology averted unjustified laparotomy for resectional surgery in 6 (30%) patients, 3 patients with pancreatic head tumours, 2 patients with distal bile duct tumours; 1 patient with pancreatic body and tail tumours and none in patients with tumours of the ampulla of Vater. The lesions that were detected by staging laparoscopy and missed by standard radiological staging were superficial liver metastasis, peritoneal seedlings and minimum ascites.*
Conclusion. *In view of the results, we recommend the routine use of staging laparoscopy with peritoneal cytology in patients with pancreatic and bile duct tumours and not in patients with tumours of the ampulla of Vater.*

Keywords: *endoscopy, assessment, neoplasms.*

INTRODUCTION

An unnecessary laparotomy is a frustrating situation that surgeons try hard not to inflict on patients with inoperable cancer. Staging laparoscopy of periampullary and pancreatic body and tail tumours has been reported to improve the assessment of resectability and avoid such unnecessary exploratory laparotomies.[1-6] This advantage is mainly attributed to the fact that laparoscopy enables the detection of small superficial liver and peritoneal metastasis that are easily missed with preoperative radiological staging.[7]

The addition of ultrasound examination to laparoscopy increases its accuracy as it adds new dimensions to its staging capability.[8-12] It enables surgeons during laparoscopy to assess the presence of deep-seated liver metastasis, evaluate peritumoural vascular invasion, and regional lymph node involvement or enlargement. However, this advancement comes with a financial burden secondary to the high cost of the sonographic equipment and training required to acquire the necessary skills for its proper use. This burden limits the wide spread use of laparoscopic ultrasound, not to mention, the inhibiting effect of such cost on its use in communities with limited financial resources.

Peritoneal cytology is another procedure, with minimum financial burden, used to increase accuracy of staging laparoscopy of abdominal malignancies.[13,14] This procedure has been shown to successfully predict unresectability of pancreatic tumours.[15] The aim of this

study is to assess the value of performing laparoscopic staging and peritoneal cytology preliminary to definitive surgical treatment of patients with periampullary and pancreatic body and tail tumours proven to be resectable by standard radiological staging.

PATIENTS AND METHODS

Patient population. The study was carried out on patients suffering from periampullary or pancreatic body and tail tumours admitted to the Medical Research Institute and Faculty of Medicine Hospitals, University of Alexandria for their definitive management within a 6 months period.

Diagnostic criteria. Periampullary tumours were defined as tumours of the ampulla of Vater, pancreatic head, intrapancreatic portion of the bile duct, and duodenum.

Exclusion criteria. Patients were excluded from the study if they had, on CT examination of the abdomen, liver metastasis, tumour involvement of the superior mesenteric-portal vein axis, superior mesenteric artery, celiac artery; or enlarged lymph nodes around the liver hilum or major vessels (aorta and inferior vena cava).

Clinical work-up. Patients were clinically examined to assess the presence of distant metastasis e.g. supraclavicular lymph nodes.

Laboratoy investigations. Blood samples were withdrawn to assess their haematological profile, renal and liver functions, and electrolyte balance.

Diagnostic work-up and assessment of resectability. All patients had a CT examination of their abdomen with special emphasis on tumour site, size, direct extension, vascular involvement, lymph node enlargement, liver metastases. All patients had a plain X-ray chest to rule out pulmonary metastasis.

Endoscopic retrograde cholangiopancreatography (ERCP). ERCP was performed to all patients presenting with jaundice to define the level of biliary obstruction and to insert a stent for preoperative biliary drainage.

Diagnostic laparoscopy. Laparoscopy was performed under general anaesthesia. A nasogastric tube was inserted into the stomach. An open technique was used for pneumoperitoneum using a Hasson blunt cannula. Carbon dioxide gas was used for inflation starting at a low flow rate of 1-3 L/min and maintained during the diagnostic procedure at a rate of 6 to 8 L/min with a maximum abdominal pressure of 14 to 15 mmHg. Inspection of the abdominal cavity was carried out with a 30° angled telescope with the aid of a palpating probe inserted in the right upper quadrant. The abdominal organs and cavity were examined in a standardized sequence of 10 steps and table positions.[16]

Peritoneal cytology. Peritoneal cytology was performed before taking any biopsies or attempting to enter the lesser sac. Cytologic washing was taken after instillation of 200 cc of normal saline in the upper abdomen. The patient was then placed in a 20° reverse Trendlenburg position and specimens were aspirated from the right and left subdiaphragmatic spaces after abdominal agitation. In the presence of ascites, it was sufficient to aspirate the ascitic fluid for cytologic examination.

Examination of the pancreas. Examination of the pancreas required the insertion of a second cannula in the left upper abdomen. Examination of the pancreas was not attempted in patients with tumours of the ampulla of Vater.

1) Supragastric method

The palpating probe introduced through the right accessory cannula was used to elevate the liver, thereby exposing the gastrohepatic omentum. A window was cut through an avascular area in gastrohepatic omentum and extended along the stomach axis. The palpating probe was then advanced through the aperture and used to elevate the liver substance above the lesser sac. The lower margin of the window in the lesser omentum and adjacent stomach (lesser curvature) were then pulled down using an atraumatic grasping forceps. The telescope was then introduced inside the lesser sac for inspection of the anterior surface of the pancreas.

2) Infragastric method

A similar window was cut through an avascular area in the gastrocolic omentum distal to the gastroepiploeic arcade and the stomach lifted with a palpating probe. The telescope was then advanced through the window into the lesser sac for inspection of the anterior surface of the pancreas with the help of a grasping forceps that kept the window widely open during inspection.

Laparoscopic biopsies. Biospies from peritoneal or omental nodules were taken with biopsy forceps. Nodules in liver were most easily sampled with a Tru-cut needle inserted directly through the abdominal wall and guided with laparoscopy. Cytology was obtained from the pancreas using fine needle aspiration cytology.

Completion of laparoscopy. Once the procedure was completed, the ports were all removed under direct vision to ensure that there was no bleeding from the port sites. The fascial defects and skin were closed after local infiltration with bupovicaine.

Cytological examination of the aspirated fluid. Freshly collected fluid was kept to settle down for 1 hour. The upper half of the fluid was removed, while the rest was shacked and poured in clean test tubes to be centrifuged at 5000 RPP, for

at least 15 minutes. The supernatant was discarded and the precipitate was gently mixed and dropped on clean glass slides. Glass slides were smeared and kept for semidrying, then dipped directly into 96% alcohol. Conventional H&E staining was performed. Thorough screening of both slides was done and a marker pen marked specific cells to be examined under an oil-immersion lens.

Ethical considerations and informed consent. The study protocol was approved by the local ethical committee. The study was explained to each patient and his/her informed consent was obtained prior to entry into the study**.**

RESULTS

A total number of 38 patients with periampullary or pancreatic body and tail tumours were initially included in the study. Preoperative assessment of respectability revealed that 18 patients (47.1%) suffered from advanced disease and as a result were excluded from the study (Fig. 1). As a result 20 patients entered the study after obtaining their informed consent; their characteristics are shown in Table 1.

All nine patients with pancreatic tumours, regardless of its intrapancreatic site, showed a hypodense mass on CT. One out of the six patients with distal bile duct tumour showed an enhancing soft tissue mass on CT. All patients with ampulla of Vater tumours had no mass lesions detected by CT. There was no ascitic fluid in any of the 20 patients as detected by CT. ERCP was attempted in all patients presenting with jaundice (15 patients). ERCP failed in one patient who had duodenal stenosis secondary to a tumour in the pancreatic head. Otherwise, ERCP was successful in defining and confirming the level of obstruction to be at the distal bile duct and a 10 French stent was successfully inserted in all 14 patients.

Staging laparoscopy was successfully performed in all 20 patients without any morbidity or mortality. Laparoscopy revealed suspicious lesions in 10 (50%) patients as shown in Table 2. Out of these 10 patients, 4 patients were confirmed to harbour malignant cells as shown Table 2. All patients with ascites (3/3) had malignant cells in their ascitic fluid and two patients (2/3) with ascites had also malignant liver deposits.

Peritoneal cytology was done in all 20 patients successfully; in the three patients with ascites, the ascitic fluid was aspirated directly. Six (30%) patients had a positive peritoneal cytology for adenocarcinoma cells. Table 3 shows the laparoscopic findings in the six patients with positive peritoneal cytology. In all six patients peritoneal cytology revealed representative malignant cellular yields made up of variable sized groups and small sheets of pleomorphic and hyperchromatic carcinoma cells attaining a ductal like configuration, with a background of few chronic and acute inflammatory cells.

Direct inspection of the pancreas was successfully performed in 9/15 (60%) patients. The infragastric approach was used in most patients [7/9 (77.8%)]. Direct inspection of the pancreas or its palpation or fine needle cytology did not yield any positive information that affected tumour staging or subsequent management.

The six patients who had positive peritoneal cytology were managed non-operatively except for two patients who underwent a double bypass surgery (cholecysto-jejunostomy with an anterior gastro-jejunostomy) secondary to duodenal stenosis / obstruction. Patients with negative peritoneal cytology were offered definitive resectional surgery, except for 3 patients who refused further surgery, as shown in Fig. 1.

Laparoscopy and peritoneal cytology averted unjustified laparotomy for resectional surgery in 3/5 (60%) patients with pancreatic head tumours, 2/6 (33.3%) patients with distal bile duct tumours; 1 /4 (25%) patients with pancreatic body and tail tumours and none in patients with tumours of the ampulla of Vater. However, two patients with pancreatic head tumours were subsequently operated upon for gastric outlet obstruction, as mentioned before, and shown in Fig. 1.

Table 1. Patient characteristics

Items		
Mean (min-max) age in years	57.4 (35-69)	
Female : Male	12 : 8	
Tumour site		
Periampullary tumours	16 (80%)	
Ampulla of Vater		5 (25%)
Pancreatic Head		5 (25%)
Distal common bile duct		6 (30%)
Pancreatic body and tail	4 (20%)	
Presenting symptom(s)		
Periampullary tumours		
Jaundice		13 (75%)
Jaundice and vomiting		2 (10%)
Pain		1 (5%)
Pancreatic body and tail		
Pain		4 (20%)

Table 2. Staging laparoscopy

Items	
Mean time required in minutes (SD)	71.34 (12.9)
Laparascopic findings (10 patients)	
Peritoneal adhesions	1 (5%)
Ascites	3 (15%)
Suspected peritoneal seedlings	3 (15%)
Suspected liver metastasis	7 (35%)
Positive samples (4 patients)	
Ascites	3/3
Peritoneal seedlings	1/3
Liver metastasis	2*/7

* Both patients suffered from ascites

Table 3. Laparoscopic findings in patients with positive peritoneal cytology (6 patients)

Items	
Peritoneal seedlings	1/6
Ascites	1/6
Ascites with liver metastasis	2/6
No macroscopic findings	2/6

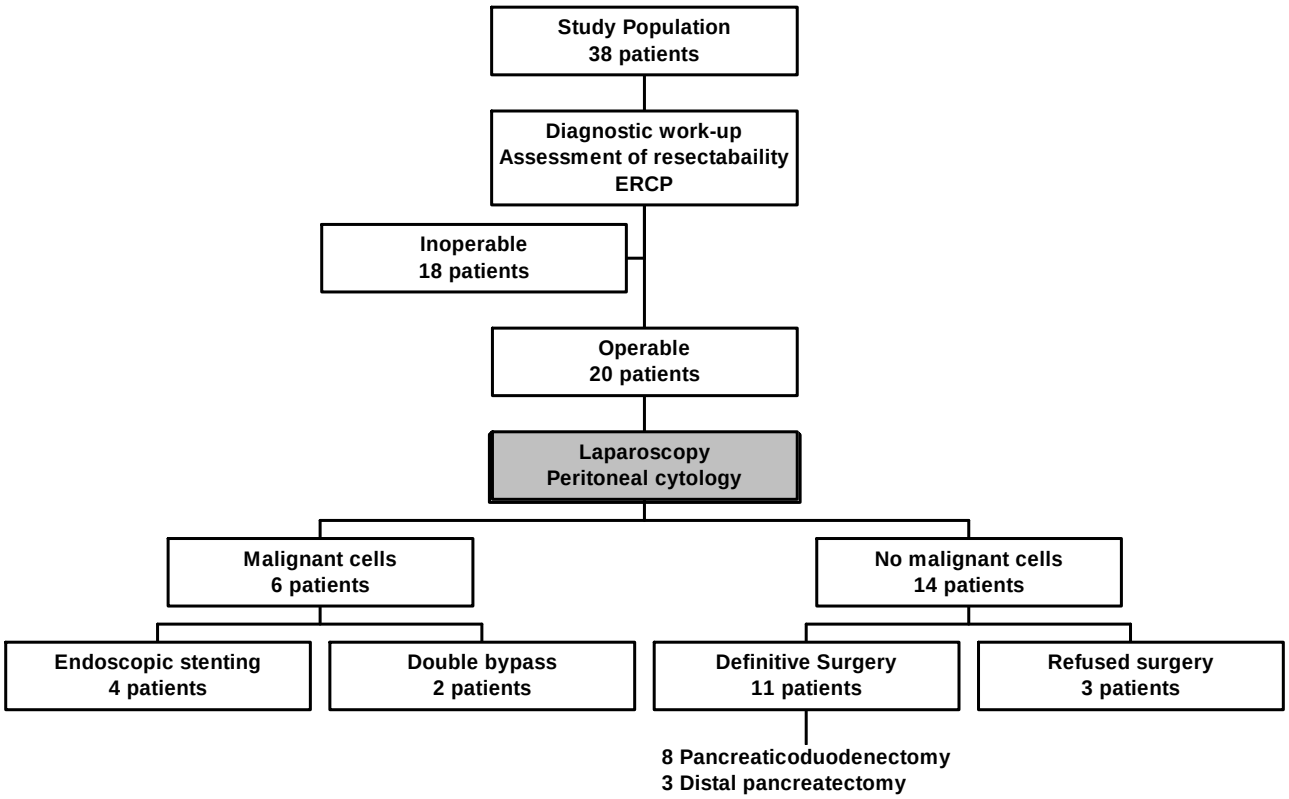

Fig. 1 Study flow chart

DISCUSSION

Laparoscopy is an invasive surgical procedure, which carries a certain risk for complications especially as it requires general anaesthesia.[17] Performing staging laparoscopy on patients with periampullary and pancreatic body and tail tumours, of whom most are elderly, may be considered an unnecessary risk taken on behalf of the

surgeons. This study has shown that staging laparoscopy could be performed safely on such group of patients. None of the studied patients suffered from any morbidity or mortality. However, larger studies performed on hundreds of patients revealed that complications, which are usually minor are expected in less than 5% of patients.[18] Furthermore, port site metastasis are rare and are usually presented in the world literature as case reports.[19]

Staging laparoscopy in our study took a longer time (71 minutes) to perform than expected in comparison to other reported studies which range from 39 to 60 minutes.[1,20] The main reason behind this is the time required to enter the lesser sac which is expected to decrease with an increase in the learning curve and also with the use of modern laparoscopic dissecting instruments such as the harmonical scalpel. Nonetheless, we did not gain any information from entering the lesser that contributed to a change in the management of our patients. Therefore, we do not recommend the routine examination of the lesser sac in patients with periampullary and pancreatic body and tail tumours.

The true superiority of laparoscopic staging in comparison to standard radiological staging is the detection of minimum ascites, peritoneal seedlings and superficial liver metastasis.[2,18,21,22,23,24] This was detected in 20% of our studied patients and corresponds with current literature in which staging laparoscopy averted exploratory laparotomy in 13% to 27% of patients scheduled for definitive resectional surgery.[23,25] The presence of ascites, even if minimum, is associated with advanced disease and is an ideal aspirate for cytology as it almost always harbours malignant cells. On the other hand, peritoneal and superficial liver lesions are not always associated with advanced disease as they prove to be malignant in only a third of patients as elaborated in this study.

The value of peritoneal cytology can be interpreted in multiple ways. First, malignant cells are always found in the peritoneal aspirate of patients with malignant macroscopic lesions such as peritoneal seedlings and/or superficial liver metastasis. Most complications, although minimum, arising from staging laparoscopy such as bleeding, bowel perforation, or bile leakage are the result of direct biopsy of suspected lesions.[18] Whether peritoneal cytology can totally replace direct biopsy of suspected lesions during staging laparoscopy and thus avert its complications requires further study. Second, peritoneal cytology increases the detection rate of patients with advanced disease and increases the number of patients that are saved an unnecessary exploratory laparotomy. [13,14,15] As a result of peritoneal cytology 30% of patients in this study were saved a formal exploratory laparotomy. Third, immediate macroscopic examination of the aspirate can be performed and might overcome many of the uncertainties encountered with frozen section of tissue samples. This will enable surgeons to perform their formal laparotomy immediately after the staging laparoscopy. However, this policy of staging and resecting at the same session has many logistical problems, which arise when advanced disease is found and exploratory laparotomy cancelled, in the form of lost dedicated operative time and hospital beds. This fact will hinder the widespread use of laparoscopic staging and exploratory laparotomy at the same session in patients with malignant disease.

Is staging laparoscopy useful in every patient and does it fit with all departmental management policies? The answer to both questions seems to be "No". First, patients with tumours of the ampulla of Vater did not benefit from staging laparoscopy as none of them were shown to harbour advanced disease and none of them had their management plan changed as a result of undergoing this endoscopic staging procedure. Therefore, we do not recommend the routine use of laparoscopic staging in patients with tumours of the ampulla of Vater after endoscopic examination confirms the presence of a tumour in the ampulla and the radiological staging reveals its resectability. On the other hand, we recommend laparoscopic staging in all patients with pancreatic and bile duct tumours as it has a bearing on their subsequent management and averts many unnecessary exploratory laparotomies in this group of patients.

Second, departments, which prefer to pursue a more surgical approach in their palliation do not favour the routine use of staging laparoscopy and will opt for an immediate exploratory laparotomy after standard radiological staging.[23] If the patient proves to harbour an advanced tumour they will perform a double bypass as they believe that it will, on the long-term, serve the patient better as these patients are considered the better end of the spectrum of patients with pancreatic and bile duct tumours and are expected to live for a relatively longer time. On the other hand, departments, which pursue a non-operative approach to patients with advanced disease, such as ours, will see much benefit in the use of staging laparoscopy as it will totally avert laparotomy in all patients with advanced disease except for those who suffer or develop gastric outlet obstruction.

Staging laparaoscopy with peritoneal cytology will always avert unnecessary exploratory laparatomies. The accepted percentage of aversion, that will make the routine use of staging laparoscopy attractive, depends upon departmental treatment strategies and level of accuracy of preoperative radiological staging.[21] In view of our results and departmental policy, we recommend the routine use of staging laparoscopy with peritoneal cytology in patients with pancreatic and bile duct tumours and not in patients with tumours of the ampulla of Vater.

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