

# Diagnostic accuracy of laparoscopy in staging of pancreatic cancer patients

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## Introduction

Pancreatic cancer is a devastating malignancy with nearly as many deaths as newly diagnosed cases each year. The 5-year survival rate is reported in the range between only 15 and 25% in most series. Accurate staging of patients with pancreatic cancer is crucial to clarify whether meaningful resection is indeed possible. Staging laparoscopy (SL) has been suggested as a tool for staging, which may spare up to two-fifth of these patients from undergoing nontherapeutic laparotomy. This study aimed at assessment of the role of laparoscopy in preoperative staging of patients with pancreatic cancer.

## Patients and methods

This study was a prospective cross-sectional study, in which 26 patients with pancreatic cancers from May 2014 till May 2017 were included at Suez Canal University Hospital. Patients were subjected to undergo abdominal ultrasonography and abdominal computed tomography scan with pancreatic protocol. Patients had undergone SL with standard technique.

## Results

Our study found that one patient in the resectable group was metastatic (1/16), whereas three patients in the borderline group were metastatic (3/10), with overall four patients (4/26) having metastasis on SL. Pattern of metastasis was liver metastases in 4% and peritoneal metastases in 11%. Male patients, older than 63 years, diabetic, cancer antigen (CA) 19-9 level more than or equal to 352 U/ml, tumors located at head, larger than 3 cm, and borderline resectable by computed tomography all may predict laparoscopically detectable metastases ( $P < 0.05$ ).

## Conclusion

SL is necessary for patients with suspicious occult distant organ metastasis; but it is not a substitute of high-quality imaging.

## Keywords:

borderline metastases, laparoscopy, pancreatic cancer, staging

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## Introduction

According to the American Cancer Society's estimates, pancreatic cancer accounts for ~3% of all cancers in the USA and ~7% of all cancer deaths [1].

The prognosis of those diagnosed with pancreatic cancer is dismal, with most patients succumbing to disease in less than 1 year. Surgical resection remains the only chance for long-term survival [2].

With only one in five patients deemed acceptable for resection, the importance of staging these patients is imperative to accurately assess the extent of disease, direct appropriate treatment, and avoid unnecessary intervention in a safe and cost-efficient manner [3].

The role of laparoscopy for staging purposes appeals to both patients and surgeons. When compared with staging at exploratory laparotomy, laparoscopic staging offers reduced surgical morbidity, decreased hospital stay, shorter recovery time, and less time to

administration of adjuvant therapy. Laparoscopy has been shown to identify intra-abdominal disease unappreciated by other staging modalities [4].

Although triple-phase high-resolution computed tomography (CT) is the staging of choice in patients with suspected or known pancreatic cancer, small tumors can be missed, or recognized as too small to characterize, and are often too small to biopsy percutaneously. Several studies have shown that 23–40% of those initially thought resectable by CT were found unresectable at the time of laparoscopic staging [5].

Despite the advantages mentioned for laparoscopic staging, the procedure is not performed routinely in

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many institutions. Some studies have not shown justification for performing laparoscopy as a routine diagnostic procedure to balance the additional surgical time and expense of the procedure for a relatively low yield of patients. Other reasons for infrequent use may be lack of adequate training, lack of understanding, or more likely the argument concerning palliation [4].

In this study, we performed staging laparoscopy (SL) to avoid unnecessary laparotomies.

## Patients and methods

### Patients

The current prospective cross-sectional study included all patients who fulfilled the inclusion criteria selected till the estimated sample size ( $n=26$ ) was reached. This research has been reviewed by our Research ethics committee in Faculty of medicine-Suez Canal University at its meeting on 24/06/2014 with reference number (#2168). A written and verbal informed consent was taken from the selected patients. The patients with pancreatic cancers attending the surgical oncology outpatient clinic and surgery ward from May 2014 till May 2017 were included. Inclusion criteria were all patients of both sex, any age, and diagnosed with resectable pancreatic cancer by triphasic CT (pancreatic protocol). Exclusion criteria were patients with unresectable, metastatic pancreatic cancer, patients' choice, or contraindication to laparoscopy.

### Procedure

All patients who attended the surgical oncology outpatient clinic diagnosed with pancreatic cancer (thorough history taking, general and local examination, cancer antigen (CA) 19-9 bilirubin level pelvi-abdominal triphasic CT scan with pancreatic protocol) were subjected to SL, which was done under general anesthesia in supine position; then after insertion of the ports, the patient was placed in reverse Trendelenburg position of 30°.

Pneumoperitoneum was established at 15 mmHg using Veress needle through a supra-umbilical incision. A 10-mm trocar 30° laparoscope was inserted through the supra-umbilical incision, and secondary 5- or 10-mm trocars were inserted in the right or left subcostal area.

On entering the peritoneal cavity, a systematic assessment should be made of all four quadrants. Evaluation of peritoneal surfaces included inspection of the suprahepatic and infrahepatic spaces, surface of

the bowel, small bowel mesentery, ligament of Treitz, paracolic gutters, and pelvis.

When there was no ascitic fluid, the peritoneal cavity was washed with 100 ml of 0.9% saline solution. The fluid was distributed throughout the peritoneal cavity and then all possible amount of fluid was aspirated for cytological examination. The peritoneal lavage cytology (PLC) results were considered positive if malignant cells or cells highly suspicious for malignancy were found at cytological examination [6]. The patients were categorized into two groups according to the respectability of the tumor:

- (1) Metastatic (unresectable) group, in which there was a visible metastasis to the liver, peritoneum, omentum, or bowel surface (no surgical intervention).
- (2) Nonmetastatic (resectable) group in which Whipple operation was done.

## Results

Our study included 15 (58%) male patients and 11 (42%) females, with mean age of  $57 \pm 6.5$  years, ranging from 49 to 68 years. Moreover, 10 (38.5%) patients were nonsmokers, whereas 16 (61.5%) were smokers; 17 (65%) patients were nonobese, whereas nine (35%) patients were obese; 20 (72%) patients had no history of chronic pancreatitis, whereas six (23%) patients had chronic pancreatitis; and 12 (46%) patients were nondiabetics, whereas 14 (54%) patients were diabetics (Table 1).

We investigated in our study tumor characteristics, and we found that tumor size by CT had a mean size of  $3.5 \pm 1$  cm, ranging from 2 to 5.6 cm. In 12 (53.8%) patients, tumor was equal or larger than 3.5 cm,

**Table 1 Patient characteristics**

Patient's characteristics	N (%)
Sex	
Male	15 (58)
Female	11 (42)
Tobacco smoking	
Nonsmoker	10 (38.5)
Smoker	16 (61.5)
Obesity	
Nonobese	17 (65)
Obese	9 (35)
Chronic pancreatitis	
Absent	20 (72)
Present	6 (23)
Diabetes mellitus	
Nondiabetic	12 (46)
Diabetic	14 (54)

whereas in 14 (46.2%) patients, tumor was smaller than 3.5 cm. Regarding tumor location by CT, 25 (96%) patients had tumors located at the head of pancreas, whereas one (4%) patient had tumors at body and tail of pancreas. Regarding the tumor grade, six (27%) cases were high grade and 13 (59%) cases were moderate. However, three (14%) cases showed low grade of differentiation. Regarding lymph node status, three (14%) cases were lymph node negative, whereas 19 (86%) cases were lymph node positive. Regarding blood vessel invasion (BVI), three (14%) cases showed no BVI, whereas 19 (86%) cases showed evidence of BVI. Regarding perineural invasion, only 59% of the studied cases showed evidence of perineural invasion whereas the rest 41% did not show any evidence of perineural invasion (Table 2).

Obstructive jaundice was the main symptom at time of diagnosis representing 54% (14/26) of patients, with 23% (6/26) of patients with weight loss and 23% (6/26) of patients with epigastric pain (Fig. 1).

Mean hemoglobin level was  $10\pm 0.9$  g/dl, ranging from 8.9 to 13 g/dl; mean serum albumin level was  $3.3\pm 0.3$  g/dl, ranging from 2.6 to 3.8 g/dl; mean serum bilirubin level was  $8.5\pm 4.8$  mg/dl, ranging from 2.6 to 16.5 mg/dl, and mean CA 19-9 level was  $728\pm 672$  U/ml, ranging from 45 to 2758 U/ml (Table 3).

Triphasic CT found that 61.5% (16/26) of patients were resectable, and 38.5% (10/26) of patients were

**Table 2 Tumor characteristics**

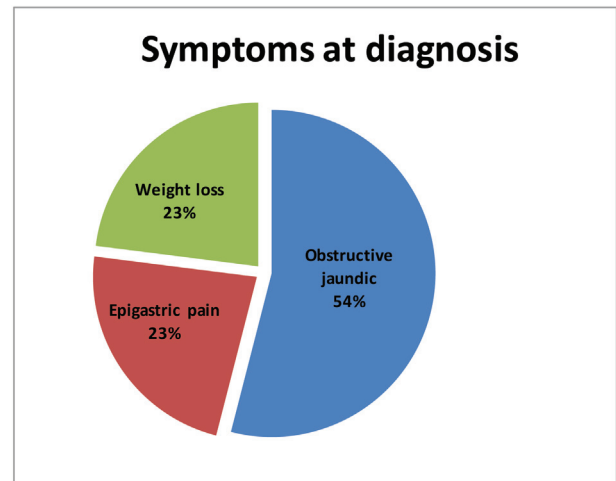
Tumor characteristics	N (%)
Location (by CT)	
Head	25 (96)
Body and tail	1 (4)
Size (by CT) (cm)	
$\geq 3.5$	12 (53.8)
$< 3.5$	14 (46.2)
Pathological grade	
High grade	6 (27)
Moderate grade	13 (59)
Low grade	3 (14)
Lymph node status	
Negative	3 (14)
Positive	19 (86)
Blood vessel invasion	
Absent	3 (14)
Present	19 (86)
Perineural invasion	
Absent	9 (41)
Present	13 (59)

CT, computed tomography.

borderline resectable. Twenty six patients who were resectable or borderline resectable by triphasic CT had undergone SL (Fig. 2).

SL of those patients found that one patient of resectable group was metastatic (1/16), whereas three patients of borderline group were metastatic (3/10),

**Fig. 1**



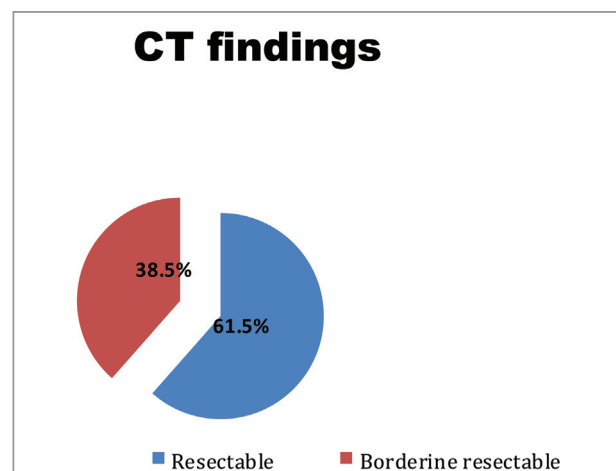
Symptoms at diagnosis.

**Table 3 Preoperative workup results**

Preoperative workup	Mean $\pm$ SD (range)
Hemoglobin level (g/dl)	$10\pm 0.9$ (8.9–13)
Serum albumin (g/dl)	$3.3\pm 0.3$ (2.6–3.8)
Serum bilirubin (mg/dl)	$8.5\pm 4.8$ (2.6–16.5)
Tumor marker CA 19-9 (U/ml)	$728\pm 672$ (45–2758)

CA, cancer antigen

**Fig. 2**

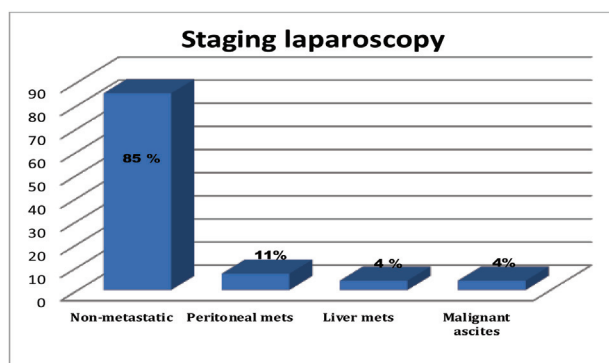


CT finding. CT, computed tomography.

**Table 4 Predictor factors of metastases in laparoscopy of pancreatic cancer**

Variables	n (Total=4)	P value
Sex		
Male	3	0.004
Female	1	
Age (years)		
<63	1	0.05
≥63	3	
DM		
Diabetic	3	0.005
Nondiabetic	1	
CA 19-9 (U/ml)		
<352	0	0.001
≥352	4	
CT findings		
Tumor location		
Head	3	0.06
Body and tail	1	
Tumor size (cm)		
<3	0	0.003
≥3	4	
Resectability		
Resectable	1	0.05
Border resectable	3	

CA, cancer antigen; CT, computed tomography; DM, diabetes mellitus.

**Fig. 3**

Staging laparoscopy findings.

with overall four patients (4/26) were metastatic on SL (Table 4).

Pattern of metastasis was liver metastases (1/4), peritoneal metastases (2/4), and malignant ascites (1/4) (Fig. 3).

Our study reported that predictors of laparoscopically detectable metastases were being a male patient, older than 63 years, diabetic, CA 19-9 level more than or equal to 352 U/ml, tumors located at head, larger than 3 cm, and borderline resectable by CT ( $P < 0.05$ ) (Table 3).

## Discussion

Our study included 26 patients with diagnosed pancreatic cancer who underwent preoperative triphasic CT, which revealed that 61.5% of patients (16/26) were resectable and 38.5% of patients (10/26) were borderline resectable. These patients had undergone SL to avoid unnecessary laparotomies.

We included 15 (58%) male patients and 11 (42%) females, with a mean age of  $57 \pm 6.5$  years, ranging from 49 to 68 years. This pattern that reflect slight tendency of male sex to have pancreatic cancer is consistent with Ibrahim *et al.* [7] whose results of cancer incidence in Egypt showed that pancreatic cancer is estimated to be 2.3% in males and 1.4% in females.

In our study, 10 (38.5%) patients were nonsmoker, whereas 16 (61.5%) were smokers; this can be explained by the fact that tobacco smoking is the leading preventable cause of pancreatic cancer, with an estimated 2.5-fold increase in risk when compared with nonsmokers [8].

In this study, 17 (65%) patients were nonobese, and 9 (35%) patients were obese; these findings are contrary to Michaud *et al.* [9] who stated that excessive body weight appears to increase the risk of pancreatic cancer, as obesity has a positive association, with a relative risk of 1.72.

Our study showed that 20 (72%) patients had no history of chronic pancreatitis, whereas six (23%) patients had chronic pancreatitis; these results are in contrast to Hurley *et al.* [10], who found that there is an 18-fold increase in risk of pancreatic cancer in patients of chronic pancreatitis compared with the general population. This can be explained by the fact that alcohol consumption is higher in western countries, raising the possibility of chronic pancreatitis [10].

We found that 12 (46%) patients were nondiabetics, whereas 14 (54%) patients were diabetics; these findings are concordant with a recent systematic review and dose-response meta-analysis including nine prospective studies, which showed that every 0.56 mmol/l increase in fasting blood glucose is associated with a 14% increase in pancreatic cancer incidence [11].

It was found that obstructive jaundice was the main symptom at the time of diagnosis, representing 54% of patients, with 23% (6/26) of patients with weight loss and 23% (6/26) of patients with epigastric pain. This can be explained in the light of the fact that



presentation of pancreatic cancer depends largely on tumor location. Carcinomas in the region of the ampulla and pancreatic head tend to present earliest with signs and symptoms of biliary tree obstruction [12].

Our current study reported that the mean hemoglobin level was  $10 \pm 0.9$  g/dl, ranging from 8.9 to 13 g/dl, and this is closely related to Satoi *et al.* [13], who found that the mean hemoglobin was 11.7 g/dl, ranging from 8 to 14.7 g/dl.

The mean serum albumin level was  $3.3 \pm 0.3$  g/dl ranging from 2.6 to 3.8 g/dl, and this is closely related to Satoi and colleagues, who found that the mean serum albumin was 3.6 g/dl, ranging 2.3–4.5 g/dl (17). These results are important in prediction of resectability as stated by Chiang *et al.* [14], who found that patients in the resection group showed higher albumin levels than those in the nonresection group.

Moreover, we found that the mean serum bilirubin level was  $8.5 \pm 4.8$  mg/dl ranging from 2.6 to 16.5 mg/dl, and this is closely related to Satoi *et al.* [13], who found that the mean serum bilirubin was 0.8 mg/dl, ranging 0.3–10 mg/dl. Chiang *et al.* [14], found that bilirubin levels were similar in both groups of patients undergoing resection and nonresection.

We noticed that the mean CA19-9 level was  $728 \pm 672$  U/ml, ranging from 45 to 2758 U/ml; this is closely related to Satoi *et al.* [1], who found that the mean CA19-9 level was 232 U/ml, ranging from 1 to 3978. Chiang *et al.* [14] found that lower mean CA 19-9 levels in the resection group than in the nonresection group, and CA 19-9 level less than 37 was independent predictive factor for resectability.

In this study, 26 patients who were resectable or borderline resectable had undergone SL. Most patients were nonmetastatic representing 85%, whereas 15% were metastatic, and this was consistent with Clarke *et al.* [15], who stated that even after appropriate preoperative imaging, 11–48% of patients are found to have unresectable disease during laparotomy.

SL in our study found that one patient of resectable group was metastatic (1/16), whereas three patients of borderline group were metastatic (3/10), with overall four patients (4/26) being metastatic on SL.

In our study, pattern of metastasis was liver metastases in 4% and peritoneal metastases in 7%; moreover, PLC

sampling was positive for malignancy in 12% of patients. Clark *et al.*, 2010, reported that SL for resectable and borderline resectable showed occult distant organ metastasis in 29% including positive peritoneal lavage cytology in 20%, liver metastasis in 13%, and peritoneal metastases in 3% [15].

The mean tumor size by CT was  $3.5 \pm 1$  cm, ranging from 2 to 5.6 cm. In 12 (53.8%) patients, tumor was equal or larger than 3.5 cm, whereas in 14 (46.2%) patients, tumor was smaller than 3.5 cm. Satoi *et al.* [13], found that the mean size was 3.7 cm ranging from 2.8 to 8.5 cm. Chiang *et al.* [14], found that tumor size less than 3 cm was an independent predictive factor for resectability.

In our study, concerning tumor location, 25 (96%) patients had tumors located at head of pancreas, whereas one (4%) patient had tumors at body and tail of pancreas, as it is estimated that ~65% of pancreatic cancers occur in the head of the pancreas, whereas 15% occur in the body and tail; the remaining lesions diffusely involve the gland [16].

Regarding tumor grade, six (27%) cases were high grade, and 13 (59%) cases were moderate. However, three (14%) cases showed low grade of differentiation. This finding can be explained in light of aggressive malignant biology [17].

It was found that three (14%) cases were lymph node negative, whereas 19 (86%) cases were lymph node positive. These findings were slightly higher than Kanda *et al.* [18], who reported that lymph node metastasis has been in 35–60% of patients with pancreatic cancer.

Concerning BVI, three (14%) cases showed no BVI, whereas 22 (86%) cases showed evidence of BVI. Perineural invasion occurred only in 59% of the studied cases, whereas the rest 41% did not show any evidence of perineural invasion; these findings can be explained in light of aggressive malignant biology [17].

In our study, it was found male patient, older than 63 years, diabetic, CA 19-9 level more than or equal to 352 U/ml, tumors located at head, larger than 3 cm, and borderline resectable by CT all may predict laparoscopically detectable metastases. These findings are concordant with Fong *et al.* [19], who stated that male patient, borderline resectable tumor, and CA 19-9 more than or equal to 397 U/ml were more likely to have laparoscopically detectable metastases. However, Fong *et al.* [19], found that patients with lesions in body or tail

were more likely to have laparoscopically detectable metastases.

## Conclusion

In conclusion, SL can be used as a minimally invasive method to improve the staging of pancreatic adenocarcinoma. We concluded that male patients with pancreatic cancer, older than 63 years, diabetic with CA 19-9 level more than or equal to 352 U/ml, tumors located at head, larger than 3 cm, and borderline resectable by CT all may predict laparoscopically detectable metastases.

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## Conflicts of interest

There are no conflicts of interest.

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