The Role of Laparoscopy in Advanced Pancreatic Cancer Diagnosis

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Abstract
Background/Aims: Histological diagnosis between ductal and endocrine carcinoma is imperative in patients with advanced and unresectable pancreatic malignancies because of the different treatment modalities and prognoses. Whenever percutaneous and endoscopic ultrasound-guided pancreatic fine needle aspiration (FNA) fails to obtain a diagnostic specimen, a laparoscopic approach may be employed.
Methods: Between October 2002 and July 2004, 19 patients with demonstrated unresectable pancreatic cancer underwent laparoscopy to obtain a cytohistological diagnosis.
Results: The mean operative time was 83 min. Laparoscopy showed the presence of liver metastases in 15 patients that were correctly diagnosed by preoperative imaging in only 8 cases (53%). Overall 5 pancreatic FNA and 16 liver and peritoneal biopsies were obtained. In 1 patient the procedure was abandoned due to hypercapnia. In 16 patients (84%) a cytohistological diagnosis was obtained. There were no mortalities.

Conclusions: Laparoscopic biopsy of advanced unresectable pancreatic cancer is a feasible, safe and reliable procedure to obtain a cytohistological diagnosis whenever ultrasound-guided FNA fails.

Introduction

Only 20% of patients suffering from pancreatic cancer are amenable to surgical resection at diagnosis [1–4]. Among unresectable neoplasms it is important to distinguish between ductal adenocarcinoma and other tumors that have different management modalities and prognoses, such as endocrine carcinoma or metastases of non-pancreatic primary tumors to the pancreas. In these cases cytohistological diagnosis is mandatory in order to initiate proper medical treatment as soon as possible [5–10].

Percutaneous ultrasound (US)-guided pancreatic fine needle aspiration (FNA) is the gold standard to obtain pathological diagnoses. Whenever this approach fails to obtain a diagnostic tumor specimen, endoscopic US (EUS) FNA should be attempted. When both US and EUS FNA fail, surgery is indicated.

In patients suffering from unresectable intra-abdominal malignancies palliative chemo-radiotherapy is more likely to be quickly initiated when a diagnosis is obtained.
by laparoscopy rather than by exploratory laparotomy [5–7]. Laparoscopic surgery is now widely employed in the diagnostic workup of pancreatic cancer patients and, compared to laparotomy, does not affect survival [11].

The role of laparoscopy and laparoscopic US in staging pancreatic cancer is well established [12–18], and the procedure is considered routine before exploratory laparotomy for pancreatic resection by several high-volume centers [19–23].

The aim of the present report is to present our experience in a consecutive series of patients suffering from pancreatic malignancies selected for laparoscopic biopsy.

**Materials and Methods**

Among 388 patients presenting with pancreatic malignancies between October 2002 and July 2004 in our surgical unit, 198 (51%) were considered unresectable at preoperative staging (including US, spiral CT or MRI and laboratory blood tests) and in the absence of gastrointestinal obstructive symptoms underwent US- and EUS-guided FNA. A total of 190 (49%) patients were operated on: 106 (27.3%) had palliative or diagnostic procedures, while 84 (21.6%) underwent pancreatic resection. Overall 19 (4.9%) consecutive unresectable patients (10 females and 9 males; mean age 60.3, range 33–74 years) underwent a laparoscopic procedure in order to obtain a cytohistological diagnosis. Figure 1 shows the clinical flowchart for the preoperative workup of pancreatic cancer patients at our institution.

**Laparoscopic Technique**

**Positioning of the Patient**

The patient is placed in a supine position with the thighs fully abducted. The operating table is equipped with a 30° reversed Trendelenburg tilt. The surgeon then stands between the patient’s legs with the first assistant on the patient’s left. A laparoscopy tower is placed on the patient’s right side.

**Insufflation**

A long Verres® needle is introduced four fingerbreadths below the left costal margin in the left upper quadrant and an intra-abdominal pressure of 14 mm Hg is maintained.

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**Fig. 1.** Clinical flowchart for the preoperative work-up of pancreatic cancer patients. CWMRI = Continuous wave MRI.
Placement of Trocars

A 10-mm optic trocar for the optical system is introduced above the umbilicus; a 5-mm trocar is placed just below the xiphoid, a 10-mm operating trocar is placed where the Verres needle was introduced, and a 5-mm trocar for atraumatic grasping forceps is placed in the right lower quadrant.

Instrumentation

Bipolar forceps or a harmonic scalpel is used to obtain a liver specimen. In the case of a locally advanced pancreatic mass in the body of the gland, when FNA of the tumor is performed the lesser sac is opened and a biopsy is obtained under vision with a percutaneous 25-gauge peridural needle after intraoperative US. All histological tissue is extracted with an Endocatch bag. Whenever possible intraoperative frozen sections or cytology are obtained.

Results

Overall 5 pancreatic FNA and 16 liver and peritoneal biopsies were obtained. The tumor site was the body–tail in 14 patients, head or uncinate process in 4, and unknown in a patient with gastrinoma metastatic to the liver. In 16 patients (84%) diagnostic specimens were obtained by laparoscopy; these included 14 positive diagnoses of ductal adenocarcinoma, and 2 endocrine tumors. In 1 patient the procedure was abandoned due to hypercapnia; this patient was operated on 6 days later with an open procedure and a tissue sample was obtained that was positive for ductal cancer. In 2 patients undergoing laparoscopy the specimen was not adequate for definitive diagnosis. These 2 patients refused additional surgical procedures. The laparoscopic procedure demonstrated the presence of liver lesions of <1 cm in diameter associated with pancreatic cancer in 15 patients. Table 1 shows the details of the preoperative workup, the sites of biopsy, and the final pathological results.

The mean operative time was 83 (range 35–160) min, including the time required for intraoperative cytology or histology on frozen sections. There were no mortalities. One patient experienced hypercapnia. The overall postoperative mean hospital stay (HS) was 4 (range 2–13) days. Patients could be divided into 3 groups: the first (n = 10) group underwent only laparoscopic biopsy with a mean HS of 2.3 (range 2–3) days; the second (n = 7) group underwent celiac plexus percutaneous block for intractable pain with a mean HS of 5.8 (range 4–7) days, and the third group consisted of only 2 patients, 1 who underwent laparotomy 6 days after laparoscopy, and the second, who underwent laparoscopy to exclude the possibility of draining the biliary tract because of diffuse tumor infiltration, was subsequently subjected to percutaneous biliary drainage placement due to preexisting jaundice and was discharged on day 13.

Follow-up data were available for 17 patients. Overall survival was 14 (range 3–27) months. For the 15 patients diagnosed with ductal adenocarcinoma the median survival was 11 (range 3–27) months after chemotherapy,

Table 1. Details of the workup and surgical procedures with final pathological results

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Metastases at laparoscopy</th>
<th>Site of biopsy or FNA</th>
<th>Pathological results</th>
<th>Preoperative imaging</th>
<th>Preoperative workup results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>Pancreatic FNA</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>2</td>
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<td>Pancreatic FNA</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>Liver biopsy, pancreatic FNA</td>
<td>Ductal adenocarcinoma</td>
<td>US, CT scan and MRI</td>
<td>Vascular infiltration, liver metastases</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>Liver biopsy</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, liver metastases</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>PEritoneal and liver biopsy</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, liver metastases</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>Liver biopsy</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, liver metastases</td>
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<tr>
<td>7</td>
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<td>Liver biopsy</td>
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<td>US and CT scan</td>
<td>Liver metastases</td>
</tr>
<tr>
<td>8</td>
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<td>Liver biopsy</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, liver metastases</td>
</tr>
<tr>
<td>9</td>
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<td>Liver biopsy</td>
<td>Endocrine carcinoma</td>
<td>US and CT scan</td>
<td>Liver metastases</td>
</tr>
<tr>
<td>10</td>
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<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>11</td>
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<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
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<td>12</td>
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<td>Liver biopsy, pancreatic FNA</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>13</td>
<td>Yes</td>
<td>Liver biopsy</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>14</td>
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<td>Liver biopsy</td>
<td>Ductal adenocarcinoma</td>
<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
</tr>
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<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
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<td>16</td>
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<td>US and CT scan</td>
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<td>17</td>
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<td>Procedure not performed</td>
<td>–</td>
<td>CT scan and MRI</td>
<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>18</td>
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<td>Inadequate sampling</td>
<td>US and CT scan</td>
<td>Vascular infiltration, no metastases</td>
</tr>
<tr>
<td>19</td>
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<td>Liver biopsy</td>
<td>Inadequate sampling</td>
<td>US and CT scan</td>
<td>Liver metastases</td>
</tr>
</tbody>
</table>

Laparoscopy and Pancreatic Cancer Diagnosis

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which consisted of gemcitabine (in 1 patient associated with oxaliplatin) in 14 and chemoradiotherapy in 1 case. Two patients affected by metastatic endocrine carcinomas received transarterial chemoembolization of liver metastases and long-acting octreotide (20 mg every 4 weeks) and survived for 27 and 14 months, respectively. Two patients who refused further investigations were lost to follow-up.

Discussion

Cytohistological diagnosis is mandatory in patients suffering from unresectable pancreatic neoplasms as medical treatment varies according to the type of tumor (e.g. ductal versus endocrine carcinoma). In fact, in addition to common ductal adenocarcinoma, rarer tumors such as endocrine cancer and pancreatic metastases are found with increasing frequency in the effort to better define all pancreatic masses [5–7]. In order to obtain a tumor specimen, the gold standard is FNA cytology using percutaneous US or EUS guidance.

The impossibility of obtaining a cytohistological diagnosis with FNA is a challenge for the surgeon: in fact to get an adequate tissue specimen exploratory laparotomy or laparoscopy should be performed. A surgical open approach for unresectable pancreatic neoplasms should be carefully considered because of the poor prognosis of this patient subgroup, and the relative immunological impairment. The possible delay of chemotherapy must also be considered as a major adverse event for these patients. In order to minimize the clinical impact of the surgical procedure, a minimally invasive approach may be a viable alternative to exploratory laparotomy [5–7].

In the recent literature much attention has been given to the role of laparoscopy in the staging of pancreatic cancer. Several authors have demonstrated that laparoscopy is both safe and feasible to better assess resectability in pancreatic cancer patients before resorting to an open resective procedure, especially when associated with laparoscopic ultrasound [12–18]. Moreover, other authors have reported that such an approach can be adopted on a routine basis [19–23].

The policy in our unit is to resort to an open surgical technique whenever patients present symptoms of upper gastrointestinal obstruction with or without jaundice and have no evidence of liver metastases on preoperative staging with intraoperative FNA to confirm the diagnosis. In patients suffering from metastatic disease every effort is made to obtain a pathological diagnosis with percutaneous US-guided FNA, performing endoscopic palliation in patients with obstructive jaundice. In the vast majority of patients this approach can be considered the gold standard with the accuracy of percutaneous diagnostic procedures varying in the literature from 83 to 94% [24, 25].

In the minority of patients without obstructive symptoms, whenever a diagnosis cannot be obtained by US and EUS FNA, a laparoscopic approach should be considered. During the period under examination, this technique was employed in 19 cases (4.9% of the total number of patients) and had an 84% success rate with no mortality and negligible morbidity. In 16 of these patients, US-guided FNA was unsuccessful either because of the small size of the lesions or because of the proximity of the lesions to major vessels, rendering the procedure unsafe. In 3 patients in whom US and CT scan did not demonstrate involvement of major vessels and/or liver metastases with a high level of CA 19.9 (>5,000 U/ml), laparoscopy was performed without previous US-guided FNA, and we were able to obtain both correct staging and pathological diagnoses, which were stage IVb due to hepatic or peritoneal spread of ductal adenocarcinoma.

Whenever possible we requested an intraoperative diagnosis that confirmed the presence of malignancy in 13 patients. In 1 patient the specimen was not diagnostic and the procedure had to be abandoned due to hypercapnia. In 5 patients due to the presence of small liver lesions intraoperative diagnosis was not requested for the sole purpose of obtaining a more accurate, definitive diagnosis. Although intraoperative diagnosis prolonged the operative time in this series, we recommend it whenever possible.

Furthermore in our experience, laparoscopy can add more information regarding the patients’ staging compared with preoperative evaluations. In fact, preoperative imaging studies correctly identified only 8 (53%) of 15 patients with metastatic disease. This finding confirms the limits of radiological imaging in identifying small metastases on the hepatic surface and peritoneum [26]. The short HS in the subgroup that underwent only laparoscopic biopsy demonstrates the clinical benefit for the patients.

In conclusion, laparoscopic biopsy of advanced, unresectable pancreatic cancer is a feasible, safe and reliable procedure for selected patients to obtain a cytohistological diagnosis whenever US-guided FNA fails and the avoidance of non-therapeutic exploratory laparotomy is warranted. In selected cases laparoscopy represents an ‘all-in-one’ procedure to provide the best staging together with definitive diagnosis.
References


