The Impact of Laparoscopy and Laparoscopic Ultrasound on the Management of Pancreatic Cystic Lesions

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Hypothesis: Laparoscopic ultrasound examination combined with biopsy of the cystic wall and aspiration of cystic fluid improves differential diagnosis of pancreatic cystic lesions contributing to surgical decision making.

Study Design: A prospective evaluation of the impact of laparoscopic ultrasound on surgical decision making in patients with pancreatic cysts.

Setting: A general community hospital; the department of surgery serves as referral for pancreatic surgery.

Patients: During a 36-month period, 15 patients with pancreatic cystic lesions were prospectively evaluated by laparoscopy and laparoscopic ultrasound with ultrasound-guided biopsy of the cystic wall and aspiration of cystic fluid for cytologic study, viscosity, and determination of levels of amylase and tumor markers (carcinoembryonic antigen, cancer antigen 19.9).

Results: Laparoscopic ultrasound contributed new, additional data in 8 patients (53%) when compared with compiled imaging data obtained by conventional ultrasound, computed tomography, magnetic resonance imaging, and endoscopic ultrasound. A solid cystic component was detected in 6 patients and additional small (<1 cm) cysts in 3 patients. Amylase and tumor marker levels, biopsy of the cystic wall, and cytologic examination had significant impact on surgical decision making in 6 patients. Nine patients underwent resection of the cystic lesion. Three patients diagnosed as having benign cysts had laparoscopy with laparoscopic ultrasound only. Three patients with suspicious lesions refused surgery. Laparoscopic ultrasound predicted correctly the nature of the cyst in 7 of 9 surgically treated patients (sensitivity, 78%). Two patients with serous cystadenoma had high levels of tumor markers (false-positive).

Conclusion: Although a rather invasive procedure that requires general anesthesia and hospitalization, laparoscopy with laparoscopic ultrasonography was found to significantly contribute to the differential diagnosis of pancreatic cystic lesions.


Pancreatic cystic lesions are being recognized with increasing frequency with widespread use of advanced imaging techniques. In most cases the clinical as well as radiological presentation of pancreatic cysts is complicated and differentiation among the various cyst types may be difficult.

The recent development of the laparoscopic ultrasonographic probe and the possibility of laparoscopic ultrasound (US)–guided biopsy and aspiration enables a thorough laparoscopic evaluation and staging of pancreatic cystic lesions.

We report our experience and the impact of the new modality on surgical decision making.

RESULTS

Fifteen patients with cystic lesions of the pancreas qualified for the study (9 women and 6 men, aged 40-78 years; mean age, 65.7 years). Six patients were asymptomatic and the cyst was disclosed as an incidental finding, or was found by routine follow-up examinations (2 patients with previous breast cancer and 1 patient with lung cancer). Two patients experienced abdominal pain and weight loss and the cyst was revealed during the diagnostic evaluation. One patient had a palpable mass in the left upper abdomen and 3 patients with cystic lesions in the head of the pancreas experienced symptoms of bile duct obstruction.

Table 2 shows the localization of the cysts and features revealed by laparoscopic US. Although most patients had cystic lesions larger than 2 cm in diameter, LAPUS also demonstrated cysts smaller...
PATIENTS AND METHODS

During a 36-month period (1996-1999), patients presenting with pancreatic cysts were screened for this study. Patients with a history of recent pancreatitis, abdominal trauma, or radiological evidence of a pancreatic pseudocyst were excluded. All patients had a conventional US study, abdominal computed tomography (CT), and in most cases, endoscopic retrograde cholangiopancreatography prior to laparoscopic evaluation. Six patients underwent endoscopic ultrasound (EUS) examination. Patients considered candidates for surgery were offered the option of laparoscopy and laparoscopic ultrasound (LAPUS) as a separate procedure, prior to the final determination of treatment. The project was approved by the hospital review board and informed consent was obtained from all participants. Treatment followed the general guidelines of differentiation between benign cysts and cystic neoplasms.10

LAPUS was performed under general anesthesia by a standard technique. Briefly, 2 disposable 10-mm cannulae were introduced at the umbilicus and right upper abdominal quadrant. Additional ports were inserted as needed for dissection or for entering the lesser sac. Inspection of the abdominal cavity was performed with a 30° telescope. Laparoscopic US was performed with a 10-mm 8-MHz sectoral contact US probe (Sharplan Usight laparoscopic ultrasound system, Tel Aviv, Israel) enabling simultaneous view of the laparoscopic and ultrasonographic images using “picture in picture” visual mixing. The head of the pancreas could be examined directly, while examination of the body and tail of the pancreas necessitated entrance into the lesser sac through a small aperture in the gastrocolic ligament. Laparoscopic US-guided biopsy was performed with an 18-gauge biopsy needle (Quick core biopsy needle; Cook, Bloomington, Ind). All patients were prospectively studied using a protocol. The various LAPUS parameters recorded are presented in Table 1.

Table 1. Laparoscopic Ultrasound Parameters for the Evaluation of Pancreatic Cysts

- Presence of chronic pancreatitis
- Presence of additional cystic lesions
- Nature of the cyst’s wall (thickness, uniformity, regularity)
- Relationship with pancreatic ductal system and vascular structures
- Biopsy of the cystic wall
- Aspirate of the cyst for
  - Amylase levels
  - Levels of tumor markers (carcinoembryonic antigen, cancer antigen 19.9)
  - Viscosity of the fluid
  - Cytologic examination

than 1 cm in diameter (3 patients). Most lesions (n = 8) were in the pancreatic head, 5 were found in the body, and 2 were in the tail of the pancreas. Involvement of the pancreatic duct was demonstrated in 3 patients (in 2 patients a dilatation of the duct distal to the cyst was found and in 1 patient a communication of the cyst with the pancreatic duct was demonstrated). LAPUS features of the cyst wall were recorded in all patients and revealed a solid component or irregularity of the wall in 6 patients. Biopsy of the cystic wall was performed in 12 patients and results were negative for malignancy in all cases. In the remaining 3 patients the cystic wall was thin (<1 mm), precluding biopsy. Cytologic examination of the aspirate revealed mucinous cells in 1 specimen only, whereas in the other instances the study was negative for cells, or demonstrated pancreatic ductal cells without atypia or granulocytes. Determination of markers in the aspirate revealed high levels of carcinoembryonic antigen (CEA) and cancer antigen 19.9 (CA19.9) in 8 patients, 5 patients had levels within the normal range, one patient had high levels of CA19.9 with normal levels of CEA, and in 1 patient the sample was insufficient for evaluation.

Amylase levels were high in 4 patients. In 2 of these patients the cysts were finally diagnosed as pseudocysts. The third patient with increased concentrations of amylase also had high levels of CEA and CA19.9 in the aspirated fluid and was found to have a mucinous cystadenoma in the head of the pancreas. The fourth patient was found to have a cystadenocarcinoma communicating to the main pancreatic duct, with high levels of tumor markers (CEA, 192 ng/mL; CA19.9, 256 U/mL); ultrasonographic features of chronic pancreatitis with thickening and edema of the pancreas were also demonstrated.

There were no complications following the LAPUS procedure and the hospitalization stay ranged from 1 to 3 days (mean, 1.5 days).

When compared with imaging data obtained from the compiled information of conventional US, CT, and magnetic resonance imaging, the LAPUS contributed new, additional information in 8 patients (53%). A solid cystic component (Figure) was detected in 5 patients and additional small cysts (<1 cm) were identified in 3 patients.

When compared with EUS findings (6 patients only), LAPUS findings and interpretation were similar in 3 patients—2 patients with lesions of the head of the pancreas (a pseudocyst and a serous cystadenoma) and 1 patient with a cystadenocarcinoma of the tail of the pancreas. Two patients with mucinous cystadenomas, 1 in the tail of the pancreas (2 × 1 cm) and 1 in the head of the pancreas (2 × 2.5 cm) were not visualized by EUS. A third patient had a mucinous cystadenoma in the head of the pancreas that was visualized but misdiagnosed by EUS as serous cystadenoma. These 3 lesions were visualized and correctly diagnosed by LAPUS.

Data obtained by LAPUS indicated resection of the pancreatic cyst in 11 patients. The other 4 patients were finally diagnosed as having benign cysts. Of these, 2 patients were diagnosed as having a pseudocyst and 2 patients a serous cystadenoma. Diagnosis was based on results of biopsy of the cystic wall, nor-
mal or absent levels of CEA and CA19.9, and high levels of amylase. These patients are observed by repeated CT and US examination. One of the patients with serous cystadenoma, correctly diagnosed by LAPUS, was operated on for a symptomatic (8 cm) cyst in the body of the pancreas.

Nine patients finally underwent operation. Two patients underwent pancreaticoduodenectomy. Enucleation of the cyst was performed in 2 patients—1 with a cystic lesion in the head of the pancreas and 1 with a cystic lesion in the body of the pancreas. Five patients have had a distal pancreatectomy for lesions of the body and tail. Three patients with suspicious lesions refused surgery: 2 patients with lesions in the head of the pancreas, suspected as mucinous cystadenomas, 1 with high levels of CEA, and 1 with LAPUS evidence of a solid component in the wall of the cyst. The third patient with a cyst in the tail of the pancreas, which was not demonstrated on EUS revealed at LAPUS 2 small additional cysts, an irregular cystic wall, and septa in the cyst, yet the tumor markers (CEA and CA19.9) were not elevated.

Histological findings are presented in Table 2. Four patients were found to have mucinous cystadenomas of the head of the pancreas, and 2 had cystadenocarcinomas. One patient was found to have a serous cystadenoma of the head of the pancreas, and 1 patient had a simple pancreatic cyst in the body of the pancreas (false-positive). These 2 patients had high levels of tumor markers in the cystic fluid aspirate: the patient with serous cystadenoma had elevated levels of CEA (225 ng/mL; normal range, 0.05-5 ng/mL) and CA19.9

Table 2. Laparoscopic Ultrasound (US) Evaluation of Pancreatic Cysts

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Cyst Size, cm</th>
<th>Positive US Parameters</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4 x 2.5</td>
<td>Dilated pancreatic duct</td>
<td>Mucinous cystadenoma</td>
<td>Resection</td>
</tr>
<tr>
<td>2</td>
<td>3.2 x 1.8</td>
<td>Solid* component, dilated pancreatic duct</td>
<td>Serous cystadenoma</td>
<td>Observation</td>
</tr>
<tr>
<td>3</td>
<td>2 x 2.5, 1 x 1</td>
<td>2 Cysts*</td>
<td>Mucinous cystadenoma</td>
<td>Refused operation</td>
</tr>
<tr>
<td>4</td>
<td>0.5 x 1</td>
<td>†</td>
<td>Pseudocyst</td>
<td>Observation</td>
</tr>
<tr>
<td>5</td>
<td>3.5 x 3</td>
<td>†</td>
<td>Serous cystadenoma</td>
<td>Resection</td>
</tr>
<tr>
<td>6</td>
<td>3 x 3</td>
<td>Solid* component</td>
<td>Mucinous cystadenoma</td>
<td>Refused operation</td>
</tr>
<tr>
<td>7</td>
<td>8 x 6</td>
<td>Solid* component</td>
<td>Mucinous cystadenoma</td>
<td>Enucleation</td>
</tr>
<tr>
<td>8</td>
<td>2 x 1</td>
<td>Tissue fragments,* communication to pancreatic duct</td>
<td>Pseudocyst</td>
<td>Observation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Cyst Size, cm</th>
<th>Positive US Parameters</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>1 x 0.8, 1 x 0.6</td>
<td>2 Cysts</td>
<td>Mucinous cystadenoma</td>
<td>Resection</td>
</tr>
<tr>
<td>10</td>
<td>5 x 4, ≤0.5*</td>
<td>Chronic pancreatitis, irregular thick wall, 2 small cysts*</td>
<td>Cystadenocarcinoma</td>
<td>Resection</td>
</tr>
<tr>
<td>11</td>
<td>2 x 1</td>
<td>†</td>
<td>Mucinous cystadenoma</td>
<td>Resection</td>
</tr>
<tr>
<td>12</td>
<td>8 x 5</td>
<td>†</td>
<td>Serous cystadenoma</td>
<td>Resection</td>
</tr>
<tr>
<td>13</td>
<td>2 x 2</td>
<td>Multilocular cyst, calcifications</td>
<td>Simple cyst</td>
<td>Enucleation</td>
</tr>
<tr>
<td>14</td>
<td>3 x 2, 0.6 x 0.8</td>
<td>2 Small cysts,* solid* component</td>
<td>Cystadenocarcinoma</td>
<td>Refused operation</td>
</tr>
<tr>
<td>15</td>
<td>3 x 4</td>
<td>Solid* component, thick irregular wall</td>
<td>Cystadenocarcinoma</td>
<td>Resection</td>
</tr>
</tbody>
</table>

* Additional, new information obtained by laparoscopic ultrasonography.
† There were no positive US parameters found.
Cystic lesions of the pancreas include inflammatory pseudocysts (70%), true cysts, serous cystadenomas, mucinous cystic tumors with malignant potential, and cystadenocarcinomas. Differentiation of various types of pancreatic cysts presents a diagnostic and therapeutic challenge, particularly since about 15% of the pancreatic cysts are actually cystic neoplasms that are potentially curable with timely resection.

Clinical presentation, no history of pancreatitis, and normal serum levels of amylase suggest a cystic neoplasm. Modern imaging techniques have added certain features of pancreatic cysts that should raise suspicion that a cystic neoplasm is present. However, these criteria are not uniformly reliable in the diagnosis of pancreatic cystic neoplasms. Endoscopic retrograde cholangiopancreatography contributes additional information with regard to relationship of the cyst to the pancreatic ductal system. Although it is assumed that demonstration of ductal changes of chronic pancreatitis, or a direct communication with the cyst and high levels of amylase within the cyst, supports the diagnosis of pseudocyst, there are exceptions. The association between chronic pancreatitis and pancreatic tumors is well established, and in the rare instance of the so-called duct-ectatic cystic neoplasm, a neoplastic transformation in one of the pancreatic ducts creates a cyst that does communicate with the ductal system as occurred in one of our cases. Aspiration of cystic fluid for analysis and biopsy of the cyst’s wall have been of considerable interest. However, the percutaneous CT or US-guided needle aspiration carries the risk of needle tract and peritoneal dissemination of tumor cells as well as spillage of malignant cyst’s contents. Even intraoperative examination of biopsy material may fail to correctly differentiate cystic lesions in as many as 20% of the cases. Contact laparoscopic US-guided puncture of the cyst minimizes the risk of spillage since it is performed under laparoscopic visualization and control, using laparoscopic instruments. Indeed, the technical development of a laparoscopic sectoral US system that enables a LAPUS-guided biopsy significantly enhances diagnosis.

The introduction of EUS enables visualization of pancreatic cystic lesions as well as aspiration of cystic fluid without the need for general anesthesia. Endoscopic ultrasound has a high sensitivity in diagnosing pancreatic lesions; however, the specificity rates are lower, in the range of 75% to 80% for pancreatic malignancy. In our setting, EUS enables a fine needle aspiration biopsy (22-gauge needles) for cytologic examination only, while LAPUS offers the possibility to obtain a core biopsy (tru-cut) with an 18-gauge needle, for histopathologic examination as well as aspiration of the fluid for cytologic examination. Since only 6 patients in this study underwent EUS, comparison is difficult at this stage. We currently believe that EUS and LAPUS are complementary studies, yet our results may suggest that LAPUS offers more comprehensive information in instances where the EUS results are inconclusive.

The presence of mucin, malignant cells and determination of neoplastic markers in the cystic fluid are useful in differentiating mucinous from serous cystic lesions whereas high pancreatic enzyme content usually suggests a pseudocyst. The markers commonly used are CEA, CA19.9, CA15.3, CA72.4, and tissue polypeptide antigen. The data obtained from our patients supports the high specificity of increased CEA and CA19.9 levels in mucinous cystadenomas and carcinomas. We, like others, have learned to consider raised CEA levels as more important than CA19.9 levels, which may be elevated in benign conditions. However, our 2 false-positive findings in patients with serous cystadenoma and simple cyst both had significantly increased levels of CA19.9 and one even elevated CEA levels. We have learned to consider the ultrasonographic characteristics of the cyst’s wall as an important parameter for differentiation. Thus, a uniformly thin and regular wall is suggestive of a benign nature while an irregular or focally thickened cystic wall or a cyst having a solid component indicates a malignant potential. These ultrasonographic parameters can be observed accurately by direct contact US examination. Moreover, biopsy and aspiration of the cyst is sometimes met with difficulty or is impossible because of proximity to major vessels. The LAPUS study enables these procedures since an “ultrasound window” is usually found, as happened in 2 of our patients where proximity to the mesenteric vessels and splenic vessels precluded CT-guided puncture. Histologic examination of cystic wall and cytologic examinations of cystic aspirate contributed to the decision not to operate in 3 patients (2 patients with pseudocysts and 1 with serous cystadenoma), while the other patient with serous cystadenoma underwent resection because of symptoms caused by the size of the cyst.

Decision regarding resection of a particular cyst is based on analysis of all obtained information. Indeed, the demonstration of malignancy, or mucinous cyst components, is a clear indication for resection, but in the absence of this information, decision is based on the ultrasonographic nature of the cystic wall and its histologic characteristics and the levels of tumor markers obtained from cystic aspirate. The presence of high amylase levels or a direct communication with the pancreatic ductal system indicate a benign cyst, only in the absence of elevated levels of tumor markers.

In conclusion, although a rather invasive procedure that requires general anesthesia and hospitalization, the LAPUS study was found to significantly contribute to the differential diagnosis of pancreatic cystic lesions.
REFERENCES


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chater and his coworkers have presented us with a small but intriguing prospective study of the value of LAPUS in assigning a specific diagnosis to lesions previously diagnosed by conventional imaging techniques as “pancreatic pseudocysts.” In their series, 6 of 15 patients were significantly impacted by the additional information provided by laparoscopic ultrasound.

This article directly addresses a currently vexing clinical problem—how to make a precise diagnosis of pancreatic pseudocysts. Despite modern imaging techniques, including CT scanning, magnetic resonance imaging, endoscopic retrograde cholangiopancreatography, and EUS, a definitive diagnosis of pseudocyst may not be possible. In fact, as many as 15% of “pancreatic pseudocysts” diagnosed by conventional imaging are actually cystic neoplasms. Moreover, when other lesions of the pancreas capable of successfully masquerading as “pseudocysts,” such as postnecrotic collections (necromas), cavitated tumors, and rare benign cysts are considered, the potential diagnostic error approaches 20%. It is possible, therefore, that each general surgeon over the course of a career could mistreat one of these lesions under the misdiagnosis of “pseudocyst,” if internal drainage were performed. The consequences of maltreatment range from disastrous in the case of a cystic malignancy to recurrence, depending on the precise lesion present.

The approach recommended by the authors (LAPUS, biopsy of the cyst wall, and tumor marker analysis of cystic fluid) is a further step, albeit expensive, in the definitive diagnosis of cystic pancreatic lesions, and one that could be applied by many clinicians today. It is conceivable that in the future LAPUS could act as an immediate precursor to definitive laparoscopic surgery, but only if a rapid, accurate, differential diagnostic test could be established. This work is a step in the right direction.

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