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Laparoscopic Ultrasound Enhances Standard Laparoscopy in the Staging of Pancreatic Cancer

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Objective

To define the role of laparoscopic ultrasound (LUS) in the staging of pancreatic tumors.

Summary Background Data

Laparoscopy has recently been established as a valuable tool in the staging of pancreatic cancer. It has been suggested that the addition of LUS to standard laparoscopy could improve the accuracy of this procedure.

Methods

A prospective evaluation of 90 patients with pancreatic tumors undergoing laparoscopy and LUS was performed over a 27-month period. LUS equipped with an articulated curved and linear array transducer (6 to 10 MHz) was used. All patients underwent rigorous laparoscopic examination. Clinical, surgical, and pathologic data were collected.

Results

The median age was 65 years (range 43 to 85 years). Sixty-four patients had tumors in the head, 19 in the body, and 3 in the tail of the pancreas. Four patients had ampullary tumors. LUS was able to image the primary tumor (98%), portal vein (97%), superior mesenteric vein (94%), hepatic artery (93%), and superior mesenteric artery (93%) in these patients. LUS was particularly helpful in determining venous involvement (42%) and arterial involvement (38%) by the tumor. This resulted in a change in surgical treatment for 13 (14%) of the 90 patients in whom standard laparoscopic examination was equivocal.

Conclusions

LUS is useful in evaluating the primary tumor and peripancreatic vascular anatomy. When standard laparoscopic findings are equivocal, LUS allowed accurate determination of resectability. Supplementing laparoscopy with LUS offers improved assessment and preoperative staging of pancreatic cancer.

An estimated 28,000 new cases of pancreatic cancer occur each year in the United States.[1] The incidence appears to be stable, with most occurring in the seventh or eighth decade of life. More than 28,000 deaths per year are caused by the disease, making it the fourth leading cause of cancer-related death, surpassed only by lung, colorectal, and breast cancers. The prognosis is bleak, with an overall 5-year survival rate of 2% to 3%. Surgical resection offers the only prospect of cure. However, symptomatology is often vague, and most patients have advanced disease, which precludes potentially curative therapy.[2,3]

Despite recent advances in pancreatic imaging and the development of nonsurgical techniques for relief of biliary obstruction, most patients still undergo an exploratory laparotomy for accurate staging and palliation.[4–6,7] Exploration does not offer any benefit and is associated with significant morbidity and mortality rates, affecting both the quality and duration of survival in patients who do not require palliative procedures.[7,8] With current techniques for endoscopic palliation, the need for laparotomy for palliative bypass is also questionable. The financial, emotional, and psychological implications of a surgical procedure that does not help are obvious but poorly documented.

The concept that laparoscopy can avoid unnecessary exploration in patients with pancreatic cancer is not new. However, its role in the management of pancreatic cancer is still being defined. Several centers have recently reported their success with laparoscopy as a modality in the preoperative and surgical staging of pancreatic cancer.[9–11] In a recent report from our institution, better instrumentation and

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techniques have shown that laparoscopy can achieve accurate surgical staging.[12]

Standard laparoscopy is a two-dimensional modality, with disadvantages being the lack of tactile sensation and the inability to identify small intrahepatic lesions or retropancreatic vascular involvement. Surgical ultrasound has the potential to overcome this deficiency, but its role has not been clearly defined. The aim of this study is to define the role of laparoscopic ultrasound (LUS) in the staging of pancreatic tumors.

MATERIALS AND METHODS

Between September 1993 and December 1995, 90 patients with peripancreatic malignancy were enrolled in a prospective, institutional review board-approved protocol to assess the efficacy of LUS examination. Before the laparoscopic examination, all patients underwent assessment with a complete medical history and physical examination, complete blood count, biochemical screening profile, chest x-ray, and a rapid-sequence, contrast-enhanced, thin-cut computed tomographic (CT) scan of the abdomen.

Patients were classified as having resectable, unresectable, or equivocal findings based on the CT assessment. Patients with hepatic or peritoneal metastases were considered to have unresectable disease. The presence of ascites or vascular encasement was a relative criterion for unresectability. Patients with CT evidence of unresectability who had only evidence of locally advanced disease were eligible for this protocol because they required laparoscopic staging before entering several treatment protocols.

All patients underwent laparoscopy and LUS. A multiport laparoscopic technique for staging, previously described by Conlon et al.,[12] was used in all cases. The following summarizes the steps in the laparoscopic assessment.

- Examination of peritoneal cavity
- Placement of laparoscopic trocars
- Instillation of 200 ml normal saline and aspiration of cytological specimens
- Assessment of primary tumor
- Examination of the liver and porta hepatis
- Division of gastro-hepatic omentum, examination of caudate lobe, vena cava, celiac axis, and lesser sac
- Identification of the ligament of Treitz, inspection of the mesocolon, duodenum, and jejunum
- Laparoscopic ultrasound

In brief, this procedure mimics the assessment of resectability performed at a standard open exploration. The peritoneal cavity was assessed, cytologic specimens from the right and left upper quadrants were taken, adhesions were divided if required, and the liver was examined using both a 5-mm and a 10-mm instrument. The hepatoduodenal ligament and the foramen of Winslow could be exposed by elevating the falciform ligament. The duodenum could be examined at this point, although mobilization of the duodenum was not performed. The patient was then placed into a slight Trendelenburg position, and the ligament of Trietz was exposed. When this was accomplished, the patient was put back into the supine position, and attention was turned to dividing the gastrohepatic omentum and exposing the celiac axis, the hepatic artery, and the superior surface of the pancreas. After completion of this examination, an assessment of resectability was made and recorded.

LUS using the Tetrad Surgical Ultrasound (Tetrad Corp., Englewood, CO) was then performed. This sophisticated prototype system allowed for simultaneous imaging and pulsed Doppler and color-flow Doppler for vascular assessment. The ultrasound probes used curved and linear array technology with a high-frequency performance and a range in the frequency of 6 to 10 MHz. This allowed images of high resolution to be obtained and detected lesions as small as 0.2 cm. A flat scanning surface facilitated acoustic coupling, which minimized tissue distortion. The following probes were used: an articulated 6-MHz probe, an articulated 10-MHz probe, a laparoscopic biopsy probe, and a rigid 7.5-MHz probe.

The LUS probe was inserted through a 10-mm or 12-mm laparoscopic port placed in either the right or left upper quadrant. In most patients, the right side was used because this facilitated scanning of the hepatoduodenal ligament. The following is the sequence of examination:

- Insertion of laparoscopic ultrasound
- Examination of liver - left lateral segment, right lobe
- Transverse scan of hepatoduodenal ligament
- Identification of superior mesenteric artery, portal vein and splenic vein
- Examination of pancreas
- Assessment of the tumor

The liver was examined using the articulated 6-MHz probe. The examination began with the probe placed transversely over the left lateral segment. Using Couinaud's description of the segmental anatomy of the liver as a guide, segments 1, 2, and 3 were examined in turn. The ultrasound was then placed over the dome of the right liver; the articulated probe facilitated this maneuver. The vena cava was identified at the back of the liver and followed forward to the porta hepatis. The hepatic veins were identified as they entered the vena cava. The liver was examined sequentially by moving and rotating the probe slowly over the surface of each of the hepatic segments. The portal vein (PV) was identified at the porta hepatis, with the probe placed on segment 4. The right PV and its anterior and posterior sectorial branches and associated bile ducts were followed to the periphery of the right hemiliver. The gallbladder and right kidney were examined, using the liver as an acoustic window with the ultrasound probe on segment 5. The hepatoduodenal ligament was examined with the transducer probe placed transversely across the ligament. The PV was identified superior to the vena cava. This was followed

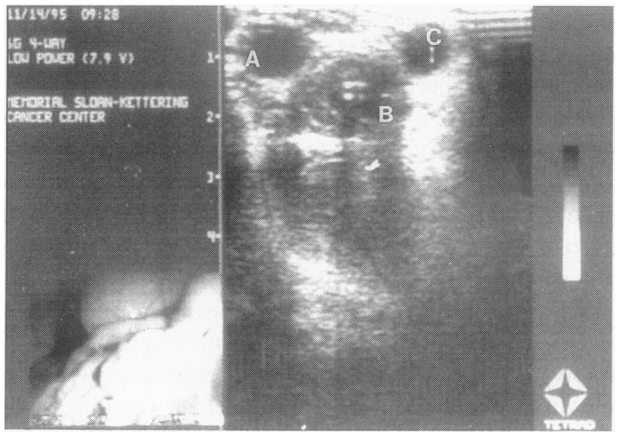

Figure 1. Transverse image of the hepatoduodenal ligament. The portal vein (A) and hepatic artery (C) can clearly be seen. A distended bile duct with a biliary stent is also visualized (B).

toward its junction with the splenic vein and superior mesenteric vein. The common hepatic duct, common bile duct, and hepatic arteries were identified during this part of the examination (Fig. 1). Identification of these structures was aided by the use of both pulse and color-flow Doppler.

When this portion of the examination was concluded, the superior mesenteric artery (SMA) and the confluence of the PV and superior mesenteric artery were examined. The was achieved by placing the transducer transversely on the gastrocolic omentum. The SMA was identified from its origin on the aorta and followed distally. In so doing, the confluence of the PV and the SMA was identified, and the relation, if any, of a tumor to this and the SMA was assessed (Fig. 2). The pancreas was then examined by placing the transducer through the window previously created in the gastrohepatic omentum and directly onto the surface of the gland. The tumor was identified and its relation to the pancreatic duct noted. In addition, gentle rotation of the probe allowed assessment of the celiac axis and proximal hepatic artery.

Biopsy samples were readily taken from intraparenchymal liver lesions or suspicious nodes with a Tru-Cut needle or biopsy forceps under sonographic guidance. In selected cases, particular attention was paid to the displacement or invasion of the regional vessels (celiac, hepatic, or superior mesenteric arteries or portal or superior mesenteric veins).

After LUS, findings were recorded and an assessment of resectability was made. Laparoscopic findings that made the tumor unresectable for cure were:

- Metastasis (hepatic, serosal, or peritoneal, or malignant ascites)
- Extrapancreatic extension of the tumor (mesocolic involvement)
- Evidence, proven by biopsy, of node involvement in the celiac or portal areas
- Invasion or encasement of the celiac axis or hepatic artery, or gross encasement by tumor of the portal or superior mesenteric veins or the SMA.

In all cases, unresectability was proven histologically at laparoscopy. For patients in whom vascular encasement was the only contraindication to resection, biopsy samples were taken from the site of encasement, either directly, after laparoscopic dissection, or by using the LUS biopsy probe. If unresectability was not proven histologically at laparoscopy, patients were considered to be resectable for the purposes of this study and underwent open exploration. In addition, patients with suggestive portal or mesenteric vein involvement were considered potentially resectable and therefore underwent exploration.

For patients with histologic proof of unresectability, no further procedures were performed and the procedure was terminated. Patients considered to have resectable disease after laparoscopy and LUS underwent open exploration with standard surgical techniques performed to assess resectability.[2] If there were no contraindications to resection, an appropriate surgical procedure was performed.

Demographic, clinical, radiologic, and surgical findings were obtained at the time of the procedure and collected in a prospective laparoscopic database. The laparoscopy and LUS findings were collated and a comparison was made using a 2 × 2 matrix analysis in which tumor resectability was correlated with the predicted resectability by the surgeon after laparoscopy and LUS.[13–15] The modalities were compared on their specificities, sensitivities, and positive and negative predictive values in determining the actual resectability of the tumors.

RESULTS

Between September 1993 and December 1995 at Memorial Sloan-Kettering Cancer Center, 90 patients with peripancreatic malignancy were entered into this study and evaluated by LUS. Forty-eight women and 42 men were

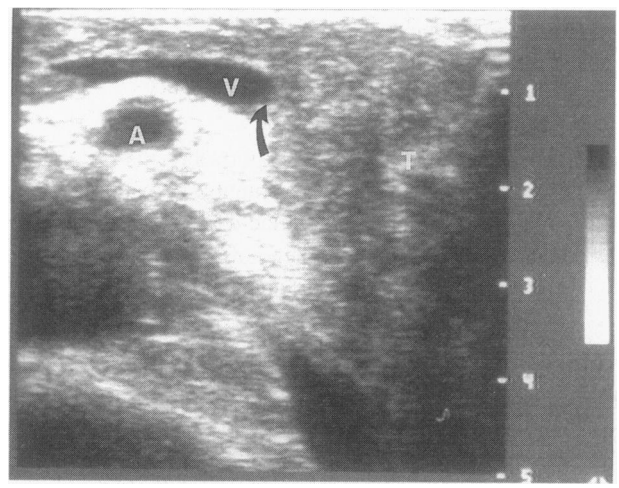

Figure 2. An uncinate tumor (T) is demonstrated involving the portal vein (V) at its junction with the splenic vein. The superior mesenteric artery (A) is also demonstrated with its characteristic halo of hyperechoic fat.

evaluated. The median age at presentation was 65 years (range 43 to 85 years).

Sixty-four patients (72%) had tumors in the head of the gland, 19 (21%) in the body, and 3 (3%) in the tail; 4 patients (4%) had ampullary tumors. Malignant disease was present in all 90 cases and was predominantly adenocarcinoma in histology. All patients underwent thin-slice contrast-enhanced CT scans of the upper abdomen and either a transabdominal ultrasound or endoscopic retrograde cholangiopancreatography to evaluate the bile duct or duodenum. This conventional imaging reported that 65 (72%) patients had resectable disease and 17 (19%) had unresectable disease; findings were equivocal in 8 (9%).

A complete laparoscopic examination was performed in all 90 patients. After laparoscopic examination, 36 (40%) patients were found to have resectable disease and 41 (46%) patients were found to have unresectable disease; 13 (14%) patients had equivocal findings. Disease was deemed unresectable because of the presence of hepatic metastases in 10 patients, vascular invasion or encasement in 15 patients, extrapancreatic or peritoneal involvement in 9 patients, and celiac or portal lymphatic metastases in 7 patients.

All 90 patients then underwent LUS evaluation. LUS was able to image the primary tumor in 88 (98%) patients, the PV in 87 (97%) patients, the superior mesenteric vein in 85 (94%) patients, and the hepatic and superior mesenteric artery in 84 (93%) patients each. Involvement of the portal, superior mesenteric, or splenic vein was imaged in 38 patients (see Fig. 2). Involvement of the hepatic, celiac, or superior mesenteric artery was imaged in 34 patients. The ultrasound confirmed resectability in the 36 patients whose disease was thought to be resectable by standard laparoscopy and also confirmed unresectability in the 41 patients thought to be unresectable by standard laparoscopy. LUS was most useful in determining resectability in the 13 patients with equivocal findings at laparoscopy, 12 of whom were considered to have vascular involvement and 1 possible nodal disease.

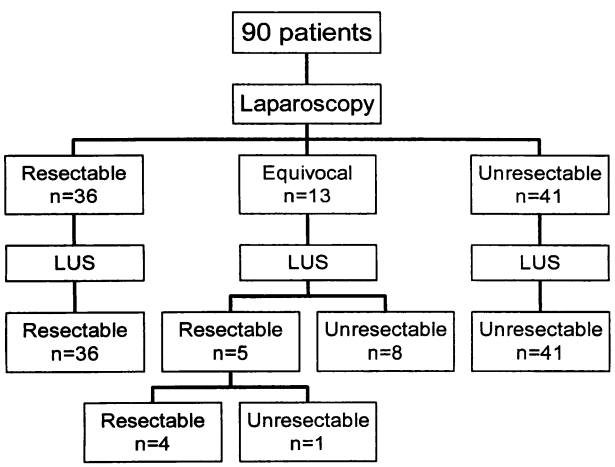

Figure 3. Flow chart of the algorithm-based analysis of the data collected in the 90 patients.

Table 1. LAPAROSCOPY/LUS

Assessment	Resected	Unresectable
Resectable	39	1
Unresectable	0	50

Sensitivity-100%, Specificity-98%; Accuracy-98%.

Figure 3 summarizes the design and results of this study in an algorithm-based analysis.

After LUS in the 13 equivocal cases, 8 patients were found to have unresectable disease. Three patients were noted to have extensive involvement of the PV and three encasement of the superior mesenteric vein or artery; one patient had encasement of the proximal celiac axis as well as a liver metastasis, and one patient with a large tumor of the neck of the gland was noted to have encasement of the hepatic artery and celiac axis. These findings were confirmed at open exploration in four of these patients through limited incisions, with two of the patients requiring biliary–enteric bypasses. The other four patients did not undergo open exploration, with unresectability confirmed by laparoscopic biopsy of the primary lesion or suspicious-appearing tissue at or near the area of identifiable vascular invasion or encasement. In two of the patients, there was common hepatic artery invasion, with frank invasion at the porta hepatis of the PV and the hepatic artery. The remaining two patients had biopsy samples taken of the primary tumor at the head of the pancreas after LUS revealed complete or near-complete obstruction of the splenic and SMV/PV confluence. All four of these patients had significant vascular invasion that was not fully appreciated by preoperative CT scanning; thus, the use of LUS avoided an unnecessary operation.

The other five equivocal cases evaluated with LUS were thought to have resectable disease. Of these patients, four truly had resectable disease and underwent resection. However, one patient at exploration was found to have unrecognized vascular involvement of the celiac axis and is reported as the only false-negative result in this study. The positive predictive index, negative predictive index, and accuracy of laparoscopy with the addition of LUS were 100%, 98%, and 98%, respectively (Table 1). There were no reportable complications specifically related to the use of LUS.

DISCUSSION

In the United States, pancreatic cancer remains one of the leading causes of cancer-related death, ranking fourth among all cancers in deaths per year, with an incidence that appears to be rising.[1] Complete removal of the tumor and the surrounding lymphatic tissue offers the only prospect for prolonged survival. Usually the resectability rates in pan-

creatic cancer are exceedingly low, and palliative procedures unfortunately have no impact on the bleak survival associated with unresected pancreatic cancer.[2,3,12]

Despite recent technologic advances in imaging techniques (*i.e.*, dynamic contrast-enhanced CT scanning), lesions of <1 cm can still evade detection. However, this advanced CT technique remains the diagnostic and staging modality of choice for these patients.[16,17] Fuhrman et al.[18] in 1994 reported on 42 patients with pancreatic malignancies in whom thin-section contrast-enhanced CT scans were used as the preoperative staging modality predicting resectability. A pancreatic resection was performed in 37 patients for a resectability rate of 88%. The other five patients had unrecognized locally advanced or metastatic disease identified at exploration, rendering them unresectable. This study reports the best resectability rates in the literature based on imaging alone. Other reports show similar results, but none with rates of resectability exceeding those in this study.

Although CT scanning has become a valuable tool in the staging of pancreatic malignancies, exact assessment of resectability and curability can be achieved only at laparotomy.[19] However, laparotomy in patients with unresectable disease has been associated with considerable mortality and morbidity rates, significant hospital stays, incisional pain, and delays in the initiation of other forms of treatment (*i.e.*, chemotherapy or radiation).[12] Therefore, a more precise means of staging these patients before surgery would have a significant and much-needed impact on management.

Minimal-access surgery has been proposed for the diagnosis, staging, palliation, and treatment of various malignancies. The concept that laparoscopy can prevent unnecessary exploration in patients with pancreatic malignancies is not new. Bernheim in 1911 at the Johns Hopkins University first reported the use of laparoscopy in the United States.[20] The procedure, which was performed on one of Halsted's patients with pancreatic cancer, allowed him to conclude that the technique might reveal general metastases or a secondary nodule in the liver, thus rendering further procedures unnecessary and saving the patient a prolonged convalescence. Our recent experience seems to support this hypothesis.

In 1996, Conlon et al.[12] reported on 115 patients with potentially resectable pancreatic tumors who underwent laparoscopy as part of their staging. After laparoscopic examination using a multiport technique, a correct assessment of resectability was made in 61 of 67 patients (91%). Disease was understaged at laparoscopy in six patients, five of whom had hepatic metastases not appreciated on CT scanning. The overall resectability rate in this series was 76%, a significant improvement over previously reported resectability rates at our institution. In a similar study, Warshaw et al.[9] reported on 40 patients considered to have localized disease who underwent laparoscopic examination as staging for pancreatic cancer. Laparoscopy resulted in a change of therapy in 14 patients, of whom 6 had hepatic, 7 had peritoneal, and 1 had omental metastases, obviating the need for exploration. Numerous other institutions have reported similar results as to the utility of laparoscopy as a tool in staging pancreatic malignancies.[9,11,21,22]

Although laparoscopy has enjoyed significant success as a new tool in the surgical oncologist's armamentarium, there still seem to be substantial limitations in the ability of the surgeon to assess the primary tumor directly. There have been reports of direct assessment of pancreatic tumors through the lesser sac, using both the supragastric and infragastric routes. However, assessment of the primary tumor with respect to its immediate environment (vascular structures, retroperitoneum) pushes the limits of the laparoscopic examination.[23,24] Further, the lack of tactile sensation limits the ability to assess smaller intraparenchymal lesions in the head of the pancreas, as well as previously undetected intraparenchymal metastatic lesions of the liver. With our experience using ultrasonography during liver surgery and in localizing pancreatic neuroendocrine tumors, the logical next step would be to introduce LUS.[4–6,25–27] This would enable direct visualization of the primary tumor and its association with the vasculature and peripancreatic lymphatic and soft tissue, as well as the identification of small hepatic metastases.

In this study, we examined the role of LUS in the staging of pancreatic malignancies in patients who were thought to have normal or equivocal CT scans with regard to resectability before surgery. This study differs from one previously reported from our institution in that the previous study evaluated patients thought to have clearly resectable disease on the preoperative CT scan.[12] LUS allowed us to identify the primary tumor and provided us with images of such high resolution that we could more accurately assess the peripancreatic soft tissue and vascular anatomy. It also partially replaced the need for tactile sensation by allowing visualization of tumors as small as 0.5 cm that were located intraparenchymally in the liver or the pancreas. These high-resolution images also allowed us to identify small but suspicious lymphadenopathy that could not be accurately assessed by conventional means (*i.e.*, CT scan, transabdominal ultrasound). Therefore, the use of LUS enabled us to predict resectability more reliably in these patients.

The addition of LUS did not improve resectability in patients thought to be either resectable or unresectable after the standard laparoscopic evaluation. However, when resectability could not be firmly appreciated by standard multiport laparoscopy, the addition of LUS proved to be extremely effective in predicting patients who ultimately underwent resection. Thus, the accuracy of predicting resectability in this study, when combining standard laparoscopy with LUS, was improved to approximately 98%, allowing us to clarify the surgical management in 13 (14%) of the patients. Hunerbein et al.[28] reported similar results, finding that in 40 patients with upper gastrointestinal malignancies, laparoscopy with the addition of LUS improved staging in 23 of the patients, ultimately sparing 16 patients

an unnecessary operation. Several other authors have also reported that the addition of LUS identified tumors and associated tissue, allowing improved accuracy in staging (predicting resectability or identifying distant metastatic spread).[14,21,29,30]

In summary, this study demonstrates that laparoscopy is a valuable tool in assessing the resectability of peripancreatic tumors, with a reported accuracy that exceeds that of conventional preoperative staging modalities. However, standard laparoscopy is only two-dimensional, with the absence of tactile sensation and the ability to identify small intraparenchymal lesions as its major disadvantages. LUS complements both dynamic contrast-enhanced CT and the laparoscopic evaluation by enabling the surgeon to overcome the two-dimensional limitations of standard laparoscopy. This allows a more reliable means of determining resectability in patients with equivocal standard laparoscopic examinations. We conclude that combining standard preoperative imaging with multiport laparoscopy and in equivocal cases LUS offers an accurate, safe, and cost-effective[12,31] means of staging peripancreatic malignancies.

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