The Value of Laparoscopic Staging in Upper Gastrointestinal Malignancy

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ABSTRACT

The goal of the clinical staging of malignant disease is to accurately define the extent of disease, direct appropriate therapy and avoid unnecessary intervention. Recent reports have suggested that laparoscopy can play a useful and complementary role in the staging of abdominal malignancy. This paper reviews the recent experience with laparoscopy in the staging of patients with upper gastrointestinal malignancy. The Oncologist 1997;2:10-17

INTRODUCTION

The goal of clinical staging is to accurately define the extent of disease, direct appropriate therapy, and avoid unnecessary intervention. Despite an increasingly sophisticated radiological diagnostic armamentarium, many patients with gastric, hepatic, or pancreatic malignancy continue to have the diagnosis of unresectable or metastatic disease made at exploratory laparotomy. For those who do not require a palliative procedure, exploration confers little benefit and may be associated with significant morbidity and mortality affecting both the quality and duration of their survival.

Recent reports have suggested that laparoscopy can play a complementary role in the staging of abdominal malignancy [1-10]. Laparoscopic examination can visualize the primary tumor, identify hepatic metastases, diagnose regional nodal metastases, and detect small-volume peritoneal disease unappreciated by other noninvasive staging modalities such as computerized tomography, magnetic resonance imaging, or ultrasonography.

Diagnostic laparoscopy is not a new modality. A Russian gynecologist, Dimitri Ott, is credited with the first recorded human laparoscopic examination in 1901. The term “laparoscothorakoskopie” was coined by H.C. Jacobaeus, who in 1911 reported the first clinical experience with this technique [11]. He noted that cirrhosis, malignancy, tuberculosis, and syphilis could be identified. The first recorded laparoscopic procedure in the United States was performed in 1911 by B.M. Bernheim of Johns Hopkins University on a patient with pancreatic cancer [12]. He felt that the technique “...may reveal general metastases or a secondary nodule in the liver, thus rendering further procedures unnecessary and saving the patient a rather prolonged convalescence.” Despite this early promise, poor optics and inadequate instrumentation confined the acceptance of the procedure to a few enthusiasts [13]. It was not until the development in the 1960s of the rod-lens system by Hopkins, and instrumentation for controlled pneumoperitoneum by Semm that laparoscopy began to be more widely practiced [13]. The subsequent development of videoendoscopy, better instrumentation, and the description of operative procedures such as laparoscopic cholecystectomy have accelerated the incorporation into general surgical practice.

The aim of this article is to review the recent experience with laparoscopy in the staging of patients with upper gastrointestinal malignancy.

Pancreatic Cancer

Patients with pancreatic cancer have much to gain from the addition of laparoscopy to the diagnostic armamentarium (Fig. 1). Most patients have unresectable disease at the time of presentation [14, 15]. However, due to the inability of the current preoperative diagnostic modalities to accurately assess the extent of disease, the majority still undergo surgical exploration for accurate staging or palliation [14-17].

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As the nonoperative management of biliary obstruction has improved in recent years, an exploratory laparotomy in most cases is unnecessary. In order to avoid such surgery, many centers now routinely perform laparoscopic examination prior to open exploration.

Seminal works by Cuschieri from Dundee, Scotland [3] and Warshaw from the Massachusetts General Hospital [4] demonstrated that small hepatic or peritoneal implants can be detected with considerable accuracy by standard laparoscopy. Warshaw’s group recently updated their experience in 114 patients with localized pancreatic cancer [18]. Metastases were identified in 27 patients (11 liver, 5 peritoneum/omentum, 11 multiple sites). None of these patients required open exploration. Forty-two patients were excluded from further surgery by angiography, and 40 came to open operation, 30 of whom were resected. Similar results were reported by John and colleagues, who demonstrated unsuspected metastatic spread in 12 cases, resulting in a specificity of only 50% in predicting tumor resectability.

In an attempt to improve the ability to determine resectability, John and colleagues also investigated the role of laparoscopic ultrasonography (LUS) [19]. LUS has the potential to partially overcome the lack of tactile sensation present in standard laparoscopy. Initially developed for the assessment of hepatic disease, it has recently been utilized in benign biliary disease [20]. John et al. were able to obtain satisfactory images of the primary tumor in 82% of cases. The LUS examination added information regarding tumor stage in 20 patients. This information changed the decision regarding resectability in 10 patients, resulting in an accuracy in predicting tumor resectability of 89%. Bemelman and coworkers also used LUS in combination with diagnostic laparoscopy for staging pancreatic head tumors [21]. Metastatic disease was demonstrated in 21 of 70 patients (30%). In those without metastatic disease, 21 of 22 patients considered to have resectable disease after LUS were resected, compared with 6 of 13 with “probably resectable” and 2 of 14 with “irresectable” disease. The sensitivity and specificity of LUS in determining resectability was 67% and 96%, respectively.

In contrast to the above studies, at Memorial Sloan-Kettering Cancer Center (MSKCC) we have utilized a multiprofessional technique to stage and assess resectability of peripancreatic malignancy [1]. In contrast to previous reports, this technique mimics the surgical assessment of resectability performed at open operation. Patients who, after radiologic examination (contrast-enhanced, dynamic CT of the abdomen), are considered to have resectable disease undergo laparoscopic staging prior to open exploration. All studies are performed under general anesthesia. An open technique for creation of the pneumoperitoneum is utilized in all cases. A 30-degree angled telescope is placed through the umbilical port. Trocars are placed in the right (10 mm, 5 mm) and left (5 mm) upper quadrants. A systematic examination of the peritoneal cavity is performed (Table 1). Suspicious peritoneal deposits, hepatic lesions (Fig. 2) or enlarged celiac, portal, or peripancreatic nodes (Fig. 3) are biopsied and sent for frozen section. Cytological washings are taken prior to any biopsy from the upper abdomen as part of a prospective evaluation of the prognostic importance of peritoneal cytological findings in pancreatic cancer. Unresectability is determined if one or more of the following are confirmed histologically: A) hepatic, serosal/peritoneal, or omental metastases; B) extrapancreatic extension of tumor (i.e., mesocolic involvement); C) celiac or portal nodal involvement by tumor, or D) invasion or encasement of the celiac axis, hepatic artery, or superior mesenteric artery. Patients who are found to have portal or mesenteric vein encroachment by tumor are considered potentially resectable and thus undergo exploratory laparotomy.

**Table 1. Sequence of the laparoscopic examination**

- 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 hepatitis
- Division of gastrohepatic 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

**Figure 1. Diagnostic algorithm for suspected peri-pancreatic cancer.** US: ultrasonography; CT: computerized tomography; MRI: magnetic resonance imaging; PTHC: percutaneous transhepatic cholangiography; ERCP: endoscopic retrograde cholangiopancreatography; Angio: angiogram; PET: positron emission tomography; EUS: endoscopic ultrasonographic.
Between December 1992 and December 1995, 243 patients with radiologically “resectable” peripancreatic tumors underwent multiport laparoscopy as described above. There were 114 male and 129 female patients. Mean age was 65 years (range 21-86 years). An antecedent history of abdominal surgery was obtained in 105 (43%) patients. In addition, a prior biliary drainage procedure had been performed in 86 patients (35%). A full laparoscopic staging procedure was successfully performed in 220 patients. Of these, 79 patients were noted to have unresectable disease. The reasons for unresectability are shown in Table 2. Unresectability was confirmed histologically in all cases. One hundred forty-one patients were considered to have resectable disease, and a resection was ultimately performed in 129 (91%) patients (Fig. 4). This resulted in a 100% positive predictive index, a 91% negative predictive index, and 95% accuracy for laparoscopic staging. Of the patients with unresectable disease, 64% had a laparoscopic procedure only. None of this group have required a subsequent open operation.

The combination of a contrast-enhanced, dynamic CT of the abdomen and laparoscopic staging has significantly reduced the percentage of patients with peripancreatic malignancy who undergo open exploration without resection at MSKCC (Fig. 5). It is important to note that this reflects

Table 2. Reasons for unresectability at laparoscopy (MSKCC results 12/92-12/95)

<table>
<thead>
<tr>
<th>Reason for unresectability</th>
<th>Number of patients</th>
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<tr>
<td>Liver metastases</td>
<td>36</td>
</tr>
<tr>
<td>Extrapancreatic disease</td>
<td>32</td>
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<tr>
<td>Nodal disease</td>
<td>17</td>
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<tr>
<td>Vascular invasion</td>
<td>32</td>
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Figure 2. Liver and peritoneal metastases demonstrated at laparoscopy in a case of pancreatic cancer.

Figure 3. Dissection of a suspicious mesenteric lymph node in a patient with adenocarcinoma of the pancreas.

Figure 4. Results of laparoscopic staging in patients with peri-pancreatic malignancy admitted to MSKCC between 12/92 and 12/95.

Figure 5. Effect of laparoscopic staging on the percentage of patients resected after open laparotomy. Of 243 patients in whom laparoscopy was attempted (12/93-12/95), 185 underwent open exploration. Explored/byp. = exploration with or without biliary or gastric bypass.
improved selection of patients rather than an increase in the resectability rate per se.

We have also had preliminary experience with LUS. Currently, we are using laparoscopic ultrasound probes which utilize curved and linear array technology, and have a high-frequency performance with a range in frequency of 6-10 MHz (Tetrad Corporation; Englewood, CO), allowing detection of lesions as small as 0.2 cm. In an initial study of 20 patients, LUS was felt to have given additional information in seven cases (Fig. 6), and to have altered the surgical approach in six patients [22]. Despite this early experience, the true assessment of the utility of this modality awaits further study.

At Memorial Hospital, we have found that the combination laparoscopy with state-of-the-art diagnostic modalities such as contrast-enhanced, dynamic CT scanning is an accurate, cost-effective, and safe means of staging peripancreatic malignancy which can avoid needless operations in some patients while not denying potentially curative surgery to those who would benefit.

**Hepatobiliary Cancer**

Recent reports have suggested that laparoscopy has much to offer in the staging of primary and secondary liver tumors [5-7, 23-25]. Despite a sophisticated diagnostic armamentarium which includes duplex ultrasonography, computerized tomography (contrast-enhanced, portography), magnetic resonance imaging, and selective visceral angiography, 40%-70% of hepatic tumors are found to be unresectable at the time of open exploration [26, 27].

Considerable controversy currently exists as to the criteria for resectability of liver tumors. In many centers, the presence of extrahepatic tumor spread, multifocal or bilobar disease, or the presence of significant cirrhosis constitute absolute contraindications for curative resection. In other centers, these factors are considered relative criteria. Thus, the impact of a staging modality such as laparoscopy is difficult to ascertain from the literature. Nonetheless, some insight on the efficacy of laparoscopy in diagnosing and staging hepatic tumors and avoiding unnecessary open exploration in those patients with advanced disease can be obtained from published data.

Brady and coworkers utilized laparoscopy to evaluate 25 patients with a clinical suspicion of either hepatic or peritoneal malignancy but normal computed tomography scans [28]. Twelve patients were found to have malignant disease (five liver, five peritoneal, two both) at laparoscopy. Of the remainder, seven had benign hepatic disease. The authors concluded that laparoscopic examination was the procedure of choice for evaluating this group of patients, allowing accurate differentiation between benign and malignant liver disease. Similar results were reported by Crantock et al., who performed diagnostic laparoscopy in 200 consecutive patients with liver disease [29]. Malignancy was documented in 25 patients (12.5%) and cirrhosis diagnosed in a further 72 cases. A targeted laparoscopic biopsy has also been suggested as an accurate means of diagnosing “early” hepatocellular carcinoma in high-risk cirrhotic patients [30, 31].

Lightdale demonstrated the efficacy of laparoscopic staging in an earlier publication from MSKCC [32]. Thirteen of 16 patients with primary hepatocellular carcinoma were found to be unresectable at laparoscopy due to multifocal or bilobar disease, extrahepatic metastases, or severe cirrhosis. Similar results were reported by Jeffers and colleagues, who studied 27 patients [33]. Unresectable disease was identified in all cases at laparoscopy by virtue of disseminated intrahepatic disease in 21, advanced cirrhosis in 23, and peritoneal metastases in two cases. Histological confirmation of disease was obtained in all cases at laparoscopy. More recently, Babineau et al. prospectively studied 29 patients with hepatic malignancy (12 primary, 17 metastatic) thought to be resectable by CT and ultrasonography criteria [6]. Laparoscopic examination was successfully performed in all patients despite a history of prior abdominal surgery in 19 patients (66%). Laparoscopy demonstrated “irresectability” in 14 patients (eight primary, six metastatic). Ten patients had unresectable or metastatic disease, and four hepatic cirrhosis. An additional four patients were noted to have unresectable disease at laparotomy not identified laparoscopically. The authors also reported that the hospital stay of patients undergoing a laparoscopic procedure alone was significantly shorter than for a group of historically matched controls undergoing open exploration alone (1.2 ± 0.5 versus 6.6 ± 1.6 days, p = 0.001).
John and associates studied the added impact of laparoscopic ultrasound in a cohort of 50 consecutive patients with “resectable” liver tumors [7]. Laparoscopy identified factors which precluded resection in 23 patients. Additional information regarding irresectability was obtained by LUS in 18 patients; in seven of these patients, this information led to a change in therapy. Fourteen patients considered to be resectable following laparoscopy and LUS underwent exploration, and 13 (93%) were resected with curative intent. Cuesta and coworkers evaluated a heterogenous group of 25 patients with hepatobiliary and pancreatic malignancy and reported that LUS provided additional information in 20 patients leading to an alteration in the surgical approach [34].

The combination of ultrasonography and laparoscopy has also been suggested for the diagnosis and staging of gallbladder cancer. Kriplani and associates studied 48 patients with both modalities [35]. The combination of ultrasonography and laparoscopy achieved a diagnostic accuracy of 100% in this study. Advanced disease was correctly identified laparoscopically in 40 patients, avoiding unnecessary exploration. In addition, laparoscopic examination correctly identified localized disease in five of six patients.

In an interesting application, Tung and colleagues from Barnes Hospital in St. Louis have used laparoscopy to detect hepatic metastases in patients with persistent/recurrent medullary thyroid cancer, thus avoiding unnecessary re-exploration of the neck [36]. They reported on a group of 37 patients with persistent hypercalcitoninemia following initial surgical therapy who were staged by computerized tomography and/or magnetic resonance imaging of the abdomen prior to laparoscopy. Laparoscopic staging demonstrated liver metastases in eight patients, seven of whom had normal radiological studies. These metastases appeared as multiple small (<5 mm), whitish nodules on the surface of the liver.

**Eosophageal/Gastric Cancer**

The ability of laparoscopic staging to prevent unnecessary exploration clearly defines its applicability in patients with pancreatic and hepatobiliary cancer. In esophageal and gastric cancers, the issue is less well-defined. Historically, the majority of patients with esophageal or gastric cancer have undergone some form of surgical resection or bypass regardless of the extent of the disease. However, as the multidisciplinary approach to these tumors develops and patients are offered choices between surgical extirpation, radiation therapy, investigational neoadjuvant chemotherapy, palliative chemotherapy and/or radiotherapy, or supportive palliative care alone, the need for accurate preoperative staging becomes evident.

The current staging modalities for esophageal cancer are listed in Table 3. Thoracoscopy is currently being evaluated as a staging modality for esophageal cancer, but as yet its usefulness has not been determined. A number of recent studies have attempted to define the role of laparoscopy in the staging of esophageal cancer, in particular defining the groups of patients which would obtain the most benefit from its utilization [9, 10, 37-44]. Molloy and colleagues prospectively evaluated 244 patients with cancer of the gastric cardia and esophagus [9]. Laparoscopy detected advanced local or metastatic disease in 92 patients (38%). Hepatic metastases were the predominant cause of unresectability in 75 patients. Laparotomy was performed in 118 patients, 85 of whom were resected. Laparoscopy failed to identify advanced local or metastatic disease in 22 patients. Overall, laparoscopy had a sensitivity of 96% in detecting hepatic metastases and 82% for assessing the feasibility of a subdiaphragmatic resection in this study. Dagnini et al. reported on 369 patients with esophageal (n = 280) and gastric cardia (n = 89) cancers who underwent laparoscopy [38]. Unresectable disease was found in 88 cases. In 52 patients, this was due to intra-abdominal metastases. The risk of having intra-abdominal metastases appeared to be related to the site of the primary tumor. In 28 patients with disease in the upper third of their esophagus, only one abdominal metastasis was found. However, for middle third, lower third, and cardia lesions, the figures were 8/96, 32/156, and 49/89, respectively, suggesting that the major benefit of laparoscopic staging may be for patients with lesions in the lower third of the esophagus or gastric cardia. In contrast, Bemelman and associates using laparoscopy and laparoscopic ultrasonography in a prospective study of 56 patients found that the benefit was confined to patients with tumors of the gastric cardia with distal esophageal involvement [10]. In this group, laparoscopy resulted in a change in stage in 41% of cases. Only 6% of patients with middle or lower esophageal tumors had their stage altered by the examination. Clearly, these studies demonstrate a role for laparoscopy in the staging algorithm; however, the true benefit remains to be defined.

A number of recent reports have also addressed the diagnostic value of laparoscopic staging in gastric cancer [39-45]. The ability of laparoscopy to detect small-volume hepatic and peritoneal disease was recognized by Possik et al., who reported a sensitivity of 87% for

<table>
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<th>Table 3. Diagnostic and staging modalities in esophageal cancer</th>
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<tr>
<td>• CXR</td>
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<tr>
<td>• Barium swallow</td>
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<tr>
<td>• CT chest/abdomen</td>
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<tr>
<td>• Bronchoscopy (upper and middle third lesions)</td>
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<td>• Bone scan (symptomatic patients)</td>
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<td>• Endoscopy and biopsy</td>
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<td>• Endoscopic ultrasonography</td>
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<td>• Laparoscopy</td>
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<td>• Thoracoscopy</td>
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the detection of hepatic metastases and 83% for peritoneal dissemination [39]. Gross and colleagues evaluated 46 consecutive patients with adenocarcinoma of the stomach [40]. Metastatic disease was identified in 27 cases (57%) at laparoscopy. A gastrectomy was ultimately performed on 16 of 18 patients (89%) considered resectable after laparoscopy. They concluded that laparoscopy can avoid unnecessary exploration and is effective in directing therapy. Similar results were noted by Kriplani and Kapur who reported a diagnostic accuracy of 92% for laparoscopic staging [41]. In their series of 40 patients, laparoscopy revealed metastases in five (13%) and locally advanced disease in 11 (28%) cases. Resectability was predicted in 87% of patients explored.

The impact of laparoscopic examination on staging was emphasized by Sendler and associates [42]. In a series of 111 patients, 23% were found to have carcinomatosis undetected by conventional staging modalities. Overall staging was altered in 47% of cases. Similarly, Ajani and colleagues reported on 39 patients with clinically staged, localized lesions who underwent laparoscopy. Of these, eight (21%) were found to have gross peritoneal disease and five (13%) had positive cytology for malignant disease [43].

We believe that laparoscopy is indicated for the majority of nonobstructed, nonbleeding patients with gastric cancer. The risk of disseminated disease is low for those with “early” (T1) tumors, and these patients should proceed to laparotomy. We have used a similar operative approach in this patient population to that described for patients with pancreatic cancer. Our preliminary experience in 92 patients appears to support the contention that laparoscopic examination can accurately identify intraperitoneal dissemination and avoid unnecessary exploration [46]. Metastatic disease unappreciated by conventional preoperative imaging modalities was noted in 31 patients in this cohort (Fig. 7). No patient to date with advanced disease who underwent a laparoscopic procedure alone has required a subsequent open operation.

We are also assessing the role of LUS as part of the staging procedure. Extrapolating from the endoscopic ultrasonographic (EUS) literature [47, 48], we feel that LUS may provide useful prognostic information. Gastric cancers staged as T3 or T4 by EUS are at significant risk for recurrence following curative resection. The identification of patients at high risk on the basis of sonographic evidence of serosal invasion may allow appropriate selection for neoadjuvant treatment. Our initial experience with LUS suggests that it may be particularly useful in the assessment of the primary tumor T stage [8]. Excellent images of the gastric wall and primary tumor can be obtained (Fig. 8). We are

Figure 7. Carcinomatosis identified in a case of gastric adenocarcinoma.

Figure 8. Laparoscopic ultrasound images (10 MHz probe) of the normal stomach (A) and stomach with a carcinoma (B). The layers (mucosa, muscularis propria, serosa) of the gastric wall can clearly be seen.
currently prospectively evaluating LUS in comparison with computerized tomography or EUS as a staging modality.

SUMMARY

Our experience at MSKCC suggests that laparoscopy has a role to play in the staging of patients with upper gastrointestinal malignancies. It appears to be a safe, effective, and cost-effective means of directing appropriate therapy and avoiding unnecessary exploration. Further experience is required to define the long-term risks of the procedure, particularly in relation to dissemination of disease (i.e., port site implantation). Also the role and value of LUS remain to be clarified. Prospective studies currently ongoing will help answer these questions.

REFERENCES


