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THE ROLE OF LAPAROSCOPY IN THE MANAGEMENT OF PANCREATIC CANCER

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1. ABSTRACT

Video laparoscopy has undergone significant advancements in the past several years. This technology can be applied to the management of patients with pancreatic carcinoma. Laparoscopy can be used to achieve the following goals when treating patients with pancreatic cancer: (1) to accurately stage the disease including diagnosis of intraperitoneal and extrapancreatic disease, (2) to evaluate resectability, (3) in resectional therapy and, (4) in palliation of unresectable disease. This chapter reviews in detail these four applications of the laparoscopic surgical approach in the management of patients with pancreatic carcinoma.

2. INTRODUCTION

Pancreatic carcinoma is a devastating disease that accounts for 28,000 deaths per year in the United States. Less than 3% of patients diagnosed are alive after five years (1). Surgical resection continues to be associated with the highest probability of long-term survival. Unfortunately, only 10-20% of patients are candidates for surgical resection. Therefore, accurate staging of disease is very important to select the appropriate patient group for surgical treatment while preventing the morbidity of unnecessary laparotomy. Although there has been considerable advances in radiographic and endoscopic imaging in recent years, there are still limitations in these technologies with regards to staging.

Since the majority of patients are not candidates for surgical resection, a significant proportion of treatment strategy is aimed at palliation of complications from this disease. Three main symptoms are commonly associated with pancreatic cancer. These include biliary obstruction, duodenal obstruction, and pain. Again, these symptoms have been traditionally approached by open surgical procedures. Since these patients have a very limited life expectancy, emphasis has been placed on efficacious, yet less invasive procedures to achieve palliation. A variety of procedures and approaches continue to develop for these patients.

Laparoscopic surgery has undergone a significant improvement and its role in the management of patients with pancreatic cancer continues to evolve. The advantage of the laparoscopic approach is its versatility. Laparoscopy can be applied as a diagnostic tool for accurate diagnosis and staging. Also, laparoscopy can be to provide palliation of symptoms or possibly even treatment of disease. The main benefit of laparoscopic surgery is its effectiveness while minimizing perioperative morbidity.

3. THE ROLE OF LAPAROSCOPY

3.1. Staging for metastatic disease

Current radiographic techniques using high-resolution helical CT scans are reliable used in evaluating the local extent of disease as well as in visualizing metastatic lesions. However, a significant number of patients may have peritoneal metastases and/or superficial liver metastases which can not be visualized by current imaging techniques. These metastases are commonly 1-2 mm. in diameter and thus cannot be demonstrated radiographically (2).

Peritoneal metastases have been identified in greater than 50% of patients with pancreatic cancer at the time of autopsy. This is the second most common pattern of metastases after liver metastases (3). Laparoscopic detection of peritoneal metastases has been described since 1911 and has been reported in a number of clinical series (4). The incidence in these studies ranges from 24-73% (3, 5-8). Recent reports in the age of high-resolution helical CT scanning and better radiographic identification of metastatic disease, state an incidence of occult peritoneal metastases in the 20-30% of patients (9-11).

Our current approach is to routinely perform staging laparoscopy prior to surgical exploration with the intent to resect the pancreatic carcinoma. The patient is prepared and draped in the standard fashion for laparotomy. A 10 mm laparoscopic port is inserted into the abdomen. The abdominal cavity is then insufflated with carbon dioxide to a pressure of 15 mmHg. A 10 mm. or 5

mm. video laparoscope is inserted into the abdomen. I personally routinely use an angled 30^0 or 45^0 laparoscope, which improves visualization in poorly visible areas of the abdomen. The peritoneal surfaces are then examined in a systematic fashion. Both hemidiaphragms, liver surfaces, abdominal wall, pelvis, and intestinal surfaces are examined. Occasionally, the lesser sac is examined by opening the gastro-colic omentum by using the laparoscopic coagulating shears (LCS, Ethicon Endosurgery Inc., Cincinnati, Ohio). The LCS is available in 5mm and 10mm models. Pancreatoscopy can then be performed with examination of the pancreas and the posterior gastric surfaces.

Two maneuvers are currently controversially used in staging laparoscopy. First, is the Kocher maneuver, which involves mobilization of the 2nd portion of the duodenum to inspect the peri-pancreatic nodal bed as well as the posterior surface of the pancreatic head. Prescence of peri-pancreatic/portal node involvement or tumor extension to the posterior surface of the pancreas, are not contra-indications for resection. Therefore, examination of these areas has a very limited role. Second, is the role of peritoneal cytology. Warshaw and others have published several articles reviewing the use of peritoneal cytology (3,12) in the staging of pancreatic cancer. From a technical aspect, the upper abdomen is irrigated with 250-500 cc. of normal saline. The fluid is aspirated and sent for cytological examination. The fluid is centrifuged and the cell pellet is examined. Patients without visible peritoneal metastases have a positive cytology in 20% of the cases. Interestingly, patients who have undergone percutaneous pancreatic biopsy have a positive cytology in 70% of cases. Warshaw reports a significant decrease in survival in patients with positive cytology and suggests that these patients do not benefit from surgical resection (3). These results should be viewed with caution. We perform peritoneal cytologic evaluation but do not consider a positive cytology as a contra-indication to resection. Cytologic examination may be used as a prognostic indicator. However, further studies are needed to determine its value in patient management.

Currently, staging laparoscopy is of benefit prior to surgical exploration with the intent to resect the tumor since about 20% of patients with peritoneal metastases will be spared from the morbidity of laparotomy. Patients with locally advanced disease will undergo neoadjuvant treatment with paclitaxel and external beam radiation according to the Brown University Oncology Group protocol. It is imperative that any patient entering a clinical trial with neoadjuvant treatment, with the later intention to resect the tumor, has the most accurate pre-treatment staging of their disease. Therefore, these patients undergo staging laparoscopy with peritoneal cytologic evaluation prior to the neoadjuvant treatment (13).

3.2. Assessment of resectability

Laparoscopy, in particular in conjunction with laparoscopic ultrasound, can be used to assess the resectability of pancreatic tumor. This role for laparoscopy has been reviewed in a number of series in the early 1990's (14-17). Results have been mixed due to the non-uniformity of the procedures carried out. With current generation of high resolution CT scanners, MRI, and endoscopic ultrasound, the role of laparoscopy for assessing resectability is becoming more limited (18,19).

The exploration is carried out in a similar fashion as described in section 3.1. of this chapter. When metastatic disease has been rule out, assessment of resectability is then commenced. The areas to be assessed are the superior mesenteric vein (SMV) and portal vein, as well as the celiac lymph nodes. The simplest way to perform this is to retract the stomach inferiorly. A linear laparoscopic ultrasound probe is then inserted into the abdomen. Ideally, the ultrasound device should have Doppler and color flow monitoring to help distinguish vascular structures. The probe is passed under the left lateral segments of the liver and over the gastro-hepatic ligament (lesser omentum). By ultrasound, the aorta and celiac axis are identified. Suspicious lymph nodes in the area can then be biopsied. Positive celiac or para-aortic nodes are generally considered to denote unresectability (20).

Invasion of the portal vein is then evaluated. This can be performed in two ways. First, is to perform the ultrasound, examining the pancreas trans-gastrically. The probe is past over the anterior gastric surface until the neck of the pancreas is identified. Careful investigation is then carried out to determine if the portal vein is invaded with tumor. A slightly more accurate method is directly examining the pancreas by ultrasound. The gastro-colic omentum is divided, as previously described, utilizing the laparoscopic coagulated shears (LCS). The lesser sac is opened and the anterior surface of the pancreas is visualized. The ultrasound probe is passed posterior to the stomach and directly onto the pancreas (21). The probe is then passed over the tumor to determine the extent of disease, as well as to determine presence of invasion of the SMV/portal vein. Direct tumor extension into the lumen of the portal vein is a sign of unresectability. Often the tumor may extend to the SMV/portal vein. The desmoplastic reaction may be difficult to distinguish from tumor. Doppler and color flow monitoring as well as using a high frequency (10mHz) probe can be helpful to determine portal vein invasion versus juxtaposition (22).

Recent advancements in other imaging modalities are decreasing the need for laparoscopic assessment of resectability. The late generation of high resolution helical CT scanning can accurately assess celiac lymphadenopathy and SMV/portal vein invasion(23). Additionally, when this imaging technique is equivocal in determining resectability, endoscopic ultrasound can be used (24). Early version ultrasound probes had a 360^0 radial field of view (25). Now, linear array endoscopic ultrasound probes are more versatile for assessing resectability (26). Suspicious celiac lymph nodes can be biopsied using a linear probe. Additionally, linear endoscopic ultrasound probes have the advantage of Doppler and color flow monitoring to further assist in the determination of vessel invasion. Given these current imaging techniques, the role of laparoscopy and laparoscopic ultrasound to determine resectability is diminishing in institutions where these imaging modalities are available (10,27). Where high resolution helical CT and endoscopic ultrasound are not utilized, laparoscopy with ultrasound remains the most accurate means of staging pancreatic malignancies (11,14,15,28).

3.3. Laparoscopic resection

Laparoscopic approaches to various surgical procedures such as cholecystectomy and hernia repair are

commonplace. As experience with laparoscopic surgery has grown, attempts at various abdominal procedures have been carried out. Laparoscopic resection for pancreatic tumors is a developing field (29-31). Gagner and Pomp reported the first successful pancreaticoduodenectomy in 1994 (32). The procedure can be performed completely laparoscopically or by hand-assisted via a Pneumo-Sleeve (Pilling-Weck, North Carolina) device in which a small incision is made so that a hand can be inserted within the abdomen and pneumoperitoneum is maintained. Hand-assisted resections are technically significantly easier and faster to perform. Additionally, an incision needs to be made for eventual specimen removal. Certainly adequacy of resection, tumor spillage, and morbidity are significant concerns in laparoscopic pancreaticoduodenectomy. However, further experience with this approach is needed before meaningful conclusions can be made. Nonetheless, laparoscopic pancreatic resections are technically demanding and should only be performed by surgeons with extensive experience in laparoscopic procedures and open pancreatic resections, in very carefully selected patients.

3.4. Laparoscopic palliation

The overall resectability rate of pancreatic cancer remains low at approximately 15%. Therefore, the majority of therapy carried out for patients with pancreatic cancer remains to be palliation of complication. Three main complications include biliary obstruction, duodenal obstruction, and pain. These complications can be treated by radiographic, endoscopic, open surgical, and laparoscopic surgical approaches (33).

Jaundice secondary to biliary obstruction occurs in 65-95% of patients with cancer of the head of the pancreas. Patients with biliary obstruction who are not candidates for resection can be palliated most commonly by an endoscopically placed endobiliary stent. Radiographically placed percutaneous external, internal-external, and internal wall stents can be also placed. Surgical biliary bypass has been the main treatment options for years. A variety of surgical options to relieve biliary obstruction include choledocoduodenostomy, cholecystojejunostomy, and Roux-en-Y choledocojejunostomy. However, with recent developments in less invasive treatment modalities has made them more popular.

The laparoscopic approach can be used to create a durable biliary bypass that is less invasive than an open surgical procedure. The most commonly used laparoscopic bypass is the cholecystojejunostomy (34-36). Although Roux-en-Y choledocojejunostomy and choledocoduodenostomy are technically feasible, they require more advanced laparoscopic skills. To ensure successful cholecystojejunostomy, one must determine the patency of the cystic duct as well as the primary tumor being located at least 2-3 cm. from the cystic-common hepatic duct junction (37). A laparoscopic cholecystojejunostomy is performed in the following fashion. The first jejunal limb in identified at the ligament of Treitz. The jejunum is then run to a point where it can reach the gallbladder easily and without tension. The gallbladder and jejunum are then aligned in a side-to-side fashion. The lumens of the jejunum and gallbladder are entered with electrocautery or the harmonic scalpel. An endoscopic linear stapling device (Ethicon Endosurgery Inc., Cincinnati, Ohio) is fired with each arm in a lumen to create the anastomosis. The enterotomy is then closed using an intracorporeal suture of running 2-0 silk. Cholecystojejunostomies are associated with an 89% success rate and a 20% incidence of recurrent jaundice or cholangitis (33).

Duodenal obstruction occurs in 20-30% of patients with pancreatic cancer. The treatment for this complication, traditionally, has been surgical gastrojejunostomy. In recent years, development of an endoscopically placed duodenal wall stent has shown promise, however surgical bypass remains the treatment of choice (38). Once again palliation for duodenal obstruction can be achieved by laparoscopic gastrojejunostomy (34, 36, 39). Several configurations for gastrojejunostomy include ante- and retro-colic as well as ante and retro-gastric. Performance of an ante-colic retro-gastric gastrojejunostomy is described. The gastro-colic omentum is divided with the LCS. This exposes the lesser sac and the posterior gastric wall. The first limb of jejunum is identified at the ligament of Treitz. The jejunum is followed distally until is reaches the posterior gastric wall easily and without tension. A gastrotomy is made in the posterior gastric wall and a second enterotomy is made into the antimesenteric border of the jejunum. An endoscopic linear stapler is inserted into each lumen and deployed to create the gastrojejunostomy. Two or even three deployments of the stapler may be required to create the appropriate sized anastomosis. The enterotomy can then be closed using intracorporeal suturing and knot tying techniques with a running 2-0 silk suture. This procedure is not technically difficult and can be performed in an expedient fashion. Surgical outcomes following surgical gastrojejunostomy are generally favorable with the main morbidity being that of delayed gastric emptying. Early delayed gastric emptying ranges from 9-17% and late delayed gastric emptying at 2-6%. These rates of delayed gastric emptying are related to the type of gastrojejunostomy performed (40).

Another challenge for the practitioner is treating pain. Again, a variety of approaches can be carried out to control pain via chemical splanchnicectomy. Ablation of the celiac nerve plexus can be achieved by injecting 25cc of 50% alcohol to either side of the celiac axis. Again, this can be achieved by CT-guided percutaneous injections, endoscopic trans-gastric injections under linear endoscopic visualization, open surgical techniques, as well as laparoscopic techniques. The laparoscopic approach requires the use of laparoscopic ultrasonography. The ultrasound probe is placed over the lesser omentum and the celiac axis and aorta are identified by ultrasound. A long 22 gauge spinal needle is passed through the abdominal wall and under laparoscopic and ultrasonographic visualization, 25 cc. of 50% alcohol is deposited on either side of the celiac axis. Chemical splanchnicectomy has been shown in prospective randomized trials to reduce pain scores as well as to delay or lower the intensity of the onset of pain. A small subset of patients with significant pre-operative pain were also noted to have an improved mean survival when compared to placebo-treated patients (41).

4. PERSPECTIVE

Laparoscopic surgical techniques continue to play a major role in the evolving management of patients with

pancreatic carcinoma. Laparoscopy remains the best tool in the diagnosis of peritoneal metastases. This procedure is used prior to laparotomy, or in patients who undergo a neoadjuvant treatment protocol. Peritoneal cytologic evaluation is controversial in terms of its prognostic value and may not necessarily preclude surgical resection but may guide the adjuvant treatment. Resectability of pancreatic tumors is most easily predicted via current, high-resolution CT scanning and linear endoscopic ultrasonography. Laparoscopic ultrasound currently adds little when these other modalities of imaging are employed. Resection of pancreatic tumors and pancreaticoduodenectomy are technically possible, and may be carried out in highly selected patients by very experienced laparoscopic surgeons. Finally, palliation of jaundice, duodenal obstruction, and pain can be achieved via a number of means i.e. radiographic, endoscopic, open surgical, and laparoscopic means. Treatments should be based on the expertise available at a particular institution and individualization of the care of each patient with pancreatic cancer.

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