The treatment of patients with pancreatic cancer requires the expertise of medical oncologists, radiation oncologists, radiologists, and surgical oncologists. The surgeon's role

**Introduction**

The surgeon should be an integral part of the decision-making process regarding the patient with pancreatic cancer, whether it be suspected or known, and resectable, unresectable, or recurrent. The determination of resectability, the need for palliative intervention, and the likelihood of its success are a fundamental part of an oncology surgeon's training.

**Diagnosis**

**Perspectives on Neoadjuvant Therapy**

A survival benefit afforded by postoperative (adjuvant) chemoradiation in patients with pancreatic cancer has been established [11-13]. The many theoretical advantages of preoperative (neoadjuvant) chemoradiation sequencing have not resulted in longer median survival than has been achieved with postoperative therapy [28-33]. Phase III testing of this concept is required before conclusions can be made about its efficacy. Neoadjuvant therapy may provide advantages relative to local control, but enough experience has accumulated to conclude that a large majority of patients with resected pancreatic cancers will still die of metastatic cancer [31]. Although surgeons should continue to seek further improvements in patient safety during and following operations, they should also support and participate in the quest for the two major components that will eventually control this disease: optimal screening tests and an effective drug or drug combination.

**Histologic Study of Resected Specimens**

Toward the latter goal, we have studied our archival material and found that tumor cell dropout with replacement by fibrosis is the most identifiable and consistent histologic effect of chemoradiation on adenocarcinomas of the pancreas [29]. We suggest that the examination of resected specimens for this effect after treatment with various new chemotherapy and radiation therapy regimens will more readily identify increased antitumor activity than will standard methods of local control and survival analysis. Patients with most stages of pancreatic cancer are elderly and weakened and may succumb to non-cancer-related illnesses despite tumor responses or even control of their cancers. For instance, 4 of 27 patients who underwent resection after chemoradiation at Fox Chase Cancer Center have died without evidence of cancer recurrence.

We propose that histologic response identification should supplement, not supplant, traditional efficacy analysis. We are just beginning a phase I trial of gemcitabine (Gemzar) with preoperative radiation therapy and as maintenance postoperative therapy for patients with localized pancreatic cancer. Once a safe dose of the drug in combination with pancreatic radiation therapy is found, a phase II trial of the regimen will be performed. The histologic responses will be compared with our archival material of patients treated with mitomycin (Mutamycin) and fluorouracil. Since the variation in estimating the degree of fibrosis between pathologists is minimal, this method can be used to compare chemotherapy regimens.

**Summary**

The surgeon is an indispensable member of the health-care team, involved in all facets of the care of the patient with pancreatic cancer. Histologic analysis of treatment effects in resected pancreatic specimens may lead to improved multimodality therapy for this disease.
Diagnosis should be and often is made after exploratory celiotomy or even pancreatic resection in many patients with resectable pancreatic cancer. Unfortunately, these patients constitute less than half of those first reaching medical attention [1,2]. The only reasons to obtain tissue for diagnosis are to avoid surgery or to enroll the patient in a preoperative adjuvant treatment program. If one could be sure of a benign diagnosis, such as bile duct obstruction by a gallstone or pancreatitis, the treatment approach would differ from that of a presumed malignancy. If tissue can be obtained by direct biopsy or brushing at endoscopic retrograde cholangiopancreatography (ERCP), it can help differentiate benign from malignant causes. It can also allow for the detection of rarer, more curable pancreatic malignancies such as lymphoma, which may be cured without surgery, and islet-cell tumors, which usually can be cured with surgery alone [3,4].

**Fine-Needle Aspiration**

Preoperative treatment with radiation therapy and chemotherapy requires the diagnosis of malignancy. Only 10% of those with resectable pancreatic cancer have tissue available to the endoscopist for direct biopsy or for brushing within the bile or pancreatic duct. Thus, fine-needle aspiration (FNA) with guidance by CT scan, ultrasound, or fluoroscopy is needed for the majority of patients to be treated by preoperative therapy.

Opinion about the utility of FNA for the diagnosis of pancreatic malignancy remains divided in the surgical literature. Proponents of this technique cite its reasonable sensitivity (~80%), the utility of a tissue diagnosis in directing further treatment, and the ability to avoid diagnostic surgery in many cases. Opponents cite its variable sensitivity (45% to 100%) [5], high cost (~$2,000), the possibility of seeding cancer cells in the peritoneum [6], and the inability to avoid operation in the patient with a negative result. Graham et al have shown that the sensitivity of FNA decreases in smaller lesions [7].

Over the past 10 years, more than 100 FNA biopsies of the pancreas have been performed at our institution. Several patients had an initial attempt that was nondiagnostic, whereas a second attempt yielded a diagnosis. Overall, very few complications were encountered. We reviewed our last 41 patients who underwent pancreatic resection with intent to cure. Nine patients had open biopsies outside our institution. Of the remaining 32 patients, 19 had FNA biopsies of their pancreatic mass. The majority of these biopsies were needed to enroll patients in a preoperative chemotherapy trial. Fine-needle aspiration was diagnostic in 15 (80%) of 19 patients. The performance of FNA was not found to correlate with positive peritoneal cytology, peritoneal relapse of disease, or survival. These data corroborate the findings of a study by Leach et al [8]. We believe that FNA biopsy is safe and useful, especially in patients who are to be entered into preoperative chemotherapy trials or who are candidates for nonoperative palliation.

**Treatment of Resectable Lesions**

At present, there are very few controversies over whether to use surgery to treat resectable pancreatic cancer. Although one can continue to argue for therapeutic nihilism and disregard advances made in the last decade in the adjuvant therapy of pancreatic cancer, most authorities agree that resection with tumor-free margins and treatment with adjuvant chemoradiation offer more hope than any nonsurgical treatment [9-13].

Debates regarding the amount of pancreas (partial vs total pancreatectomy) and surrounding tissue (pylorus-sparing vs standard vs extended or regional pancreatectomy) to be removed continue at subdued levels, and the various surgical approaches probably never will be compared in prospective, randomized fashion. Insufficient data exist to enable us to determine whether the use of adjuvant chemoradiation permits wider or even lesser excisions. Nevertheless, it is clear that positive pathologic margins are a major adverse prognostic factor that cannot be overcome by adjuvant chemoradiation [14]. Thus, the surgeon should attempt to achieve clear pathologic margins. If this is known to be impossible prior to the "point of no return" in the procedure, resection should be abandoned in favor of bypass operations.

**Treatment of Unresectable Lesions**

Patients with unresectable lesions require coordinated, multidisciplinary treatment to palliate their biliary obstruction, potential duodenal obstruction, and pain. Although median survival in this group of patients is less than 1 year, palliative measures can optimize the quality of their remaining life.

**Surgical Bypass vs Nonsurgical Approaches**

In the past, surgical biliary-enteric and gastroenteric bypass have been the standard of care. With the development of large-channel endoscopes and larger and better biliary stents, however, other
therapeutic options besides surgery have become available. If symptoms of duodenal obstruction are present and the patient can tolerate surgery, operative double bypass should be performed. There is some evidence to suggest that traditional gastrojejunostomy does not effectively palliate symptoms of nausea and vomiting [15]. Lucas et al have shown that better relief of symptoms can be achieved with antrectomy plus gastroenterostomy [16]. If the patient cannot tolerate surgery, percutaneous endoscopic gastrostomy should be considered, along with a biliary endoprosthesis. In patients with no symptoms of nausea or vomiting, the optimal palliative approach is less clear. Studies comparing endoscopic stents and surgical bypass have shown no difference in 30-day mortality or overall survival [17-19]. Stents are, however, prone to occlusion. Even the Wallstent (Schneider AG, Bülach, Switzerland), composed of a wire mesh and expandable to 10 mm, is subject to tumor ingrowth and occlusion. This has led one group to suggest that patients expected to live longer than 6 months are better served by surgical biliary-enteric bypass [17]. Among patients in whom endoscopic or percutaneous biliary stents are placed, two large surgical series have shown that 13% to 16% will develop duodenal obstruction [20,21]. This fact must be kept in mind if a nonsurgical approach is elected.

Laparoscopic Procedures
Laparoscopic procedures to palliate pancreatic cancer are now a reality [22,23]. The development of endoscopic staplers and the technique of intracorporeal suturing have made cholecysto-jejunostomy and gastrojejunostomy possible. Enthusiasm for these techniques must be tempered by sound judgment. Before a biliary obstruction is bypassed with the gallbladder, cystic duct patency must be assured. If antrectomy is necessary for effective palliation of nausea and vomiting, this technique will have to be developed through the laparoscope. Any procedure that promises less morbidity and faster return to full function is appealing.

Pain Relief
Pain has a major impact on the quality of life of the patient with pancreatic cancer. Some patients experience pain relief with stenting or bypass alone. In others, radiation therapy can reduce pain symptoms [21,24]. The preferred method of pain relief has become direct or percutaneous injection of the celiac plexus with 50% ethanol or 6% phenol. Not only has this technique been shown to provide excellent palliation of pain symptoms, but one study demonstrated longer survival in patients who underwent this procedure [25-27]. Palliative therapy for patients with unresectable pancreatic cancer is complex, and specific therapies must be directed toward individual needs. The algorithm shown in Figure 1 should help physicians advise patients on their treatment options.

References:


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