

Preoperative staging of cancer of the pancreatic head: Is there room for improvement?

Kristopher P. Croome, MD, MS
Shiva Jayaraman, MD
Christopher M. Schlachta, MD CM

From the Department of Surgery, London Health Sciences Centre and Schulich School of Medicine and Dentistry, London, Ont.

Accepted for publication
Mar. 16, 2009

Correspondence to:
Dr. C.M. Schlachta
Canadian Surgical Technologies & Advanced Robotics
London Health Sciences Centre
University Hospital
339 Windermere Rd.
London ON N6A 5A5
fax 519 663-3481
christopher.schlachta@lhsc.on.ca

Background: Despite advances in preoperative staging, cancer of the pancreatic head is frequently found to be unresectable at laparotomy. We sought to identify potential areas of improvement in preoperative staging.

Methods: We performed a retrospective institutional review of patients referred for resection of cancer of the pancreatic head over a 2-year period. The primary outcome was the rate of metastasis or unresectable disease found at laparotomy in patients who were booked for pancreaticoduodenectomy with curative intent.

Results: During the study period, 133 patients were referred with suspected cancer of the pancreatic head. All underwent preoperative computed tomography scanning. Twenty-four also underwent preoperative endoscopic ultrasonography (EUS) and 23 also underwent magnetic resonance imaging (MRI). In total, 78 patients were deemed not to be candidates for surgery, leaving 55 patients with potentially resectable cancer who were scheduled for pancreaticoduodenectomy. Of these, 32 patients (58%) underwent successful resection with curative intent, and 23 patients (42%) were found to have metastatic or locally advanced disease not identified by preoperative staging. Reasons for nonresectability were metastases (9 patients, 16%), vascular involvement (12 patients, 22%) and mesentery involvement (2 patients, 4%). One patient had a diagnostic laparoscopy immediately before planned open exploration and was found to have peritoneal seeding precluding curative resection. Of the patients who underwent EUS, 14 were not surgical candidates because of locally advanced tumours. Ten patients were offered surgery with curative intent, and 5 patients (50%) were found to have unresectable tumours (4 metastatic, 1 locally advanced). Of the patients who underwent MRI, 11 were offered surgery, and 5 (45%) had unresectable tumours (2 metastatic, 3 locally advanced disease).

Conclusion: In our institution, preoperative staging for cancer of the pancreatic head misses a substantial number of metastatic and unresectable disease. There is clearly room for improvement, and newer technologies should be evaluated to enhance the detection of metastatic and locally advanced disease to prevent unnecessary laparotomy.

Contexte : En dépit des progrès réalisés dans la détermination du stade du cancer avant l'intervention, la laparotomie révèle souvent que le cancer de la tête du pancréas est irrésécable. Nous avons cherché à cerner les aspects possibles à améliorer dans la détermination du stade avant l'intervention.

Méthodes : Nous avons procédé à un examen rétrospectif des cas de patients référés à un établissement pour une résection d'un cancer de la tête du pancréas au cours d'une période de deux ans. Le taux de métastases ou de maladies irrésécables constatées au moment de la laparotomie chez les patients devant subir une pancréaticoduodénectomie curative a constitué le principal résultat.

Résultats : Au cours de la période d'étude, 133 patients ont été référés avec un cancer soupçonné de la tête du pancréas. Tous ont subi une tomodynamométrie préopératoire. Vingt-quatre ont subi une échographie endoscopique préopératoire et 23, une imagerie par résonance magnétique (IRM). Au total, 78 patients ont été déclarés non candidats à l'intervention chirurgicale, ce qui a laissé 55 patients avec un cancer peut-être résécable chez lesquels on a prévu une pancréaticoduodénectomie. De ce total, 32 patients (58 %) ont subi avec succès une résection curative et 23 (42 %) avaient des métastases ou une maladie localement avancée non identifiée par la détermination du stade avant l'intervention. La non-résécabilité était causée par des métastases (9 patients, 16 %), une atteinte vasculaire (12 patients, 22 %) et une atteinte du mésentère (2 patients, 4 %). Un patient a subi une laparoscopie diagnostique immédiatement avant l'exploration ouverte prévue et on a constaté une atteinte du péritoine qui a empêché une résection curative.

Parmi les patients qui ont subi une échographie endoscopique, 14 n'étaient pas candidats à l'intervention chirurgicale à cause de tumeurs localement avancées. On a offert l'intervention chirurgicale curative à 10 patients, pour constater que cinq (50 %) avaient une tumeur irrésécable (4 avec métastases et 1 localement avancée). On a offert une intervention chirurgicale à 11 des patients qui ont subi un examen par IRM; 5 (45 %) d'entre eux avaient une tumeur irrésécable (2 avec métastases, 3 maladies localement avancées).

Conclusion : Dans notre établissement, la détermination avant l'intervention du stade du cancer de la tête du pancréas rate un nombre important de métastases et de cas de maladie irrésécable. Il est clairement possible d'améliorer la situation et il faudrait évaluer des technologies nouvelles pour améliorer la détection des métastases et de la maladie localement avancée afin d'éviter les laparotomies inutiles.

Pancreatic cancer is the fourth leading cause of cancer deaths in Canada. The 5-year survival rates are low, with surgical resection providing the only possibility of cure. The appropriate treatment of pancreatic cancer depends on accurate preoperative staging. Historically, staging was performed by exploratory laparotomy. Advances in imaging technology have made it possible to determine the stage of disease without subjecting patients to surgery. In the past, the only palliation for pancreatic cancer was open surgical gastroenteric and biliary-enteric bypass. Today, less-invasive palliative techniques such as endoscopic or percutaneous placement of biliary stents, endoscopic placement of duodenal stents and laparoscopic gastroenterostomy exist.¹ By using these less invasive techniques, open palliative bypass may be avoidable in many situations. With the scarcity of available operating room time, there are also important implications of wasted operating room time if a patient is found to have an unresectable tumour at the time of surgery and if conversion to a bypass procedure is necessary.

Thus, it is important to identify patients who are candidates for curative resection and to spare patients with metastatic or unresectable disease the risks associated with surgery and allow them more direct access to proper palliation. Despite improvements in imaging modalities, a high incidence of unresectable disease is still found at the time of surgery (20%–57%).^{2,3,4} Whereas multiple preoperative staging techniques have been used in the attempt to more accurately stage disease, no consensus about the best approach in determining tumour resectability has been reached.² We designed this study to review the experience at our institution and to identify potential areas for improvement in preoperative staging.

METHODS

We identified by their billing codes all patients who were referred to pancreatic surgeons at the London Health Sciences Centre between Jan. 1, 2005, and Dec. 31, 2006, for pancreatic disease. We surveyed the records of these patients for benign and malignant disease of the pancreas as well as for jaundice, biliary obstruction and gastric outlet obstruction. The charts and operative notes of these

patients were reviewed in detail. The primary outcome was the rate of metastasis or unresectable disease found at laparotomy in patients who were booked for potentially curative resection. The operative intent in all surgeries was curative resection, which was expressed to the patient. Preoperative planning was performed for all patients and, should their disease be found to be unresectable at the time of surgery, the patients were prepared for the possibility of open palliative bypass. Informed consent was obtained in all cases for pancreaticoduodenectomy as well as for palliative bypass. Secondary outcomes were sensitivity and specificity of various imaging modalities. Pancreatic tumours were considered unresectable if there was metastatic or locally advanced disease. Metastatic disease included hepatic metastases or peritoneal seeding.

Locally advanced disease included local lymph node invasion, celiac trunk, hepatic artery/superior mesenteric artery invasion, portal vein invasion, or superior mesenteric vein invasion or encasement. The local practice is for patients to be referred to a surgeon before oncology unless there is obvious metastatic disease. We did not include referrals directly from endoscopic retrograde cholangiopancreatography (ERCP) to oncology owing to clearly metastatic disease because our goal was to evaluate the staging in patients who were thought to have potentially resectable disease.

The study protocol was approved by the University of Western Ontario's institutional ethics board.

RESULTS

In total, 133 patients were referred to pancreatic surgeons because of suspected cancer of the pancreatic head. After preoperative workup, the surgical teams felt that 55 patients had surgically resectable pancreatic cancer; these patients were booked for pancreaticoduodenectomy. At the time of surgery, 23 (42%) of these patients were found to have metastatic or locally advanced disease, despite preoperative imaging that suggested resectability. The reasons for unresectability in these patients are shown in Table 1. The procedures performed in these 23 patients were gastroenteric and biliary-enteric bypass (15 patients),

gastroenteric bypass (3 patients), biliary-enteric bypass (1 patient) and exploratory laparotomy (4 patients). A total of 32 patients underwent pancreaticoduodenectomy with curative intent.

Of the remaining 78 patients who were not felt to have resectable disease based on imaging, 9 were taken to the operating room for a palliative procedure with no intent of resection, 11 had ERCP and stenting, 3 had percutaneous transhepatic cholangiography with drainage, 16 had clear metastatic disease at presentation and were referred to oncology, and 38 patients were followed because of the patients' wishes, because the patient was unfit for surgery or because the lesion had a low suspicion of malignancy.

All of the patients taken to the operating room underwent preoperative computed tomography (CT). Ninety-six patients were staged preoperatively with CT alone. Of these, 40 patients were booked for surgery with the intent of resection; 56 patients were deemed not to be candidates for surgery. Of those who were candidates for surgery, 16 were found to have unresectable disease at the time of surgery. One patient had a diagnostic laparoscopy and was found to have peritoneal seeding.

In total, 14 patients underwent preoperative endoscopic ultrasonography (EUS) and CT scanning. Of these patients, 7 were not felt to have resectable disease because of locally advanced disease or vessel involvement, and 3 were felt to not have cancer. The other 4 patients were taken to the operating room for a planned resection. At the time of surgery, 2 patients were found to have peritoneal seeding and 2 received pancreaticoduodenectomy.

Thirteen patients underwent preoperative MRI and CT scanning. Two of these patients were not felt to have resectable disease because of locally advanced or metastatic disease, whereas 4 patients were followed because they were not felt to have cancer. The other 7 patients were taken to the operating room for a planned resection. At the

time of surgery, 4 patients were found to have unresectable disease (liver metastases 2, mesenteric nodes 1, superior mesenteric artery involvement 1), whereas the other 3 underwent pancreaticoduodenectomy.

In total, 10 patients received preoperative EUS, MRI and CT scanning. One of these patients was not felt to have resectable disease because of locally advanced or metastatic disease, and 5 were followed because they were not felt to have cancer. The other 4 patients were taken to the operating room for a planned resection. At the time of surgery, 1 patient was found to have unresectable disease because of extension into the celiac trunk and para-aortic nodes; the other 3 patients underwent pancreaticoduodenectomy.

The sensitivity of the preoperative imaging techniques is shown in Table 2. Among imaging techniques, CT and EUS and MRI had the highest sensitivity (86%), with CT and EUS having a sensitivity of 83%.

DISCUSSION

A universal staging algorithm for pancreatic cancer does not exist. Historically, surgical exploration was recommended for most patients with pancreatic cancer; however, laparotomy in patients when curative resection is not possible results in increased perioperative mortality with no increase in survival.^{5,6} Patients with unresectable disease can undergo endoscopic and percutaneous methods of palliative decompression, and, therefore, in most cases, laparotomy and bypass for palliation is unnecessary. Of the patients in our study who were thought to have resectable pancreatic cancer based on standard preoperative staging, 42% were found to have metastatic or locally advanced disease at the time of surgery. This correlates with the literature and reconfirms that a high proportion of patients are found have unresectable disease at the time of surgery. It also suggests many patients undergo unnecessary laparotomies.

In an attempt to more accurately stage pancreatic cancer before surgery, previous studies have investigated various imaging techniques, including EUS, CT and MRI. Computed tomography has been suggested to have the highest accuracy of these techniques in assessing the extent of the primary tumour, locoregional extension, vascular invasion

Table 1. Reasons for unresectable cases of pancreatic cancer identified during surgery

Reason	No. (%) patients
Metastatic disease	
Liver metastasis	5 (9)
Peritoneal seeding	3 (5)
Omental seeding	1 (2)
Total	9 (16)
Locally unresectable disease	
SMV invasion or encasement	4 (7)
Encroachment in the SMA	3 (5)
Encasement of the portal vein	3 (5)
Extension into the celiac trunk and para-aortic nodes	2 (3)
Mesentery root invaded	1 (2)
Positive mesenteric nodes	1 (2)
Total	14 (26)

SMA = superior mesenteric artery; SMV = superior mesenteric vein.

Table 2. Sensitivity of preoperative imaging techniques

Imaging	Sensitivity, % (95% CI)
Computed tomography	78 (66–86)
Computed tomography and endoscopic ultrasonography	83 (51–97)
Computed tomography and magnetic resonance imaging	60 (27–86)
Computed tomography, magnetic resonance imaging and endoscopic ultrasonography	86 (42–99)

CI = confidence interval.

distant metastasis and tumour resectability.^{2,3,7} Endoscopic ultrasound has the highest accuracy in assessing lymph node involvement.² For determining resectability, previous meta-analyses have shown that CT and MRI each have a sensitivity of 82%.³ All of the patients in our study had a preoperative CT, with a sensitivity of 79%. Resectability was more accurately predicted in patients who had EUS in addition to a CT scan (83% sensitivity). Others have found the best algorithm involving these techniques to be CT or EUS as an initial test followed by the alternate technique for patients with potentially resectable disease.² Whereas the highest sensitivity in our study was with a combination of CT, EUS and MRI (86%), there was a wide confidence interval. In addition, the lowest sensitivity was in the CT and MRI group.

Staging laparoscopy has been suggested as a modality to identify unresectable disease for patients in whom advanced disease is suspected despite imaging findings to the contrary. Laparoscopy has been suggested to prevent 10%–44% of patients from having an unnecessary laparotomy by identifying those with unresectable disease not identified by imaging.^{4,8,9} Laparoscopy has the advantage of identifying small peritoneal and hepatic lesions not identified by noninvasive imaging.⁹ In our study, the 9 patients with metastatic disease at the time of surgery could have been spared laparotomy if staging laparoscopy had been performed. The 14 patients with locally advanced disease could also have potentially been identified by staging laparoscopy. Laparoscopy has been suggested to be most beneficial in patients with presumed adenocarcinoma, compared with pancreatic neoplasms of other histologies.⁹ Liver metastasis and peritoneal seeding were 2 of the most common reasons for unresectability in the present study. Only 1 staging laparoscopy was performed, and the patient was spared an unnecessary laparotomy. The low rate of staging laparoscopy likely has multiple causes. Many surgeons are reluctant to use operative time for staging laparoscopy. There is also likely a perception of inflated accuracy with cross-sectional imaging. Because the technical skills for this method of staging exist in our institution and this study suggests its utility, perhaps staging laparoscopy will be a way to decrease the rate of unresectable disease found during surgery.

Techniques such as metal stenting of the bile duct and duodenal stenting are available as effective palliation for unresectable or metastatic cancer of the pancreatic head.^{1,10} By better identifying the patients most likely to benefit from surgery, patients with metastatic or unresectable disease can be spared the risk associated with surgery and be directed to safe, durable, less invasive palliation. This will

not only improve patient care but will also allow better use of precious operating room time.

This study has shown that there is a high rate of unresectable disease found at the time of laparotomy in patients with cancer of the pancreatic head in our institution. With the increasing availability of novel minimally invasive palliation, laparotomy should be reserved for patients for whom curative resection is planned. There may be a role for prospectively evaluating newer technologies or developing staging protocols to allow better use of operating room resources and help identify patients who have the greatest likelihood of potentially curative resection.

Competing interests: None declared.

Contributors: All authors designed the study, analyzed the data, reviewed the article and approved its publication. Dr. Croome acquired the data and wrote the article.

References

- Xinopoulos D, Dimitroulopoulos D. Endoscopic palliative treatment of pancreatic cancer. *Ann Gastroenterol* 2005;18:391-4.
- Soriano A, Castells A, Ayuso C, et al. Preoperative staging and tumor resectability assessment of pancreatic cancer: prospective study comparing endoscopic ultrasonography, helical computed tomography, magnetic resonance imaging, and angiography. *Am J Gastroenterol* 2004;99:492-501.
- Bipat S, Phoa SSK, van Delden OM, et al. Ultrasonography, computed tomography and magnetic resonance imaging for diagnosis and determining resectability of pancreatic adenocarcinoma: a meta-analysis. *J Comput Assist Tomogr* 2005;29:438-45.
- Doucas H, Sutton CD, Zimmerman A, et al. Assessment of pancreatic malignancy with laparoscopy and intraoperative ultrasound. *Surg Endosc* 2007;21:1147-52.
- Warshaw AL, Fernandez-del Castillo C. Pancreatic carcinoma. *N Engl J Med* 1992;326:455-65.
- de Rooij PD, Rogatko A, Brennan MF. Evaluation of palliative surgical procedures in unresectable pancreatic cancer. *Br J Surg* 1991;78:1053-8.
- Guthrie JA, Sheridan MB. Investigation of abdominal pain to detect pancreatic cancer. *BMJ* 2008;336:1067-9.
- Stefanidis D, Grove KD, Schwesinger WH, et al. The current role of staging laparoscopy for adenocarcinoma of the pancreas: a review. *Ann Oncol* 2006;17:189-99.
- White R, Winston C, Gonen M, et al. Current utility of staging laparoscopy for pancreatic and peripancreatic neoplasms. *J Am Coll Surg* 2008;206:445-50.
- Del Piano M, Ballare M, Montino F, et al. Endoscopy or surgery for malignant GI outlet obstruction? *Gastrointest Endosc* 2005;61:421-6.