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ORIGINAL ARTICLE

Clinical Utility of Endoscopic Ultrasound in Solid Pancreatic Mass Lesions Deemed Resectable by Computer Tomography

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ABSTRACT

Context Appropriate surgical exploration and resection of pancreatic carcinoma depends on accurate preoperative evaluation.

Objective Determine the accuracy of endoscopic ultrasound in predicting the need for surgical exploration in patients with solid pancreatic masses deemed by computer tomography to be resectable without venous grafting (absence of distant metastatic disease or major vascular involvement).

Patients All patients between March 2000 and November 2003 with focal pancreatic mass lesions deemed to be surgically resectable by computer tomography. Forty-nine patients participated (29 males, 20 females; age range: 40-86 years).

Intervention Preoperative linear-array endoscopic ultrasound.

Main outcome measure Surgical pathology compared to computer tomography and endoscopic ultrasound results.

Results Out of the 49 patients, 33 (67.3%) had pancreatic neoplasms and 16 (32.7%) had chronic pancreatitis. Endoscopic ultrasound correctly diagnosed all 16 patients with chronic pancreatitis. Endoscopic ultrasound correctly identified 18 (54.5%) of those with neoplasms as having unresectable disease while 6 (18.2%) patients were appropriately identified as resectable by endoscopic ultrasound. The remaining 9 patients (27.3%) were deemed resectable by endoscopic ultrasound, but were unresectable at the time of surgery. None of the patients were falsely designated as unresectable by endoscopic ultrasound.

Conclusion Endoscopic ultrasound is an important compliment to computed tomography in predicting resectability and in avoiding nontherapeutic laparotomy of solid pancreatic neoplasms. Moreover, endoscopic ultrasound classification did not discourage surgery of resectable pancreatic masses.

INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer deaths in the United States [1]. Surgical intervention remains the only potentially curative therapy for pancreatic adenocarcinoma and a relatively high rate of non-therapeutic explorations is currently considered acceptable. Fewer than one third of pancreatic cancers are resectable at presentation with a fraction of those achieving long-term survival [2]. The identification of factors that preclude attempts at resection prior to operation has multiple benefits, most importantly avoiding nontherapeutic

laparotomy and hastening the initiation of systemic therapy.

Patient selection remains the most important factor in determining the success of pancreatic resection. Thin cut, pancreatic protocol computer tomography (CT) is a central diagnostic test as it can demonstrate liver metastases, vascular invasion, and malignant ascites [3, 4, 5]. CT remains limited in its ability to detect local and remote malignant lymphadenopathy and extra-pancreatic extension. This is especially true for small tumors (<30 mm), neoplasms involving the transverse mesocolon, and remote lymph nodes harboring low volume malignancy [6, 7, 8].

Endoscopic ultrasound (EUS) is an excellent method for detecting and classifying pancreatic lesions and has a low complication rate [9, 10, 11, 12, 13, 14, 15, 16]. Implementation of this technique in addition to CT scanning allows more accurate preoperative evaluation of pancreatic lesions [17, 18, 19, 20, 21]. Ideally, inclusion of EUS in the management of pancreatic disorders may result in fewer non-therapeutic surgical interventions without reducing potentially curative resections [22].

The purpose of this study is to evaluate the diagnostic benefit of preoperative EUS in patients with solid pancreatic masses deemed resectable by CT. It is hypothesized that EUS would significantly enhance the accuracy of determining resectability and would decrease the rate of nontherapeutic exploration.

METHODS

This is a retrospective review identified under one surgeon's care of patients with solid pancreatic lesions deemed resectable by CT. Patients with known metastatic disease were excluded from the study. Patients in this study underwent preoperative EUS for diagnosis and evaluation of surgical resectability between March 2000 to November 2003. Presumed diagnoses included solid pancreatic malignancies and focal mass forming chronic pancreatitis. A retrospective review was performed for each patient that underwent surgical exploration in order to accrue pertinent data including age, gender, pre-operative diagnostic results, surgical procedure, and final pathologic findings. Using the above noted criteria, 49 patients were identified over the 3.7 year period. Twenty-nine were male and 20 were female (age range: 40 to 86 years; Figure 1).

Computed Tomography

All CT scans were obtained using a standardized pancreatic protocol via a multidetector scanner (Siemens Medical, New York, NY, USA). All patients were imaged with 4 mm beam collimation (nominal and effective slice thickness of 1.0 mm and 1.3 mm, respectively) and a 0.5 mm reconstruction interval, 120 kVp, 205 mA, and a pitch of 1.0 during a 15 second breath-hold. Intravenous contrast (125 mL of 60% contrast) was administered at 2.5 mL/second, with a 65-second delay before the initiation of scanning. Each CT scan was interpreted by one of nine experienced radiologists.

Endoscopic Ultrasonography

Each EUS procedure was performed by one of two experienced gastroenterologists using a linear array echoendoscope (EG3630, Pentax Precision Instruments, Orangeburg, NY, USA). In addition to interrogation of the tumor for vascular invasion and extra-pancreatic spread, lymph nodes in the mediastinum, celiac, porta hepatis and region of the superior mesenteric artery were inspected and biopsied when appropriate.

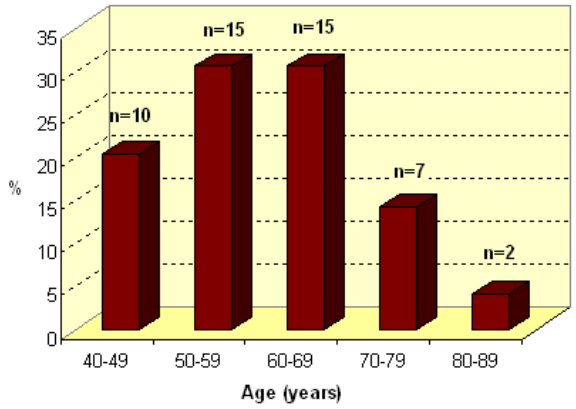

Figure 1. Age distribution of the 49 patients with solid pancreatic lesions deemed resectable by CT.

Post-EUS cytologic diagnosis and classification were compared to final surgical pathologic diagnosis which served as the gold standard.

Surgery

All surgical explorations were performed by a single surgeon. The surgical approach started with a diagnostic laparoscopy to rule out the presence of peritoneal carcinomatosis, miliary liver metastases or ascites. Laparoscopic ultrasound was available, but not employed because these patients had already undergone EUS. Contraindications to resection at exploration included identification of remote metastatic disease, resection that would require arterial reconstruction, or a clear inability to obtain an R0 resection.

Pathology

Final pathologic diagnosis was determined either via pathologic examination of the resected specimen or a positive needle aspiration/biopsy for malignancy. Thirty-four of the 49 patients enrolled in the study (69.4%) had an indication for EUS-guided fine needle aspiration (FNA) at the time of ultrasonography. A dedicated cytopathologist was present at the time of EUS-guided FNA to determine the adequacy of the specimen. It should be noted that lymph nodes in the field of resection were generally not sampled unless needed to establish tissue diagnosis as this finding would otherwise not alter the surgical plan.

ETHICS

The study protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 (as revised in Tokyo 2004) and was approved by the University of Minnesota's Internal Review Board. Written/oral informed consent was obtained from all patients for each medical technique applied according to the usual clinical practice.

STATISTICS

Absolute and relative frequencies were reported as descriptive statistics.

RESULTS

Out of the 49 patients, final pathologic diagnoses included neoplasms for 33 patients (67.3%) and chronic pancreatitis for 16 patients (32.7%). Among patients with neoplastic processes, 28 (84.8%) had pancreatic adenocarcinoma, 3 (9.1%) had ampullary neoplasia, and 2 (6.1%) had a distal cholangiocarcinoma. Patients underwent a variety of surgical procedures for these neoplasms, including 20 pancreaticoduodenectomies (60.6%), 10 explorations with a palliative procedure (30.3%), 2 distal pancreatectomies (6.1%), and one total pancreatectomy (3.0%).

Endoscopic Ultrasonography

EUS correctly diagnosed all 16 patients with chronic pancreatitis. Assessment of respectability was correct in 24 patients (72.7%) of the 33 patients with neoplasms: 18 (54.5%) as having unresectable disease and 6 (18.2%) as having resectable tumors. The remaining 9 patients (27.3%) were deemed potentially resectable by EUS, but were found to be unresectable at the time of surgery. None of the patients were falsely designated as unresectable by EUS. According to these values, the sensitivity, specificity, and the positive and negative predictive values of EUS in predicting resectability were 100% (18/18), 40.0% (6/15), 66.7% (18/27), and 100% (6/6), respectively.

Thirty-one (91.2%) of the 34 EUS-guided fine needle aspirations performed at the time of ultrasonography were accurate as proven by final pathologic findings while the remaining 3 biopsies (8.8%) were non-diagnostic.

Eight of the 33 patients with malignancies (24.2%) had duct stenting via ERCP prior to their EUS. Two of these (25.0%) were designated as resectable by EUS and were found to be unresectable at the time of surgery.

DISCUSSION

The role of EUS in the management of peripancreatic lesions remains controversial. This study demonstrates the accuracy of EUS in determining the resectability in a population of patients with solid pancreatic masses deemed resectable by CT. Our data suggest that, most importantly, EUS rarely over-classifies lesions. This in part represents a conscious decision by the endosonographers to classify lesions conservatively as not to falsely discourage resection. This conservative approach accounts in part for the 9 (27%) patients who were falsely designated as having resectable tumors. However, it also ensures that nearly every patient with resectable disease will undergo surgical resection.

EUS and CT are complimentary studies. CT should always be the first diagnostic test, since it is highly accurate at determining resectability, especially as it relates to metastatic disease and significant vascular involvement. Prior research suggests that patients with clear evidence of unresectability do not need EUS, unless a tissue diagnosis cannot be obtained in a more advantageous manner [21]. However, when CT suggests resectability, EUS can be useful in documenting histology and identifying remote disease that precludes resection (e.g. vascular invasion and non-regional lymphadenopathy). In fact, in our study over half of the patients deemed resectable by CT were correctly identified as unresectable by EUS. Employment of pre-surgical EUS should help pancreatic surgeons to avoid non-therapeutic interventions without decreasing the exploration of patients with resectable disease. In addition to its diagnostic benefit we found the added information provided by pre-operative EUS to be extremely useful during patient counseling regarding the risk/benefit ratio of surgery.

The limitations of this study are threefold. First, this is a retrospective analysis. While the criteria seem fair it raises the possibility of selection bias. Secondly, CT technology is advancing rapidly and axial scanning should be able to improve in its ability to correctly classify pancreatic cancers. Finally, the radiologists involved in this study included nine general radiologists without specific clinical interest in pancreatic malignancy, whereas the EUS exams were performed by two gastroenterologists with clinical practices focused on pancreatic disease. Had a single radiologist with an interest in the pancreas been reading the films more subtle nuances may have been identified leading to improved CT accuracy. We feel, however, that the design of this study corresponds to the current standard of care for pancreatic malignancy in the United States and therefore is clinically relevant. Currently, most pancreatic malignancies are initially evaluated at centers which do not have a focused interest in pancreaticobiliary cancer. The current study would suggest that EUS may be of significant benefit prior to surgical exploration when initial CT imaging suggests the presence of a resectable mass. Notwithstanding the limitations, this paper demonstrated the value of ancillary EUS in the evaluation of solid pancreatic lesions deemed resectable by CT. In this setting, EUS could decrease the number of non-therapeutic laparotomies with minimal falsely discouraged resections.

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Abbreviations CT: computer tomography; EUS: endoscopic ultrasound; FNA: fine needle aspiration

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