Comparison of Endoscopic Ultrasonography and Multidetector Computed Tomography for Detecting and Staging Pancreatic Cancer

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Background: **Accurate preoperative detection and staging of pancreatic cancer may identify patients with locoregional disease that is amenable to surgical resection.**

Objective: **To compare endoscopic ultrasonography and multidetector computed tomography (CT) for the detection, staging, and resectability of known or suspected locoregional pancreatic cancer.**

Design: **Prospective, observational, cohort study.**

Setting: **Single, tertiary referral hospital in Indianapolis, Indiana.**

Patients: **120 participants with known or suspected locoregional pancreatic cancer.**

Interventions: **Endoscopic ultrasonography followed by multidetector CT was performed in all patients. Patients with known or suspected pancreatic cancer deemed potentially resectable by 1 or both tests were considered for surgery.**

Measurements: **Detection, staging, and resectability of pancreatic cancer. Surgically resected pancreatic cancer with negative microscopic histologic margins was considered resectable.**

Results: **Of 120 patients enrolled, 104 (87%) underwent endoscopic ultrasonography and CT. Of the 80 patients with pancreatic cancer, 27 (34%) were managed nonoperatively, and 53 (66%) treated surgically had resectable ($n = 25$) or unresectable ($n = 28$) cancer. For the 80 patients with cancer, the sensitivity of endoscopic ultrasonography (98% [95% CI, 91% to 100%]) for detecting a pancreatic mass was greater than that of CT (86% [CI, 77% to 93%]; $P = 0.012$). For the 53 surgical patients, endoscopic ultrasonography was superior to CT for tumor staging accuracy (67% vs. 41%; $P < 0.001$) but equivalent for nodal staging accuracy (44% vs. 47%; $P > 0.2$). Of the 25 resectable pancreatic tumors in patients recommended for surgery, endoscopic ultrasonography and CT correctly identified 88% and 92%, respectively, as resectable. Of the 28 unresectable pancreatic tumors in patients recommended for surgery, endoscopic ultrasonography and CT correctly identified 68% and 64%, respectively, as unresectable.**

Limitations: **Radiologists who read the scans and endosonographers were not blinded to previous radiographic information. Because of the modest sample size, CIs of the sensitivity estimates were sometimes wide.**

Conclusion: **Compared with multidetector CT, endoscopic ultrasonography is superior for tumor detection and staging but similar for nodal staging and resectability of preoperatively suspected nonmetastatic pancreatic cancer.**

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In the United States for the year 2003, it was estimated that pancreatic cancer would be diagnosed in approximately 30 700 patients and contribute to 30 000 deaths (1). Complete surgical removal with negative histologic margins (R0 resection) is an independent predictor of postoperative survival (2–4) and remains the only potential curative treatment for pancreatic cancer. At surgical exploration, however, only 5% to 25% of the tumors are amenable to resection (5–8). Therefore, the principle goal of preoperative evaluation is to identify patients with potentially resectable disease while avoiding surgical exploration in those with unresectable disease.

There is no evidence-based consensus on the optimal preoperative imaging assessment of patients with suspected pancreatic cancer. Because of widespread availability, helical computed tomography (CT) is usually the initial study for this indication (9, 10). Dual-phase helical CT, during which postinjection contrast image acquisition is obtained in both the pancreatic (arterial) and portal venous phases, has improved detection rate and assessment of resectability in patients with suspected pancreatic cancer (11, 12). Current state-of-the-art CT imaging uses a multiple-row detector with narrow detector collimation, wide x-ray beam, and rapid table translation; these features offer faster acquisition and thinner image slices compared with single-detector CT (13–15). Whether multidetector CT offers improved detection and staging of pancreatic cancer, however, is unknown.

Endoscopic ultrasonography has been shown to be superior to conventional CT for the detection (16–20) and staging (19, 20) of pancreatic cancer. When compared with helical CT, however, endoscopic ultrasonography is reported to be either equivalent for detection (21, 22) or superior for detection or staging (23–25). To date, no comparative studies of multidetector CT with other imaging tests, including endoscopic ultrasonography, for suspected pancreatic cancer have been performed. Therefore, we conducted a prospective trial to compare endoscopic ultrasonography and multidetector CT for the detection, staging, and resectability of suspected locoregional pancreatic cancer.

METHODS

Patients

The institutional review board at Indiana University Medical Center approved this study, and all patients signed

Context

Clinicians often use multidetector computed tomography or endoscopic ultrasonography to detect and stage pancreatic cancer.

Contribution

This prospective study found that, among 80 adults with proven pancreatic cancer, the sensitivity of multidetector computed tomography and endoscopic ultrasonography for detecting a pancreatic mass was 86% (CI, 77% to 93%) and 98% (CI, 91% to 100%), respectively. Among 53 patients undergoing surgery, endoscopic ultrasonography was more accurate for staging local tumor spread, but both tests showed similar accuracy for nodal staging and detecting resectability.

Cautions

Optimal strategies to detect and stage pancreatic cancer may vary across sites depending on the expertise of radiologists and endosonographers.

–The Editors

written informed consent. Eligible patients were referred to our hospital with clinically suspected or recently diagnosed solid or cystic pancreatic cancer within the previous 8 weeks. The referral base for our hospital consists of gastroenterologists and surgeons from Indiana and the surrounding contiguous states. Patients were eligible only if they agreed to undergo endoscopic ultrasonography, CT, and surgery (if necessary) at our institution. Patients were excluded if they had previously undergone endoscopic retrograde cholangiopancreatography or endoscopic ultrasonography at our institution for suspected pancreatic cancer; declined or remained undecided about potential surgical intervention; were referred to our institution by surgeons outside our hospital system. Patients were also excluded if they were pregnant, were incarcerated, could not independently provide informed consent, or were considered high surgical risk (American Society of Anesthesiology class III to V). In addition, we excluded patients with known or suspected periampullary masses, cholangiocarcinomas, or cancer with suspected locally advanced arterial (superior mesenteric, hepatic, or celiac) involvement or metastatic disease (ascites, suspicious liver or pulmonary lesions, distant enlarged lymph nodes) detected by previous imaging studies. Patients with suspected nonocclusive involvement of the superior mesenteric vein or portal vein were considered eligible for enrollment.

Study Design

This was a prospective, single-center, observational study. All enrolled patients had to respond to an initial health and medical questionnaire, which was followed by same-day endoscopic ultrasonography. Computed tomography was performed within 1 week. Within 3 weeks after CT, a surgeon examined the patient and reviewed the results of endoscopic ultrasonography and CT to determine eligibility for potential resection. After surgery or the decision to pursue nonoperative management, we telephoned patients to assess quality of life at 1 month, 3 months, and every 6 months until death or until 24 months if clinical disease remained stable.

Endoscopic Ultrasonography Technique

Conscious sedation was performed with various combinations of intravenously administered propofol, meperidine, fentanyl, or midazolam. Initially, we examined all patients with a radial echoendoscope (Olympus GF-UM130 [Olympus America Inc., Melville, New York]). We then examined patients with a linear echoendoscope (using either Pentax FG-36UX [Pentax Precision Instruments, Orangeburg, New York] or Olympus GF-UC140P [Olympus America Inc.]). Unless cancer had been definitively confirmed previously, endoscopic ultrasonography–guided fine-needle aspiration was performed with a 22-gauge needle (Wilson-Cook Medical Inc., Winston-Salem, North Carolina) in all patients, when applicable. A cytotechnologist or cytopathologist was on-site for preliminary interpretations of all aspirations.

One of 3 experienced gastroenterologists, each of whom had performed at least 1000 pancreatic examinations, performed all procedures. The operator was not blinded to previous radiographic data. Recorded information included the presence or absence, size, echocharacteristics, location, or locoregional extension of any visualized pancreatic mass, lymph nodes, or distant metastases. Lymph nodes that were not accessible to endoscopic ultrasonography–guided fine-needle aspiration were considered malignant if 3 or more of the following criteria were present: diffuse hypoechoic echogenicity, short-axis diameter of 5 mm or greater, well-defined borders, round shape, or location within 5 mm of the tumor. Well-defined hypoechoic or hyperechoic lesions within the liver with a short-axis diameter of 10 mm or greater and not accessible to fine-needle aspiration were defined as metastases. We considered vascular involvement by the tumor to be present if any 1 of the following were noted: loss of the normal hyperechoic interface between tumor and vessel for at least 5 mm (adherence), irregular tumor and vessel interface, tumor within vessel lumen (invasion), vessel encasement, and perigastric or periduodenal collaterals with associated venous occlusion. Immediately after the examination, any visualized mass was designated by the endosonographer as surgically resectable or unresectable and assigned a tumor, node, metastasis (TNM) staging according to the 1997 American Joint Committee on Cancer (AJCC) classification (**Appendix Table**; available at www.annals.org) for staging of pancreatic cancer (26).

Multidetector CT Technique

We performed multidetector CT with a quad-channel scanner (MX 8000 Quad, Philips Medical Systems, Cleve-

land, Ohio) by using 0.5-second gantry rotation time and acquisition of 4 sections per rotation. All patients drank 500 mL of tap water as nonopaque oral intraluminal contrast media. A total of 150 mL (300 mg of iodine/mL) of low-osmolar contrast media (Isovue-300, Bracco Diagnostics, Princeton, New Jersey) was injected with a power injector (CT Envision Injector, Medrad, Pittsburgh, Pennsylvania) at a rate of 4.0 mL/s into an antecubital vein by using either an 18- or 20-gauge cannula. Examination was performed in a dual-phase mode. Image acquisition was first done during the pancreatic phase (35 seconds after the start of contrast infusion) from the top to the bottom of the pancreas with 4.0-mm beam collimation (nominal section thickness, 1.0 mm; effective section thickness, 1.3 mm), 0.5-mm reconstruction interval, 120 kVp, 205 mAs, and a pitch of 1.0 during a single breath-hold of 15 to 20 seconds. The second phase was performed during the portal venous phase (65 seconds after the start of contrast infusion) from the top of the liver to the iliac crests with 10-mm beam collimation (nominal section thickness, 2.5 mm; effective section thickness, 3.2 mm), 1.3-mm reconstruction interval, 120 kVp, 250 mAs, and a pitch of 0.875 during a single breath-hold of 15 seconds. Multiplanar (2-dimensional) reformatting was not routinely performed; however, when it was used, the entire data set was transferred to a workstation (MX View, Philips Medical Systems) for evaluation. No 3-dimensional (volume rendering) postprocessing was used in this study.

One of 3 experienced gastrointestinal radiologists who were blinded to the results of the previous endoscopic ultrasonography examination interpreted all scans. Patient information provided to the interpreting radiologist included presenting symptoms; the size, location, and vascular involvement (if known) of any visualized pancreatic mass from previous CT; and the results of any previous endoscopic retrograde cholangiopancreatography (for example, presence or absence of ductal strictures) or pathology (for example, endoscopic brush cytology). Locoregional and distant adenopathy were considered malignant if they were greater than 10 mm in short-axis dimension. Metastatic liver lesions were defined as nodular, low-attenuation lesions that lacked benign features and measured at least 10 mm in diameter. Vascular involvement by the tumor was considered to be present if any of the following were noted: encasement with fat plane obliteration of greater than or equal to 50% of vessel diameter, tumor within the vessel lumen, thrombosis or occlusion of the vessel, or presence of venous collaterals. Information recorded by the radiologist was identical to that of the endosonographer and included the staging and resectability of any suspected pancreatic mass detected.

Surgery

One of 2 experienced pancreatobiliary surgeons performed all consultations and operations. Decisions for surgery were based on a preoperative evaluation of surgical risk coupled with endoscopic ultrasonography and CT findings. Before surgery, we considered tumors to be unresectable if they had pathologically confirmed distant metastatic disease (for example, metastatic liver lesions, malignant ascites) or if they were locally advanced and were suspected of having encasement of the superior mesenteric or portal vein or involvement of the celiac artery, superior mesenteric artery, or hepatic artery. Patients with suspected nonocclusive portal venous involvement or locoregional unresectability were considered for surgery on a case-by-case basis. If there was discordance between test results, preoperative diagnostic uncertainty, or need for biliary or intestinal bypass, surgical exploration was performed.

Before tumor resection, all patients had complete abdominal exploration by laparoscopy or laparotomy. Operative criteria for attempted resection were absence of liver or peritoneal metastatic lesions; invasion of the transverse mesocolon; metastasis to distant lymph nodes; and involvement of the celiac, superior mesenteric, or hepatic arteries. Mesenteric or portal venous resection with reconstruction was done in select patients if adequate vascular control could be achieved and a high probability of margin-negative resection was anticipated. Despite successful resection and venous reconstruction, however, these patients were considered to have unresectable tumors. A standard pancreaticoduodenectomy or pylorus-preserving variant was done for tumors located in the head or uncinate process; a distal pancreatectomy and splenectomy was done for tumors located in the body or tail. Routine intraoperative histologic frozen section examinations were done on the pancreatic, bile duct, and retroperitoneal soft tissue margins. A positive pancreatic or bile duct margin mandated further surgical resection, if possible, until a negative margin was obtained. Persistently positive pancreatic margins resulted in a total pancreatectomy. Regional lymph nodes were routinely resected en bloc with the tumor specimen.

Pathology

A gastrointestinal pathologist evaluated all resected pancreatic masses. If malignant, a tumor and node stage was assigned (**Appendix Table**, available at www.annals.org) according to the American Joint Committee on Cancer 1997 classification (26).

Criteria for Pancreatic Cancer Detection, Staging, and Resectability

Reference standards for pancreatic cancer detection were either intraoperative examination alone (with or without biopsy or resection) or the results of endoscopic ultrasonography–guided fine-needle aspiration (or previously obtained cytology) and subsequent clinical follow-up. When complete surgical resection was attempted, pathologic assessment of tumor stage (T1–T3) and nodal stage (N0 or N1) was considered the gold standard. Splenic (T3) and nonsplenic (T4) vascular involvement by tumor was defined as a lack of an adequate surgical plane of dissection.

Pathologic confirmation of vascular invasion by tumor was not routinely performed. Surgically resected tumors with either microscopically (R1) or macroscopically (R2) positive histologic margins were considered unresectable despite gross tumor removal. Unresectable tumors, evaluated surgically, were also defined as any T4 vascular invasion, pathologically confirmed liver or peritoneal metastatic lesions, invasion of the transverse mesocolon or stomach, or metastasis to distant lymph nodes. Only resected pancreatic cancer with negative microscopic histologic margins (R0 resection) was considered resectable.

Statistical Analysis

The primary end point for comparison between endoscopic ultrasonography and multidetector CT was resectability of pancreatic cancer. Secondary end points were detection and staging of the tumors. On the basis of review of the surgical data at our institution from 1997 to 1999, we estimated that 60 patients each year would undergo attempted surgical resection of pancreatic cancer. Furthermore, we estimated that a 2-year sample would contain 120 patients, 40 of whom would have unresectable tumors. On the basis of 3 published series (2 of which were performed at our institution) before study recruitment (19, 21, 25), we estimated that endoscopic ultrasonography and CT would correctly identify 89% and 91% of resectable neoplasms, respectively, and 91% and 46% of unresectable neoplasms, respectively. With projected enrollment of 2 years, this study was powered at 80% to detect an absolute difference of 20% in identification of unresectable pancreatic cancers between the 2 imaging techniques. We made this projection by using an exact sign test of equality of paired proportions, with a 0.05 2-sided significance level and a 21% estimated proportion of discordant pairs (27).

Statistical analysis was performed with SAS software (SAS Institute, Inc., Cary, North Carolina). We compared baseline characteristics and characteristics of surgery and surgical pathology between patients with resectable and unresectable pancreatic cancer by using *t*-tests for continuous data and Fisher exact tests for categorical data. For patients with pancreatic cancer who had surgery, the accuracy of tumor and nodal staging was defined as the proportion of all tumors staged correctly. We used exact McNemar tests (28, 29) to compare the sensitivity for detection of malignancy and accuracy of tumor and nodal staging of endoscopic ultrasonography and CT. When we found a significant overall difference between the 2 procedures, we performed exact McNemar tests for various tumor stages and tumor sizes, and the *P* values were inflated by using the Sidak multiple comparison correction to account for the retesting of the data (30). The Sidak *P* value equals $1 - (1 - \text{unadjusted } P \text{ value})^x$, where x equals the number of comparisons. We calculated exact 95% CIs for all estimates of sensitivity, specificity, and accuracy estimates. In addition, we calculated 95% CIs for the differences in sensitivities between the 2 procedures. A 2-tailed distribution was used; *P* values less than 0.05 were considered significant. All investigators in this study had full access to the data files.

Role of the Funding Sources

The funding sources had no role in the collection, analysis, or interpretation of the data or in the decision to submit the manuscript for publication.

RESULTS

Study Sample

This study was conducted between July 2000 and October 2002; the **Figure** outlines the trial profile. Of the 482 patients screened, 154 were eligible and 120 were enrolled. No procedural complications from CT or endoscopic ultrasonography were noted. Of those enrolled, we excluded 16 persons for protocol violations: 7 did not obtain CT at our institution, and 9 opted for surgery elsewhere. Of the remaining 104 patients, 63 (61%) underwent surgery. The mean age (±SD) of these patients was 64 ± 12 years; 59 (57%) patients were men, 99 (95%) were white, 4 (4%) were black, and 1 (1%) was Hispanic. Final diagnoses (n = 63) after intraoperative and subsequent histopathologic examination were unresectable (n = 28) or resectable (n = 25) pancreatic cancer, chronic pancreatitis (n = 5), benign intraductal papillary mucinous tumor (n = 1), macrocystic serious cystadenoma (n = 1), benign neuroendocrine tumor (n = 1), accessory spleen (n = 1), and ampullary cancer (n = 1). In the patient with ampullary cancer, CT detected no mass. However, endoscopy disclosed a 22-mm periampullary mass, which was completely resected at surgery. In the remaining 9 patients with benign disease who were treated surgically, both endoscopic ultrasonography and CT showed resectable focal pancreatic masses without vascular invasion.

Of the 41 patients managed without surgery, 27 (66%) had pancreatic cancer (adenocarcinoma [n = 26] or neuroendocrine carcinoma [n = 1]). In 24 patients (89%), the diagnosis was confirmed by malignant cytology from endoscopic ultrasonography–guided fine-needle aspiration of the pancreas alone (n = 16), liver alone (n = 4), pancreas and celiac lymph node (n = 2), pancreas and ascitic fluid (n = 1), and pancreas and liver (n = 1). In 1 patient, cytology from a previously placed pancreatic stent demonstrated malignancy. In the remaining 2 patients, endoscopic ultrasonography–guided fine-needle aspiration of a pancreatic mass showed atypical cells suspicious for adenocarcinoma, and the final diagnosis of cancer was subsequently confirmed by follow-up (time to death, 352 days and 483 days, respectively). To date, 24 patients (89%) with adenocarcinoma who were managed nonoperatively have died, and the mean time to death was 197 days (range, 24 to 676 days). Despite neoadjuvant treatment and clinical evidence of persistent disease, the remaining 3 with cytologically confirmed neuroendocrine carcinoma

($n = 1$) and adenocarcinoma ($n = 2$) remain alive 686, 919, and 944 days, respectively, after initial diagnosis.

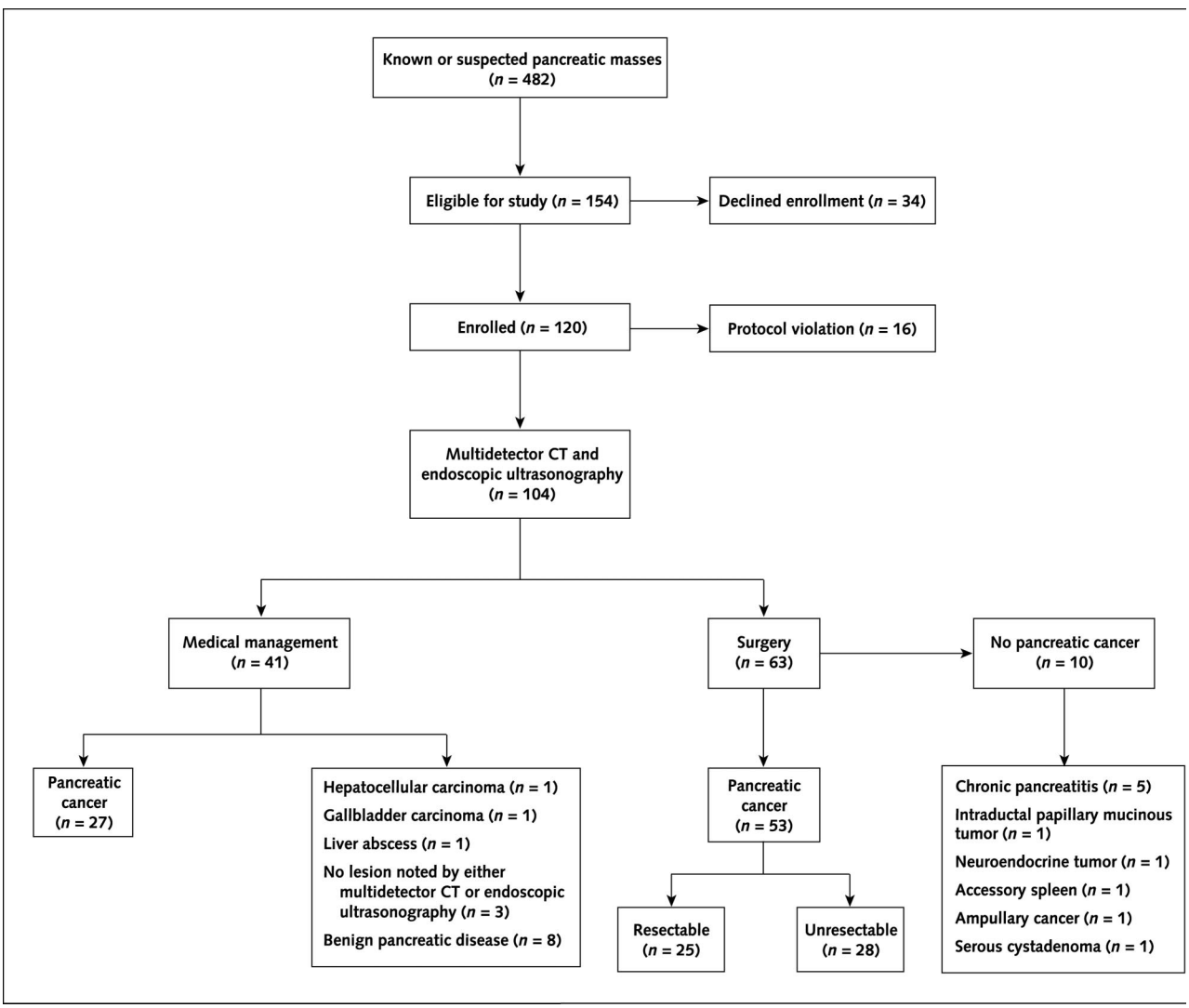
Two of the remaining 14 patients managed nonoperatively had suspected unresectable gallbladder carcinoma and hepatoma and died 26 and 33 days, respectively, after CT. Three patients had no mass seen by either endoscopic ultrasonography or CT and remain alive a mean of 708 days (range, 369 to 882 days) after CT. One patient with a suspected liver abscess died 181 days after CT. The remaining 8 patients believed to have benign disease were all alive a mean of 794 days (range, 357 to 952 days) after CT.

Table 1 shows the baseline characteristics of patients with surgically resectable and those with unresectable pancreatic cancer. Patients with unresectable tumors had significantly larger masses than did those with resectable tumors ($P = 0.012$). The 2 groups did not differ significantly for time to surgery, tumor pathology, or tumor location.

Surgery

Table 2 summarizes the results of surgery for the 53 patients with pancreatic cancer. Mean time from CT to surgery did not differ between the 2 groups. Overall, 45 of the tumors (85%) were located in the head of the pancreas, and 50 (94%) were ductal adenocarcinomas. Assessment of tumor and nodal staging was incomplete in 4 and 8 patients with unresectable tumors, respectively. Of the 28 unresectable masses, we did not attempt resection in 14 (50%) because of intraoperatively detected liver metastatic lesions ($n = 6$), distant nodal metastasis ($n = 3$), or vascular invasion ($n = 5$). In the remaining 14 masses (50%), we attempted resection; however, by protocol definition, these masses were unresectable because of portal venous reconstruction ($n = 5$), microscopically positive retroperitoneal soft tissue margin (R1 resection; $n = 5$), macroscopically positive margin (R2 resection; $n = 2$), distant nodal

Figure. **Trial profile.**



CT = computed tomography.

Table 1. **Baseline Characteristics and Results of Surgery for Patients with Resectable and Unresectable Pancreatic Cancer***

Characteristic	Resectable Cancer ($n = 25$)	Unresectable Cancer ($n = 28$)
Age, *y*		
Mean ± SD	61.9 ± 11.1	66.8 ± 10.9
Range	37–81	40–81
Race, *n (%)*		
White	25 (100)	26 (93)
Black	0 (0)	2 (7)
Sex, *n (%)*		
Male	15 (60)	16 (57)
Female	10 (40)	12 (43)
Time to surgery, *d*†		
Mean ± SD	14.4 ± 8.1	12.4 ± 7.4
Range	1–35	2–33
Pathology, *n (%)*		
Ductal adenocarcinoma	23 (92)	27 (96)
Malignant IPMT	2 (8)	1 (4)
Tumor size, *mm*‡		
Mean ± SD	26.7 ± 13.2	35.7 ± 12.1
Range	2–60	18–62
Tumor location, *n (%)*		
Head	21 (84)	24 (86)
Body	1 (4)	2 (7)
Tail	0 (0)	1 (4)
Head and body	1 (4)	0 (0)
Body and tail	2 (8)	1 (4)
Tumor (T) stage, *n (%)*		
T1	4 (16)	1 (4)
T2	3 (12)	1 (4)
T3	18 (72)	5 (18)
T4	0 (0)	17 (61)
Not staged§	0 (0)	4 (14)
Nodal (N) stage, *n (%)*		
N0	7 (28)	6 (21)
N1	18 (72)	14 (50)
Not staged§	0 (0)	8 (29)
Surgery performed, *n (%)*		
Pancreaticoduodenectomy (Whipple procedure)	6 (24)	4 (14)
PPPD	15 (60)	2 (7)
Distal pancreatectomy	3 (12)	2 (7)
Total pancreatectomy	1 (4)	0 (0)
Pancreaticoduodenectomy and PVR	0 (0)	2 (7)
PPPD and PVR	0 (0)	2 (7)
Distal pancreatectomy and PVR	0 (0)	1 (4)
Total pancreatectomy and PVR	0 (0)	1 (4)
Laparotomy with or without biopsy	0 (0)	8 (29)
Laparotomy with palliative bypass	0 (0)	6 (21)

* IPMT = intraductal papillary mucinous tumor; PPPD = pylorus preserving pancreaticoduodenectomy; PVR = portal vein reconstruction.
† Time from computed tomography examination until surgery is performed.
‡ Size was determined from surgical pathology in all patients with resectable tumors; in patients with unresectable tumors, size was determined when complete tumor removal was attempted. For the remaining patients, size was taken as the average of both preoperative computed tomography and endoscopic ultrasonography findings or from endoscopic ultrasonography assessment alone when computed tomography detected no mass.
§ Full laparotomy or resection was not completed in some patients with unresectable malignancy; therefore, assessment was incomplete.

metastasis ($n = 1$), or portal vein reconstruction and R2 resection ($n = 1$).

Detection of Pancreatic Cancer

For the 80 patients with pancreatic cancer, the sensitivity of endoscopic ultrasonography (98% [CI, 91% to 100%]) for mass detection was greater than that of CT (86% [CI, 77% to 93%]) ($P = 0.01$) (**Table 2**). Of the 53 patients with cancer who were treated surgically, the sensitivity of endoscopic ultrasonography (96% [CI, 87% to 100%]) for detection of a pancreatic mass was also greater than that of CT (81% [CI, 68% to 91%]) ($P = 0.02$). For masses that were 25 mm or smaller in diameter ($n = 19$), detection by endoscopic ultrasonography (89% [CI, 67% to 99%]) and by CT (53% [CI, 29% to 76%]) (adjusted $P = 0.077$) did not significantly differ. Similarly, for masses that were larger than 25 mm in diameter ($n = 34$), no statistically significant difference in detection between endoscopic ultrasonography (100% [CI, 90% to 100%]) and CT (97% [CI, 85% to 100%]) (adjusted $P > 0.2$) was seen. The 2 surgically resected tumors undetected by endoscopic ultrasonography were T1 tumors located in the head of the pancreas; these tumors were removed and had negative histologic margins (**Table 3**). Of the 10 tumors missed by CT and managed surgically, 9 were located in the head of the pancreas, 4 had indwelling biliary stents, and 3 were unresectable. Reasons for unresectability of these 3 lesions included metastatic distant adenopathy ($n = 1$), portal vein invasion ($n = 1$), and a positive retroperitoneal soft tissue margin (R1 resection; $n = 1$). Of the 27 patients with pancreatic cancer who were managed nonoperatively, masses were detected by endoscopic ultrasonography in 27 (100%) and by CT in 26 (96%). The one 20-mm mass undetected by CT was in a patient with adenocarcinoma of the head of the pancreas (confirmed by endoscopic ultrasonography–guided fine-needle aspiration) complicated by portal vein thrombosis and ascites. This patient died 37 days after CT.

For the 10 patients without pancreatic cancer who were managed surgically, endoscopic ultrasonography and CT detected pancreatic masses in 8 patients. Both tests correctly identified no pancreatic mass in the patient with ampullary cancer. However, both tests incorrectly detected a pancreatic mass in 1 patient who was found intraoperatively to have an accessory spleen adherent to the tail of the pancreas. No pancreatic mass was found in this patient at surgery.

Staging of Pancreatic Cancer

For the 53 patients with pancreatic cancer who were managed surgically, assessment of tumor and nodal staging was possible in 49 and 45 patients, respectively. Overall, the accuracy of endoscopic ultrasonography for tumor staging (67% [CI, 52% to 80%]) was superior to the accuracy of CT (41% [CI, 27% to 56%]) ($P = 0.007$; exact McNemar test) (**Table 4**). For staging of T1 and T2 tumors ($n = 9$) collectively, both tests demonstrated only 11% ac-

Table 2. **Comparison of Endoscopic Ultrasonography and Multidetector Computed Tomography for Detecting Pancreatic Masses in Patients with Pancreatic Cancer Managed Operatively and Nonoperatively***

Pancreatic Cancer	Patients, *n*	True-Positive Result on CT, *n*†	False-Negative Result on CT, *n*†	Sensitivity (95% CI), %		Difference in Sensitivity (95% CI), %	*P* Value
				EUS	CT		
Managed operatively and nonoperatively	Total: 80 Operatively: 53 Nonoperatively: 27			98 (91 to 100)	86 (77 to 93)	11 (4 to 19)	0.012
True-positive result on EUS		68	10				
False-negative result on EUS		1	1				
Managed operatively	53			96 (87 to 100)	81 (68 to 91)	15 (4 to 26)	0.022
True-positive result on EUS		42	9				
False-negative result on EUS		1	1				
Managed operatively with mass size ≤25 mm	19			89 (67 to 99)	53 (29 to 76)	37 (14 to 60)	0.077‡
True-positive result on EUS		9 (47)	8 (42)				
False-negative result on EUS		1 (5)	1 (5)				
Managed operatively with mass size >25 mm	34			100 (90 to 100)	97 (85 to 100)	3 (−2 to 8)	>0.2‡
True-positive result on EUS		33 (97)	1 (3)				
False-negative result on EUS		0 (0)	0 (0)				

* Size was determined from surgical pathology in all patients with resectable tumors; in patients with unresectable tumors, size was determined when complete tumor removal was attempted. For the remaining patients, size was taken as the average of both preoperative computed tomography and endoscopic ultrasonography findings or from endoscopic ultrasonography assessment alone when computed tomography detected no mass. CT = computed tomography; EUS = endoscopic ultrasonography.
† Values in parentheses are percentages.
‡ *P* values were adjusted for multiple comparisons by using the Sidak adjument.

curacy. Overall accuracy of endoscopic ultrasonography for T3 tumors (74% [CI, 52% to 90%]) was statistically superior to that of CT (30% [CI, 13% to 53%]) (adjusted $P = 0.026$); however, no difference was seen for T4 tumors (88% [CI, 64% to 99%] vs. 71% [CI, 44% to 90%], respectively; adjusted $P > 0.2$).

For nodal staging, overall accuracy of endoscopic ultrasonography (44%; 20 of 45 tumors) was similar to that of CT (47%; 21 of 45 tumors) ($P > 0.2$). Accuracy of both endoscopic ultrasonography and CT for N0 staging was 92% ($P > 0.2$). Endoscopic ultrasonography and CT were also not significantly different for staging of N1 tumors (25% vs. 28%, respectively; $P > 0.2$).

To evaluate the effect of the missing staging information in patients with incomplete surgical resection, we considered the following situations. If the accuracy of tumor staging of the 4 missing patients is assigned according to the observed combined distribution of the accuracies of both tests, the results are unchanged. Assuming that CT correctly staged all 4 patients, tumor staging accuracy did not significantly differ between the 2 tests when endoscopic ultrasonography incorrectly staged all 4 ($P = 0.11$) or 3 of the 4 patients ($P = 0.064$). If all 4 missing tumor stages were staged as T3, all hypothetical scenarios would demonstrate no statistically significant difference for staging T3 tumors between the 2 tests (adjusted $P > 0.05$ for all scenarios). Similarly, for the nodal stage, if the accuracy of nodal staging of the 8 missing patients is assigned according to the observed combined distribution, the results are unchanged. However, if all 8 patients are hypothetically staged incorrectly by endoscopic ultrasonography but correctly by CT, no statistically significant difference in accuracy between the 2 tests is noted ($P = 0.08$). These findings remain consistent even if the 8 missing nodal stages are hypothetically staged N1 (adjusted $P = 0.12$).

Resectability of Pancreatic Cancer

Of the 25 patients with resectable pancreatic tumors, endoscopic ultrasonography and CT correctly identified 88% and 92%, respectively, as resectable. Endoscopic ultrasonography incorrectly identified portal vein invasion ($n = 2$) and superior mesenteric vein invasion ($n = 1$), and CT incorrectly identified tumor invasion of the superior mesenteric vein ($n = 1$) and adrenal enlargement as metastasis ($n = 1$). Of the 28 patients with unresectable pancreatic tumors, endoscopic ultrasonography and CT correctly identified 68% and 64%, respectively, as unresectable. In 4 patients, endoscopic ultrasonography and CT incorrectly identified masses with microscopically positive retroperitoneal margins as resectable. Endoscopic ultrasonography also failed to detect invasion of the superior mesenteric vein ($n = 1$), superior mesenteric artery ($n = 1$), portal vein ($n = 1$), liver ($n = 1$), and celiac lymph node metastatic lesions ($n = 1$). Computed tomography failed to detect liver metastatic lesions ($n = 2$) and tumor invasion of the portal vein ($n = 2$), celiac trunk ($n = 1$), and superior mesenteric vein ($n = 1$). In the 41 patients for whom endoscopic ultrasonography and CT preoperatively concurred about tumor resectability, 21 of 22 (95%) were correctly identified as resectable and 14 of 19 (74%) were correctly identified as unresectable.

In 25 of the 27 patients (93%) with pancreatic cancer that was managed nonoperatively, both endoscopic ultrasonography and CT demonstrated evidence of unresect-

Table 3. **Characteristics of Masses Undetected by Endoscopic Ultrasonography and Multidetector Computed Tomography in Patients Having Surgery for Pancreatic Cancer**

Characteristic	Endoscopic Ultrasonography (n = 53)	Multidetector Computed Tomography (n = 53)
Undetected tumors, *n*		
Overall	2	10
>25 mm in diameter (n = 34)	0	1
≤25 mm in diameter (n = 19)	2	9
Size, *mm*		
Mean ± SD	11.0 ± 12.7	19.2 ± 9.4
Range	2, 20	2–35
Resectability, *n*		
Resectable	2	7
Unresectable	0	3
Tumor (T) stage, *n*		
T1	2	3
T2	0	0
T3	0	5
T4	0	2
Nodal (N) stage		
N0	1	5
N1	1	5
Location in pancreas, *n*		
Head	2	8
Head and body	0	1
Body and tail	0	1
Stent present, *n*		
Biliary	1	4
Pancreatic	0	0
None	1	6

ability. Of the other 2 patients, 1 did not undergo surgery because preoperative percutaneous fine-needle aspiration detected metastatic periumbilical lymph node and the second decided not to pursue surgery. For these 27 patients, endoscopic ultrasonography suspected T4 vascular invasion in 25 patients. In the same group, CT suspected T4 vascular invasion in 21, liver metastatic lesions in 12, and peritoneal metastatic lesions in 1 patient.

DISCUSSION

In this study, endoscopic ultrasonography was superior to multidetector CT for tumor detection and tumor staging but equivalent for nodal staging and determination of resectability of preoperatively suspected locoregional pancreatic cancer. A recent summary (31) of the 4 published trials (21–24) to date (with surgical exploration in 121 patients), which compared dual-phase helical CT and endoscopic ultrasonography, concluded that endoscopic ultrasonography was statistically superior to CT for the detection and determination of resectability for pancreatic cancer. However, direct comparison of these studies is problematic because of the inclusion of patients with ampullary cancer (21–23) and benign disease (22), use of endoscopic ultrasonography–guided fine-needle aspiration in only 1 study (24), inclusion of patients with distant metastasis detected on helical CT (23), variable CT technique and staging classifications used, and the relatively small numbers of patients enrolled. In the current study, patients with known or suspected benign disease, nonpancreatic cancer, or cancer with suspected locally advanced vascular (excluding portal vein) involvement or metastatic disease were excluded from enrollment. While these criteria may have underestimated the effect of CT obtained before enrollment, we believe they optimized identification of patients with probable locoregional malignancy who were most likely to benefit from surgery. In addition, these criteria are consistent with current standards of practice at most referral centers. In our study, 47% of the 53 patients with pancreatic cancer who underwent laparotomy had an R0 resection; this figure is higher than figures stated in previous reports (5–8).

Precisely timed image acquisition during the arterial phase of a dual-phase helical CT scan has been shown to improve dectection of pancreatic masses (12, 32, 33). As in previous studies that compared endoscopic ultrasonography to conventional (16–20) and helical (23, 24) CT, we found that the overall sensitivity of endoscopic ultrasonography was superior to multidetector CT for the detection of pancreatic cancer. For the 19 small (≤25 mm) pancreatic tumors removed surgically, however, our study demonstrated no statistical difference in detection between endoscopic ultrasonography (89%) and multidetector CT (53%; adjusted $P = 0.077$). This finding is contrary to the results of previous studies (20, 21). However, when multidetector CT fails to detect a mass in patients with suspected pancreatic cancer, we believe that endoscopic ultrasonography may help detect small neoplasms.

Our tumor staging accuracies of endoscopic ultrasonography were lower than those reported in some studies (18, 34, 35) and were principally due to poor staging of early tumors. However, these lower accuracies are similar to those observed in several recent reports (36–38). The restricted patient spectrum resulting from our strict inclusion criteria and the nonoperative management of patients with probable unresectable cancer may have underestimated the overall accuracy of tumor staging for both diagnostic tests. To better distinguish potentially resectable (T3) from unresectable (T4) tumors, the recently updated American Joint Committee on Cancer 2003 staging criteria (39) classify only vascular invasion of the celiac or superior mesenteric artery as T4 cancer. These changes may improve overall staging accuracies of pancreatic cancer in future studies.

We found that both endoscopic ultrasonography and multidetector CT were inaccurate for nodal staging of pancreatic cancer, primarily because of poor detection of N1 disease. The low accuracies for N1 staging may have been due to either poor detection of small peritumoral lymph

nodes or the strict diagnostic criteria used by each technique. Our results are similar to those of other recent studies on pancreatic cancer staging that document inaccurate assessment of malignant adenopathy for both endoscopic ultrasonography (36, 37) and helical CT (40, 41). In the current study, 72% of the 25 resectable but only 50% of the 28 unresectable pancreatic tumors had N1 malignancy. These data suggest that detection of peritumoral adenopathy is not essential for assessing resectability of pancreatic neoplasms, particularly for masses located in the head of the pancreas. Because determination of tumor resectability is more clinically relevant than staging, the effect of the relative inaccuracies of endoscopic ultrasonography and multidetector CT for tumor cancer staging is minimal.

In patients with suspected nonmetastatic pancreatic cancer, we found no significant difference between endoscopic ultrasonography and multidetector CT for preoperative determination of tumor resectability. Furthermore, concordance for resectability between these tests does not seem to improve assessment compared with either test alone. Therefore, if multidetector CT detects a pancreatic mass that appears resectable in an appropriate surgical candidate with suspected cancer, preoperative endoscopic ultrasonography does not seem to be necessary unless tissue confirmation of suspected cancer is desired. In the current study, 3 of 10 pancreatic cancers missed by multidetector CT were confirmed as surgically unresectable. Both masses missed by endoscopic ultrasonography were resectable. Therefore, when multidetector CT fails to detect a mass in patients with suspected pancreatic cancer, we believe that preoperative endoscopic ultrasonography is necessary for tumor detection. Although assessment of both endoscopic ultrasonography and multidetector CT for resectability was good, the ability of both tests to preoperatively identify unresectable malignancy was lower than expected. This is partly explained by the fact that both endoscopic ultrasonography and multidetector CT incorrectly identified as resectable 4 of the 5 tumors with histologically positive retroperitoneal margins.

Our study has several limitations. First, the nonsurgical management of 27 patients with suspected unresectable pancreatic cancer limits comparisons of endoscopic ultrasonography and multidetector CT for staging and resectability to patients with suspected locoregional cancer. Because endoscopic ultrasonography and multidetector CT concurred that 25 of these tumors (93%) were unresectable, the ability of each test to correctly identify unresectable cancer for all 80 tumors would probably have been higher than reported for the 53 patients with cancer that was managed surgically. A second limitation of our study is that neither the endosonographer nor radiologist was blinded to previous studies obtained before study enrollment. Therefore, bias about tumor staging may have been introduced before each respective examination (42). During the study, however, the radiologist was blinded to the results of the previous endoscopic ultrasonography examination. A third limitation was the small number of patients with unresectable cancer who underwent surgery. The original sample size estimate for this study was 40 patients with surgically determined unresectability, which was based on a 20% difference between the 2 tests for the identification of unresectable disease. During the study period, however, we found only an absolute 4% difference in the 28 patients with surgically proven unresectable cancer.

Table 4. **Comparison of Endoscopic Ultrasonography and Multidetector Computed Tomography for Tumor Staging of Patients Having Surgery for Pancreatic Cancer***

Test and Tumor Stage	Pathology or Surgical Tumor Stage†			
	T1	T2	T3	T4
EUS‡				
T0	2	0	0	0
T1	0	0	2	0
T2	1	1	1	0
T3	2	3	17	2
T4	0	0	3	15
Overstaged	3/5	3/4	3/23	0/17
Understaged	2/5	0/4	3/23	2/17
Accuracy, *n/n (%)*	0/5 (0)	1/4 (25)	17/23 (74)	15/17 (88)
Overall accuracy of EUS: 33/49 (67%)				
CT‡				
T0	3	0	5	2
T1	1	0	2	1
T2	0	0	7	2
T3	1	4	7	0
T4	0	0	2	12
Overstaged	1/5	4/4	2/23	0/17
Understaged	3/5	0/4	14/23	5/17
Accuracy, *n/n (%)*	1/5 (20)	0/4 (0)	7/23 (30)	12/17 (71)
Overall accuracy of CT: 20/49 (41%)				

* CT = computed tomography; EUS = endoscopic ultrasonography.
† Pathologic assessment of T1–T3 stage and intraoperative assessment of T3 (splenic) or T4 (nonsplenic) vascular invasion were considered the reference standards for endoscopic ultrasonography and multidetector computed tomography. Full laparotomy or resection was not completed in 4 patients with unresectable tumors; therefore, assessment is incomplete.
‡ T0 stage refers to masses undetected by endoscopic ultrasonography or multidetector computed tomography.

In summary, endoscopic ultrasonography is superior to multidetector CT for the detection of pancreatic cancer. Therefore, in patients with suspected pancreatic cancer, endoscopic ultrasonography may be helpful for identifying neoplasms (particularly in the head of the pancreas) that are undetected by multidetector CT. For preoperatively suspected locoregional cancer, endoscopic ultrasonography is superior to multidetector CT for tumor staging but equivalent for nodal staging and determination of resectability. Therefore, if multidetector CT detects a pancreatic mass that seems to be resectable in an appropriate surgical candidate with suspected cancer, preoperative endoscopic ultrasonography does not seem to be necessary unless tissue confirmation of suspected malignancy is desired.

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Appendix Table. **American Joint Committee on Cancer 1997 Classification for Staging Pancreatic Cancer**

Primary tumor (T)
- Tx: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: In situ carcinoma
- T1: Tumor limited to the pancreas (<2 cm in size)
- T2: Tumor limited to the pancreas (>2 cm in size)
- T3: Tumor extends directly into the duodenum, bile duct, or peripancreatic tissues
- T4: Tumor extends directly into the stomach, spleen, colon, or adjacent large vessels

Regional lymph nodes (N)
- Nx: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Regional lymph node metastasis

Distant metastasis (M)
- Mx: Distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis