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Comparison of Linear Array Endoscopic Ultrasound and Helical Computed Tomography for the Staging of Periampullary Malignancies

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Background: The purpose of this study was to compare linear array endoscopic ultrasound (EUS) and helical computed tomography (CT) scan in the preoperative local staging evaluation of patients with periampullary tumors.

Methods: Patients evaluated with EUS and CT for suspected periampullary malignancies from 1996 to 2000 were analyzed. Surgical/pathology staging results were the reference standard.

Results: Forty-eight patients (28 men and 20 women; mean age, 62 ± 4.9 years; range, 18–90 years) were identified. Malignancy was histologically confirmed in 44 patients. Parameters evaluated included tumor size, lymph node metastases, and major vascular invasion. EUS was significantly more sensitive (100%), specific (75%), and accurate (98%) than helical CT (68%, 50%, and 67%, respectively) for evaluation of the periampullary mass ($P < .05$). In addition, EUS detected regional lymph node metastases in more patients than helical CT. Sensitivity, specificity, and accuracy of EUS were 61%, 100%, and 84%, in comparison to 33%, 92%, and 68%, respectively, with CT. Major vascular involvement was noted in 9 of 44 patients. EUS correctly identified vascular involvement in 100% compared with 45% with CT ($P < .05$).

Conclusions: Linear array EUS was consistently superior to helical CT in the preoperative local staging of periampullary malignancies.

Key Words: Endoscopic ultrasound—Computed tomography—Periampullary cancer—Pancreatic cancer.

Malignancies of the periampullary region represent a heterogeneous group of tumors that often provide challenging decisions for surgeons. Complete surgical resection remains the only proven therapy for potential cure. However, most patients present with either advanced locoregional or metastatic disease that precludes curative surgical resection.[1–3] Several factors have been associated with a poor prognosis in patients with periampullary malignancies. These include larger tumor size, lymph node metastases, and infiltration into and around major extrapancreatic vessels.[1–3] Therefore, accurate preoperative evaluation of extrapancreatic tumor extension, especially the presence or absence of vascular invasion and regional nodal metastases, is important in identifying patients who may benefit from surgical interventions.

A variety of imaging techniques have been used for defining malignancies in the periampullary region, including transabdominal ultrasound,[4,5] endoscopic retrograde cholangiopancreatography,[6] magnetic resonance imaging,[7–9] visceral angiography,[4,9,10] and computed tomography (CT).[4,7–15] Currently, CT is the dominant noninvasive imaging modality used for the staging of periampullary tumors. However, several studies demonstrate

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that up to 40% of patients with periampullary malignancies are inaccurately staged by CT.[1–3,9,12–20] Sensitivity rates for the detection of lymph node metastases and major vascular involvement by CT are inconsistent and range from 38% to 74% and 36% to 70%, respectivly.[4,9,12–20]

Endoscopic ultrasound (EUS) involves the visualization of the gastrointestinal tract by means of intraluminal high-frequency (5–12 MHz) sonography via an endoscope. This allows for precise and enhanced imaging of the gastrointestinal wall and adjacent structures. EUS has emerged as a promising imaging modality for the accurate local staging of other gastrointestinal malignancies, including esophageal,[21] gastric,[22] and rectal.[23,24]

Several reports suggest that EUS is superior to other conventional radiological modalities, including CT scanning in the staging of periampullary malignancies.[4,7,13–16] They demonstrate a significantly higher sensitivity and specificity in identifying periampullary lesions, assessing major vascular involvement, and determining lymph node metastases with EUS compared with CT. However, many of these studies were often performed with conventional dynamic or nonhelical incremental CT scanners, and few studies were compared with surgical findings. In addition, advancements in endoscopic ultrasonography, such as the use of linear array imaging as compared with older first-generation circular array images, have improved the results of detecting periampullary malignancies.[25,26]

Therefore, the purpose of this study was to compare the results of linear array EUS and helical CT scan in the preoperative local staging of patients with periampullary malignancies. Parameters assessed in this study included absence or presence of a tumor, tumor size, lymph node metastases, and major vascular involvement. Surgical and pathology findings were used as the standard of reference.

PATIENTS AND METHODS

A retrospective study of all patients who underwent surgical exploration and had preoperative evaluation with linear array EUS and helical CT for the evaluation of suspected periampullary malignancies at New York Presbyterian Hospital–Cornell Medical Center from May 1996 to May 2000 were analyzed. The surgical and pathology staging results were considered the reference standard.

EUS was performed by either of the senior gastroenterologists of this report (M.P. or I.J.) with the FG32UA-type echoendoscope (Pentax, Orangeburg, NY). A curvilinear array transducer of ultrasound frequency of 5 to 12 MHz was used in all patients. Briefly, visualization of the pancreatic head and portal vein confluence were obtained from the duodenal bulb. The pancreatic body/tail and celiac vessels were scanned from the gastric fundus. For this purpose, the stomach was filled with 200 to 400 mL of water, whereas in the duodenum a water-filled balloon at the tip of the instrument was used to improve transmission of the ultrasound waves. The criteria for tumor size included the largest diameter (centimeters) of a well-demarcated lesion with an echo-poor, homogeneous pattern. Lymph nodes were considered malignant if their maximum diameter was $\geq$.5 cm, as reported previously.[4,7,13,14] If the lymph nodes did not meet the size criteria or were not visualized, the regional lymph nodes were considered benign. Major vascular involvement was determined to be positive if direct tumor extension was seen in the vessel lumen, if vascular obstruction was noted, or if there was irregularity of the vessel wall and obliteration of the hyperechoic interface between the tumor and the major vessel.[13–15,27]

Helical CT scans were obtained at our institution with a GE Hispeed CT/i scanner (General Electric, Milwaukee, WI). All patients received water-soluble oral contrast before the procedure. Contiguous sections of 3 mm were obtained of the peripancreatic area; both unenhanced and enhanced views were performed after a bolus injection of 100 mL of non-nonionic iodinated contrast material at a rate of 2 to 3 mL/second. Helical CT scanning was begun immediately after completion of the contrast injection. Scans were analyzed and reviewed by two radiologists experienced in abdominal imaging. The criteria for tumor size included the largest diameter (centimeters) of a well-demarcated lesion. Lymph nodes were considered malignant if their maximum diameter was $>$1.0 cm, as reported previously in the CT radiology literature.[17–20] Major vascular involvement was determined to be positive if direct tumor extension was seen in the vessel lumen, if vascular thrombosis was noted, or if there was irregularity of the vessel wall and obliteration of the interface between the tumor and the major vessel.

Statistical analysis was performed with PEPI version 3 (USD, Stone Mountain, GA). Sensitivity was defined as the ability of the test to detect disease when it was present. Specificity was the ability of the test to indicate nondisease when no disease was present. Accuracy was the ability of the test to determine true-positive and true-negative results in all study subjects. In addition, positive and negative predictive values were calculated. Positive predictive value indicates what proportion of the subjects who had positive test results had the disease, and negative predictive value indicates what proportion of

the subjects who had negative test results were free of the disease. Exact 95% confidence intervals were calculated for each statistical parameter.[28] The *z*-test was performed for comparison of two proportions, and statistical significance was evaluated at the $P < .05$ level.

RESULTS

Of the 48 patients evaluated in this study, all patients underwent preoperative linear array EUS and helical CT scanning followed by surgical exploration for a suspected periampullary malignancy (Fig. 1). These included 28 men and 20 women who ranged in age from 18 to 90 years, with a mean age of 62 years. In 44 patients, the diagnosis of a periampullary malignancy was histologically confirmed (pancreatic ductal adenocarcinoma in 34, neuroendocrine tumors in 6, and ampullary adenocarcinoma in 4). The diagnosis of malignancy was excluded in the remaining four patients by pathology and clinical follow-up after surgery. All four patients with a benign diagnosis were found to have focal chronic pancreatitis on pathologic examination. Tumor size, lymph node metastases, and major vascular invasion were evaluated in all 44 patients in whom surgery and pathologic examination determined a final diagnosis of malignancy.

Of the 44 patients diagnosed with a periampullary malignancy, EUS was more sensitive (100%), specific (75%), and accurate (98%) than helical CT (68%, 50%, and 67%, respectively) for detection of a periampullary mass (Table 1). The differences in sensitivity and accuracy reached statistical significance for EUS ($P < .05$) compared with CT. EUS identified a periampullary mass in all 44 patients, as opposed to only 30 patients with CT scanning. CT failed to identify any type of mass in 14 patients (31%) diagnosed with a malignancy in this study (Fig. 2A and B). Tumor size ranged from 1 to 4 cm in diameter, with a mean size of $2.7 \pm .6$ cm; no tumor in this study exceeded 4 cm in diameter. The ability of linear array EUS to determine tumor size was superior when compared with helical CT results. EUS correctly predicted the tumor size within 1 cm of pathologic or intraoperative findings in >90% (40 of 44) of the patients, compared with only 52% (23 of 44 patients) identified with CT (Fig. 3).

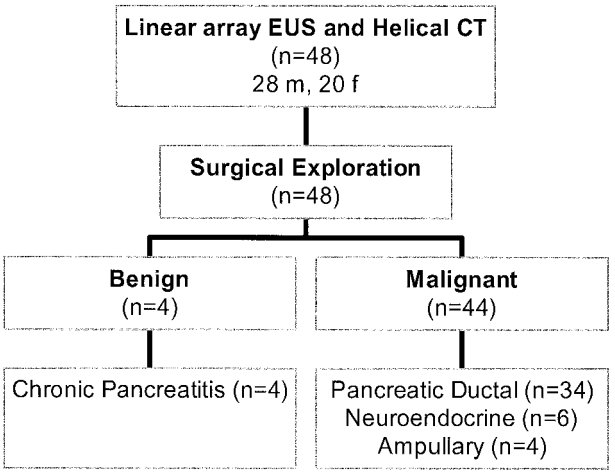

FIG. 1. Study design. All patients underwent preoperative staging for a suspected peripancreatic malignancy. Results were compared with surgical/pathology findings. EUS, endoscopic ultrasound; CT, computed tomography.

Although for lymph node staging, EUS was able to detect regional lymph node metastases in more patients than helical CT, the differences were not significant. The sensitivity, specificity, and accuracy of EUS in identifying peripancreatic nodal metastases were 61%, 100%, and 84%, in comparison to 33%, 92%, and 68%, respectively, with helical CT. However, these differences were not statistically significant (Table 2).

Major vascular involvement was noted in the final surgical/pathologic assessment in 9 of 44 patients in this study (Table 3). Of the nine patients with vascular involvement, three underwent resection of the involved major vascular structures (portal vein); two had tumor extending to but not invading the portal/superior mesenteric vein confluence, with no resection of vascular structures needed; and four patients were deemed unresectable at the time of operation because of the degree of vascular encasement around the superior mesenteric artery or portal/superior mesenteric vein confluence. EUS correctly determined vascular involvement in 100% of the cases involved (Fig. 4), as opposed to helical CT, which identified this abnormality in only 45%. These differences were significant ($P < .05$).

DISCUSSION

Tumors of the periampullary region represent a heterogeneous group of malignancies, including those from the pancreas, ampulla of Vater, distal common bile duct, and duodenum. They are however, homogenous in many regards by their highly malignant nature, late clinical presentation, and often-dismal prognosis. Surgical resection provides the only curative treatment in patients with this disease.[1–3] Unfortunately, most patients have advanced disease with rapidly aggressive locoregional tumors, which may involve major vascular structures that preclude resection or may spread through the lymph and nervous system with disseminated metastases. Early diagnosis and accurate assessment of disease staging are challenging tasks. The goal of high-quality preoperative

TABLE 1. *Comparison of linear array EUS and helical CT in detecting a periampullary malignancy (n = 48)*

	Sensitivity		Specificity		Positive PV		Negative PV		Accuracy	
Variable	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
EUS	100*	93–100	75	24–99	98	90–100	100	37–100	98*	90–100
CT	68	53–81	50	9–91	94	81–99	13	2–36	67	53–79

CI, confidence interval; PV, predictive value; EUS, endoscopic ultrasound; CT, computed tomography.
* $P < .05$.

radiological evaluation in periampullary malignancies is to determine the extent of local tumor extension, including regional lymph node metastases, major vascular involvement, and distant metastatic disease. This allows for selection of patients who may benefit from surgical resection and identification of those individuals who are better managed nonoperatively.

Although our results are representative of a selected patient population, we demonstrate that linear array EUS has a higher sensitivity, specificity, and accuracy rate in identifying and appropriately staging periampullary malignancies compared with helical CT. This was reflective in that EUS was superior to helical CT in accurately assessing major factors in staging, such as tumor size, lymph node metastases, and vascular involvement. Of the 44 patients with a periampullary malignancy in this series, EUS correctly identified a mass in all 44 patients. In contrast, helical CT defined an actual mass in only 30 of 44 patients. A total of 14 patients (31%) had no mass identified on helical CT imaging. Although this seems to be a disproportionate number, the inability of CT scans to identify masses in patients with periampullary malignancies has been well described.[19,29] In a study by Bluemke et al.,[19] helical CT failed to identify a mass in 11% of patients diagnosed with pancreatic malignancies. In a multicenter trial investigating EUS and CT scanning for pancreatic tumors, a surprising 56% of patients with pancreatic carcinoma had CT scans that revealed nonspecific enlargement of the pancreas and did not demonstrate a mass lesion.[29] Gress et al.,[30] in a study of 81 patients evaluated with EUS and helical CT, reported that CT failed to detect a mass in 26% of patients with confirmed tumor at surgery. In our own series, EUS

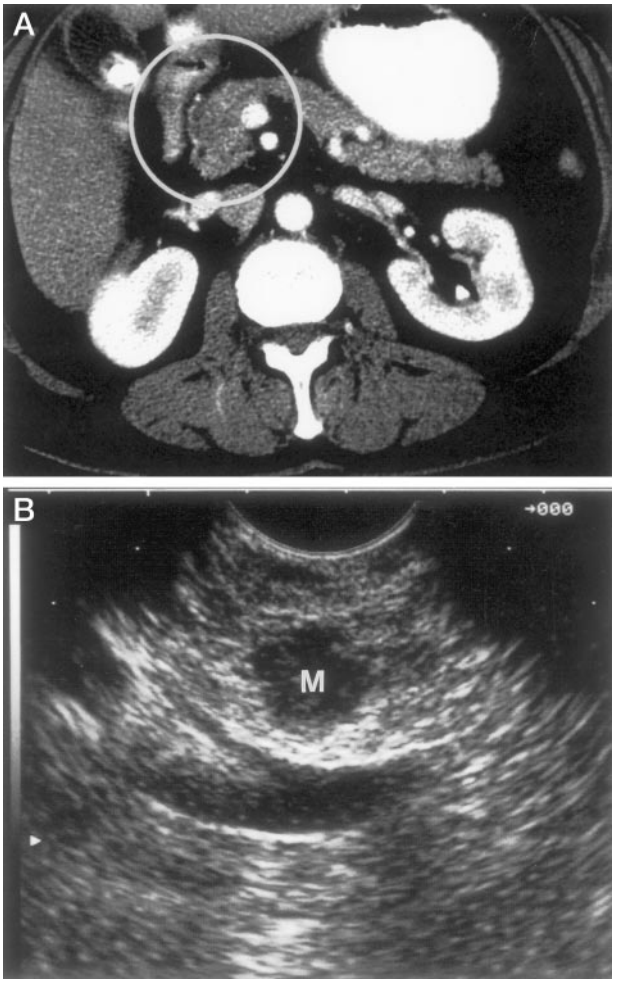

FIG. 2. Identifying the presence of a mass on helical computed tomography (CT) and endoscopic ultrasound (EUS). (**A**) No tumor was identified on helical CT; however, the same patient underwent an EUS (**B**) and demonstrated a 1.5-cm mass (M) in the head of the pancreas. Note the interface between the mass and the superior mesenteric/portal vein confluence, suggesting no vascular invasion.

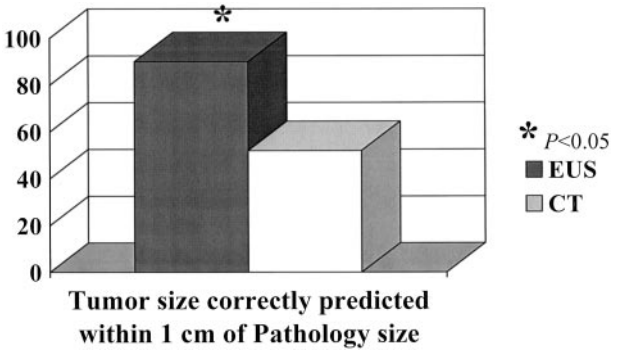

FIG. 3. Comparing endoscopic ultrasound (EUS) and helical computed tomography (CT) in predicting tumor size.

TABLE 2. *Comparison of linear array EUS and helical CT for nodal involvement in peripampullary malignancies (n = 44)*

	Sensitivity		Specificity		Positive PV		Negative PV		Accuracy	
Variable	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
EUS	61	38–81	100	89–100	100	76–100	79	62–90	84	71–93
CT	33	15–37	92	77–99	75	39–96	67	50–81	68	53–81

CI, confidence interval; PV, predictive value; EUS, endoscopic ultrasound; CT, computed tomography.

correctly identified a periampullary lesion in 100% of patients found to have a malignancy, as compared with 68% with helical CT. In addition, the size of the tumor was correctly identified within 1 cm of the pathologic measurement in 90% of patients with EUS, compared with 52% by using criteria obtained with helical CT. These differences were statistically significant. The ability of EUS to identify these lesions correctly may be reflective of the overall small size of the tumors in this study. The mean tumor size was 2.7 cm, and no tumor measured >4 cm. EUS has been reported to be particularly accurate for smaller lesions. Rosch et al.[15] compared EUS and dynamic CT for evaluation of patients with pancreatic tumors and demonstrated improved results with tumors <3 cm. They reported 100% sensitivity and 100% specificity with EUS and 55% and 53%, respectively, with CT. Additionally, Mueller et al.[7] demonstrated that EUS was more sensitive (93%) in identifying pancreatic tumors <3 cm compared with CT scan (53%).

Although peripancreatic nodal disease at our institution and others does not preclude surgical resection, it has been identified as a negative prognostic factor for survival, and its presence may be an indicator for neoadjuvant therapy.[1–3,9] The ability to detect lymph node metastasis in this study was superior with EUS compared with helical CT; however, these differences did not reach statistical significance. In this series, EUS had an accuracy rate of 84%, compared with 68% with helical CT. In a comparative study, Palazzo et al.[13] reported an accuracy rate of 67% with EUS and 55% with helical CT. Similarly, Gress et al.[30] demonstrated that the overall accuracy of nodal staging was improved with EUS compared with CT: 72% vs. 55%, respectively.

Assessment of potential tumor involvement of major regional vessels is an extremely important aspect of preoperative staging. Whereas tumor involvement of the superior mesenteric artery and celiac axis is considered an absolute contraindication to surgical resection, limited involvement of the portal/superior mesenteric vein does not preclude resection, and this is increasingly being performed safely in patients with periampullary malignancies.[1–3,9] Our series identified nine patients with vascular involvement; all of these were preoperatively identified with EUS (100%), compared with only four (45%) with helical CT. These results are similar to those in several other reports in the literature. Rosch et al.[4] demonstrated that EUS was superior to CT in determining tumor involvement of the portal venous system, in which they reported sensitivity and specificity rates of 91% and 97% with EUS, compared with 36% and 85%, respectively, with CT. Sugiyama et al.[27] investigated portal venous invasion in pancreaticobiliary carcinomas, in which they reported 91% sensitivity, 92% specificity, and 92% accuracy rates with EUS, compared with 64%, 79%, and 75%, respectively, with CT. Gress et al.[30] also demonstrated superior vascular invasion assessment with EUS compared with CT, with reported accuracy rates of 93% for EUS and 62% for CT. Selected series comparing EUS and CT in the preoperative staging of periampullary malignancies are listed in Table 4.

This study addresses preoperative staging of periampullary malignancies with the use of the most recent technology in EUS, that is, linear array imaging. In addition, we compared the results with helical CT results and used surgical/pathology results as the gold standard. Although this study is a retrospective series in a select group of patients, our results indicate that linear array EUS is consistently superior to helical CT in preoperative assessment of tumor size, lymph node metastases, and presence of tumor vascular involvement in patients

TABLE 3. *Comparison of linear array EUS and helical CT in predicting major vascular involvement (n = 44)*

	Sensitivity		Specificity		Positive PV		Negative PV		Accuracy	
Variable	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
EUS	100*	72–100	100	92–100	100	1–44	100	92–100	100	93–100
CT	45	16–76	100	92–100	100	47–100	88	74–95	88	77–93

CI, confidence interval; PV, predictive value; EUS, endoscopic ultrasound; CT, computed tomography.
*$P < .05$.

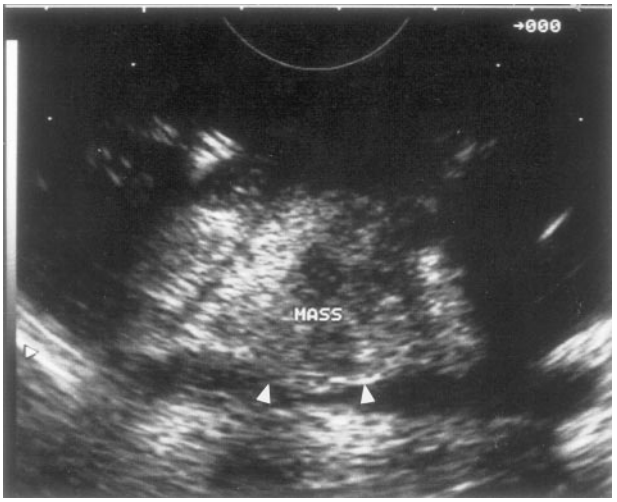

FIG. 4. Endoscopic ultrasound demonstrating vascular involvement: tumor (mass) encroaching on the portal vein (white arrows).

with periampullary malignancies. However, several considerations should be taken into account before EUS is used in all patients with a presumed periampullary malignancy. Although there were no complications in this reported series, EUS does represent an invasive modality, with the potential for complications of any invasive technique, including bleeding, gastrointestinal perforation, and hypotension from sedation. In addition, EUS is operator dependent and requires a significant learning curve. In one study, physicians who performed at least 40 EUS procedures were considered experienced.[4] However, the most important deficit of EUS is the inability to properly assess distant metastasis, such as hepatic and peritoneal involvement.

Therefore, we believe that linear array EUS should not replace high-quality helical CT scans for the routine preoperative staging of periampullary malignancies but

TABLE 4. *Selected series of EUS and CT in preoperative assessment of periampullary lesions*

Study	Year	n	EUS	CT	Comments
Current series	2003	48	100% Sensitivity 75% Specificity	68% Sensitivity 50% Specificity	EUS superior to CT in detecting tumor size and vascular involvement
Sugiyama et al.[27]	1997	91	95% Sensitivity	81% Sensitivity	EUS was superior to CT in detecting vascular involvement: 92% vs. 75%
Midwinter et al.[29]	1999	34	97% Sensitivity	76% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Gress et al.[30]	1999	81	85% Sensitivity	30% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Tio et al.[32]	1990	67	92% Sensitivity	NR	No comparison with CT was made
Howard et al.[33]	1997	21	75% Sensitivity 77% Specificity	63% Sensitivity 100% Specificity	EUS more sensitive than CT for tumor detection, but underestimates resectability
Legmann et al.[34]	1998	30	100% Sensitivity 33% Specificity	92% Sensitivity 100% Specificity	No difference between EUS and dual-phase helical CT
Akahoshi et al.[35]	1998	96	89% Sensitivity 97% Specificity	NR	No comparison with CT was made
Kubo et al.[36]	1999	35	74% Sensitivity	NR	Evaluated only ampullary lesions: no comparison with CT was made
Cannon et al.[37]	1999	37	78% Sensitivity	24% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Shoup et al.[38]	2000	37	97% Sensitivity 33% Specificity	82% Sensitivity 66% Specificity	CT overestimated vascular involvement
Schwarz et al.[39]	2001	95	71% Sensitivity	61% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Chen et al.[40]	2001	36	97% Sensitivity	39% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Skordilis et al.[41]	2002	20	82% Sensitivity	30% Sensitivity	All patients had ampullary carcinoma
Meining et al.[42]	2002	36	75% Accuracy	NR	Reviewed only T stage
Palazzo et al.[13]	1993	64	91% Sensitivity	66% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Yasuda et al.[14]	1988	42	100% Sensitivity	72% Sensitivity	EUS superior to CT in detecting vascular involvement and lymph node metastases
Rosch et al.[15]	1991	102	99% Sensitivity 100% Specificity	77% Sensitivity 53% Specificity	EUS superior to CT in detecting vascular involvement and lymph node metastases

NR, not reported; EUS, endoscopic ultrasound; CT, computed tomography.

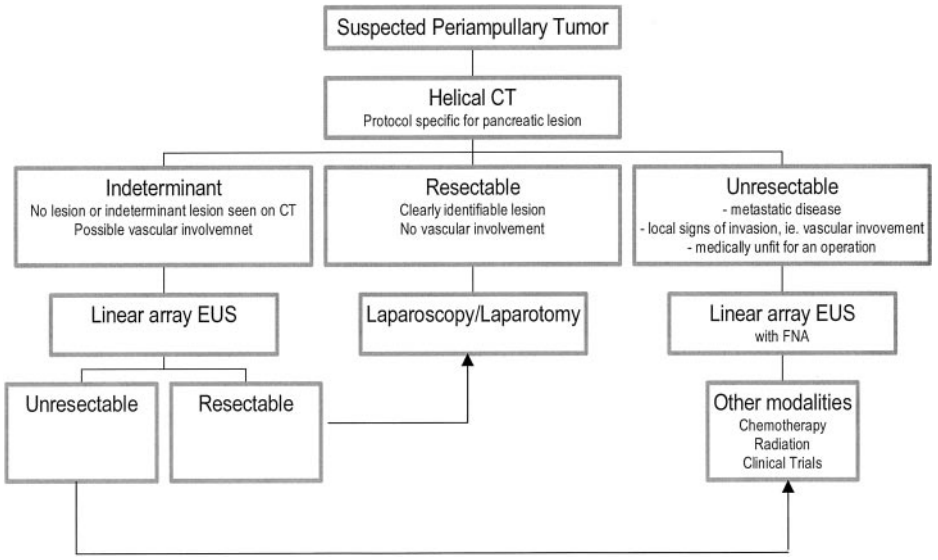

FIG. 5. Algorithm for preoperative staging evaluation in patients suspected of having periampullary malignancies. EUS, endoscopic ultrasound; CT, computed tomography; FNA, fine-needle aspiration.

that it should be used as an adjunct in a selected group of patients. These patients should include those in whom the CT scan is negative or ambiguous in defining a mass and in whom there is a high clinical suspicion of a periampullary malignancy. In addition, the disease of patients who show evidence or a suggestion of vascular invasion on CT may be better characterized by EUS, and EUS may allow for better preoperative planning. Furthermore, patients with unresectable lesions identified on CT or those medically unfit for an operation and who need histological tissue confirmation may undergo EUS-guided fine-needle aspiration.[31] An algorithm for the preoperative work-up of patients with suspected periampullary malignancies is presented in Fig. 5.

In summary, our study revealed that linear EUS is superior to helical CT in the preoperative assessment of tumor size, detection of regional nodal metastases, and detection of major vascular invasion in patients with periampullary malignancies. Linear array EUS improved preoperative local staging of periampullary malignancies when cases were compared by findings at operation. These results in a selected group of patients indicate that appropriate use of linear array EUS is useful as an adjunct in the preoperative assessment of selected patients with periampullary malignancies.

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