Role of EUS for preoperative evaluation of cholangiocarcinoma: a large single-center experience CME

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Background: Accurate preoperative diagnosis and staging of cholangiocarcinoma (CCA) remain difficult.

Objective: To evaluate the utility of EUS in the diagnosis and preoperative evaluation of CCA.

Design: Observational study of prospectively collected data.

Setting: Single tertiary referral hospital in Indianapolis, Indiana.

Patients: Consecutive patients with CCA from January 2003 through October 2009.

Interventions: EUS and EUS-guided FNA (EUS-FNA).

Main Outcome Measurements: Sensitivity of EUS for the detection of a tumor and prediction of unresectability compared with CT and magnetic resonance imaging (MRI); sensitivity of EUS-FNA to provide tissue diagnosis, by using surgical pathology as a reference standard.

Results: A total of 228 patients with biliary strictures undergoing EUS were identified. Of these, 81 (mean age 70 years, 45 men) had CCA. Fifty-one patients (63%) had distal and 30 (37%) had proximal CCA. For those with available imaging, tumor detection was superior with EUS compared with triphasic CT (76 of 81 [94%] vs 23 of 75 [30%], respectively; $P < .001$). MRI identified the tumor in 11 of 26 patients (42%; $P = .07$ vs EUS). EUS identified CCA in all 51 (100%) distal and 25 (83%) of 30 proximal tumors ($P < .01$). EUS-FNA (median, 5 passes; range, 1-12 passes) was performed in 74 patients (91%). The overall sensitivity of EUS-FNA for the diagnosis of CCA was 73% (95% confidence interval, 62%-82%) and was significantly higher in distal compared with proximal CCA (81% vs 59%, respectively; $P = .04$). Fifteen tumors were definitely unresectable. EUS correctly identified unresectability in 8 of 15 and correctly identified the 38 of 39 patients with resectable tumors (53% sensitivity and 97% specificity for unresectability). CT and/or MRI failed to detect unresectability in 6 of these 8 patients.

Limitation: Single-center study.

Conclusion: EUS and EUS-FNA are sensitive for the diagnosis of CCA and very specific in predicting unresectability. The sensitivity of EUS-FNA is significantly higher in distal than in proximal CCA. (Gastrointest Endosc 2011;73:71-8.)

Cholangiocarcinoma (CCA) originates from either the intrahepatic or the extrahepatic bile ducts, and its incidence and mortality appear to be increasing worldwide.[1,2] Preoperative evaluation of suspected CCA should attempt to visualize the mass lesion, obtain a pathologic diagnosis, and evaluate for potential surgical resectability.

Abbreviations: CCA, cholangiocarcinoma; EUS-FNA, EUS-guided FNA; MRI, magnetic resonance imaging.

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See CME section; p. 134

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Confirmation of CCA can be very difficult before surgery. The differential diagnosis includes other carcinomas (mainly pancreatic) and metastases from other primary malignancies in addition to benign biliary strictures.[3]

Preoperative imaging modalities including transabdominal US, CT, and magnetic resonance imaging (MRI) can visualize the bile duct tumor and predict unresectability with variable degrees of accuracy.[4,5] Brush cytology during ERCP has been used for the diagnosis of CCA but with variable sensitivity, ranging from 33% to 80%.[6-13] The incorporation of new tissue acquisition techniques, such as endoscopic needle aspiration[7] and endobiliary forceps,[8-11] increases the sensitivity of tissue sampling of biliary strictures compared with brush cytology alone. The addition of peroral cholangioscopy has been reported to identify extrahepatic CCA with 100% sensitivity.[14]

EUS is well suited as a diagnostic modality to evaluate the entire bile duct because of the proximity of the US probe to the course of the duct. The limited number of studies describing the role of EUS-guided FNA (EUS-FNA) in the evaluation of biliary strictures have found widely variable sensitivity for the diagnosis of CCA: from 45% to 89%.[15-21] The differential role of EUS in evaluating proximal compared with distal bile duct strictures and in assessing the surgical resectability of all bile duct tumors remains less clear. The aim of the present study was to evaluate the utility of EUS for preoperative evaluation of CCA and its ability to detect the lesion, make a tissue diagnosis, and accurately assess surgical resectability.

Take-home Message

- In this large single-center study, EUS detected the tumor in 100% of distal and 83% of proximal cholangiocarcinomas ($P < .01$). The sensitivity of EUS-guided FNA was significantly higher in distal than in proximal cholangiocarcinoma (81% vs 59%, respectively; $P = .04$).
- EUS had a sensitivity of 53% and specificity of 97% for detecting unresectability in cholangiocarcinoma. EUS is complementary to CT or magnetic resonance imaging for detecting unresectability in cholangiocarcinoma.

MATERIALS AND METHODS

Patients

This study was approved by the Indiana University Institutional Review Board. Using prospectively updated cytology and endoscopy databases, we identified all patients who underwent EUS at our institution between May 2003 and December 2009 for a known or suspected bile duct stricture or tumor. All included patients had CCA diagnosed based on surgical pathology or unequivocal cytology obtained during EUS-FNA or brush cytology in addition to clinical and imaging findings consistent with CCA. All patients with benign, indeterminate, or metastatic biliary strictures or pancreatic adenocarcinoma were excluded. When surgical resection was performed or attempted, surgical pathology was used to differentiate distal CCA from pancreatic head adenocarcinoma. When nonoperative management was pursued, EUS, MRI, and ERCP studies were reviewed to differentiate distal CCA from pancreatic head tumors. In this situation, we considered the tumor to be distal CCA based on the following criteria: (1) EUS demonstrating a tumor that is confined to the bile duct and a pancreatic duct that is normal; (2) a cholangiogram demonstrating a malignant-appearing stricture in the common bile duct; (3) a normal pancreatogram (if available); and (4) cytology (obtained by EUS-FNA or brushing during ERCP) positive for adenocarcinoma.

Medical records of enrolled subjects were reviewed, and procedural indications, previous radiographic data, patient demographics, EUS examination results, clinical outcomes, and follow-up data were abstracted.

EUS-FNA techniques

Written informed consent was obtained from each patient before the procedure. Patients received conscious sedation with appropriate cardiorespiratory monitoring. All procedures were performed by 1 of 5 experienced attending endosonographers. EUS-FNA was performed with the Olympus GF-UC140P linear-array echoendoscope (Olympus Medical Systems, Center Valley, Pa, USA) and a 22-gauge FNA needle (Cook Endoscopy, Winston-Salem, NC, USA). Doppler examination was performed before FNA to ensure the absence of intervening vascular structures along the anticipated needle path and to evaluate the visualized mass for any invasion into the portal vein, gastroduodenal artery, or hepatic artery (Fig. 1). A cytopathologist was available on site for preliminary interpretation of all procedure findings. Each sample aspirated was processed to 2 smear preparations: One slide was air dried and stained with a modified Giemsa stain for rapid on-site interpretation, and the other slide was alcohol fixed and stained by the Papanicolaou method. As part of our routine care, patients were contacted by telephone 48 hours after EUS to check for any complications.[18]

Any specimen interpreted as atypical or nondiagnostic was considered to be negative for malignancy, whereas specimens reported as adenocarcinoma or highly suspicious for malignancy were considered to be positive for malignancy. When surgical resection was attempted after EUS-FNA, histopathology was considered to be the reference standard for the presence of malignancy. When nonoperative management was pursued, the unequivocal cytology reports of adenocarcinoma (from brushing or EUS-FNA) and subsequent clinical course were considered to be the reference standard for the diagnosis of CCA.