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ORIGINAL ARTICLE

Diagnostic accuracy of endoscopic ultrasonography in patients with inconclusive magnetic resonance imaging diagnosis of biliopancreatic abnormalities

Rasoul Sotoudehmanesh · Morteza Khatibian · Mohammad-Reza Ghadir · Mohammad Bagheri · Amir Pejman Hashemi-Taheri · Nahid Sedighi · Ali Ali-Asgari · Fatemeh Zeinali · Shadi Shahraeeni · Shadi Kolahdoozan

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Abstract
Aim To determine the sensitivity and specificity of endoscopic ultrasonography (EUS) in patients with inconclusive magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/MRCP) in pancreatobiliary abnormalities.
Methods During 10 months, patients with pancreatobiliary diseases referred to endoscopic retrograde cholangiopancreatography (ERCP) because of inconclusive MRI/MRCP diagnosis were scheduled to undergo endoscopic ultrasonography. Patients were divided into four major groups: patients with (i) resectable periampullary neoplasms who were referred to a surgeon, (ii) unresectable periampullary cancer who underwent ERCP for biliary stenting, (iii) bile duct stone who were referred to ERCP for stone extraction, and (iv) normal pancreatobiliary tract. Reference standards for comparison were ERCP, surgery, a biopsy confirming malignancy, or the clinical course during follow up (at least 12 months) in cases without evidences of malignancy.
Results One hundred and seven patients (51 men; mean [SD] age 60.0 [15.5]) were included in the study. Final diagnoses were common bile duct (CBD) stone (n=24), periampullary neoplasms (n=46), others (n=23) and no pathologic findings (n=14). EUS determined the staging for clinical decision-making in 47 patients with neoplasms which showed that tumors in 34 patients (79.1%) were unresectable (advanced stage). After EUS, 47 patients (43.9%) did not require ERCP. The accuracy of EUS for the diagnosis of CBD stone and periampullary neoplasms were 96.3% and 99.1%, respectively.
Conclusions EUS is a useful modality in cases of inconclusive MRI/MRCP indicating pancreatobiliary disorders.

Keywords Cholangiopancreatography · Pancreatobiliary neoplasms · Sensitivity · Specificity

R. Sotoudehmanesh (✉) · M. Khatibian · M. Bagheri · A. Ali-Asgari · F. Zeinali · S. Shahraeeni · S. Kolahdoozan
Digestive Disease Research Centre, Shariati Hospital, Tehran University of Medical Sciences, 14117-13135-North Kargar, Ave. Shariati Hospital, Tehran, Iran
e-mail: setoodeh@ams.ac.ir

M.-R. Ghadir
Gastroenterology Department, Qom University of Medical Sciences, Qom, Iran

A. P. Hashemi-Taheri · N. Sedighi
Radiology Department, Shariati hospital, Tehran University of Medical Sciences, 14117-13135-North Kargar, Ave. Shariati Hospital, Tehran, Iran

Introduction

Accurate methods for the diagnosis of pancreatobiliary disorders in patients with obstructive jaundice are important both for surgeons and for endoscopists. Transabdominal ultrasonography (TUS) permits distinction between extrahepatic and intrahepatic cholestasis, but has a low sensitivity (50% to 80%) in identifying the etiology of biliary abnormality [1–3]. Hence, in many situations, it is necessary to use other complementary imaging techniques such as endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT), endoscopic ultrasonography (EUS) or magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/MRCP), that increase the diagnostic accuracy to 95% to 99% [3].

ERCP is the gold standard for study of the biliopancreatic region. Nevertheless, ERCP is associated with significant complication rates [4]. In addition, neoplasms in the uncinate process, accessory duct, and tail of the pancreas may not be detected. Even when the neoplasm is suspected at ERCP, it cannot be staged by this modality. In such a situation, EUS and MRI/MRCP have emerged as two low-risk diagnostic tools with acceptable performance for the diagnosis of pancreatobiliary disorders. EUS with FNA is a minimally invasive modality for imaging the pancreaticobiliary system, with no significant complications [5].

MRI/MRCP is a non-invasive technique that provides projectional images similar to those of ERCP without administration of contrast agents. Recent technical developments have led to notable improvements in this field with a clinical acceptance by gastroenterologists. However, there are some instances wherein MRI/MRCP is inconclusive since the findings do not correlate with other clinical and laboratory findings. Therefore, an additional diagnostic imaging is required before therapeutic decision-making. Examples of such situations include: diagnosis of CBD stone in a patient with significant weight loss or the diagnosis of periampullary neoplasm (pancreatic head, ampullary and distal CBD neoplasms) in the absence of jaundice.

To the best of our knowledge, the role of EUS in inconclusive (questionable but not negative) MRI/MRCP findings in pancreatobiliary abnormalities, has not been studied and patients with inconsistent clinical and imaging results after MRI/MRCP may be considered for ERCP. The aim of our study was to determine the sensitivity and specificity of EUS in patients with inconclusive MRI/MRCP in various pancreatobiliary abnormalities.

Methods

This study was conducted at the Digestive Disease Research Center, Shariati Hospital (a tertiary care university-affiliated hospital) from May 2006 to March 2007. Patients were eligible for the study if: (1) biochemical abnormalities (alkaline phosphatase or gamma glutamyltranspeptidase more than twice the normal value and serum bilirubin >2 mg/dL) or dilated bile ducts at abdominal ultrasonography or CT scan (common bile duct diameter >7 mm in patients with gall bladder in situ, and >9 mm in patients with previous cholecystectomy) were present; (2) the patient had undergone MRI/MRCP; and (3) diagnostic ERCP was requested by a gastroenterologist, because a definite diagnosis was not evident due to inconsistency of clinical, laboratory and imaging results or MRI/MRCP were inconclusive. Exclusion criteria were history of surgery with gastro-enteric anastomosis (Roux-en-Y gastrojejunostomy or Whipple's procedure), which made a successful EUS and ERCP unlikely, the presence of unresectable tumor (metastasis, vascular invasion) and refusal of informed written consent.

The study was approved by the institution Review Board of the Digestive Diseases Research Center of Tehran University of Medical Sciences, according to the declaration of Helsinki. Informed consent was obtained according to the guidelines of the institute.

Consecutive patients underwent EUS prospectively were then divided into four major groups: patients with (i) resectable periampullary neoplasms who were referred to a surgeon, (ii) unresectable periampullary cancer who underwent ERCP for biliary stenting and EUS-FNA for pancreas unresectable tumors, (iii) bile duct stone who were referred to ERCP for stone extraction, and (iv) normal pancreatobiliary tract.

A composite reference standard was defined according to the subsequent clinical decision and included the results of one of the following: ERCP, surgical report, a histologic specimen confirming malignancy (brush cytology, ampullary neoplasm biopsy, surgical specimen or cytology obtained by EUS-FNA) or the clinical course during follow up (at least 12 months) in cases without histologic proof of malignancy. All clinical, laboratory and imaging information (except for MRI/MRCP findings and images) were provided to the endosonographer and others involved in the reference standard procedures, except for the results of EUS, which were withheld from the latter group. The mean (SD) time between EUS and MRI/MRCP was 11 (13) days (range 1–73 days). ERCP was done 1–5 days after EUS.

All EUS procedures were performed, by an experienced gastroenterologist, using a radial echoendoscope (GF-UMQ 240 Olympus Optical Co Ltd, Tokyo, Japan) with a frequency of 7.5 MHz. Follow up was done by a research fellow for the results of ERCP, surgery and patients considered for clinical follow up. Study data were prospectively collected using tailored data-entry forms. The final diagnosis of EUS was compared with the defined reference standards.

Quantitative variables were presented with mean (SD). Sensitivity, specificity, positive and negative predictive values and accuracy and their 95% confidence intervals (95% CI) were calculated using standard formulae. The target conditions considered for statistical analysis were: correct diagnosis of any cause of obstruction, diagnosis of malignancy or diagnosis of CBD stone. All calculations were performed using STATA statistical software (STATA 8.0; STATA, College Station, Texas, USA).

Results

From May 2006 to March 2007, 120 patients with inconclusive results after MRI/MRCP were referred to our center for ERCP. Of these, 13 were excluded because of unwillingness to

provide consent; 107 patients were enrolled in the study. No patient had a history of surgery with gastro-enteric anastomosis. Demographic, clinical and laboratory features of patients are presented in Table 1. MRI/MRCP diagnosis was confirmed by the reference standard in 28 cases (60.9%) with neoplasms and 17 cases (70.8%) with CBD stones.

Figure 1 shows the flow diagram of the study. A cross tabulation of the final diagnoses of EUS by results of the reference standard is presented in Table 2. The observed neoplasms ($n=46$) included: 15 pancreatic, 15 distal CBD, 10 ampullary, one proximal CBD and 5 Klatskin tumors.

No complications were observed after EUS. Fifty-one patients were referred for ERCP, and 3 cases (5.9%) developed post-ERCP pancreatitis.

Table 3 shows estimates of diagnostic accuracy of EUS for various target conditions associated with biliary obstruction.

EUS was used for the staging of suspicious neoplasms in 47 patients with neoplasms and showed that 34 patients (79.1%) were unresectable (advanced stage). After performing EUS, 47 patients (43.9%) did not require ERCP, because the diagnosis of normal CBD with or without gallbladder (GB) stone, or resectable periampullary neoplasm were referred for surgery (Fig. 1). Fifty-eight patients (56.1%) needed therapeutic ERCP for CBD stone extraction or biliary stenting for unresectable pancreatobiliary neoplasms.

Table 1 Demographic, clinical, laboratory and MRI/MRCP findings

Parameters	
Male sex (*n* [%])	51 (47.7)
Age (mean [SD])	60.0 [15.5]
Disease onset, months (mean [SD])	4.8 (5.8)
Previous cholecystectomy (*n* [SD])	25 (23.4)
Clinical findings (*n* [SD])	
Abdominal pain	76 (71.0)
Jaundice	54 (50.5)
Fever	34 (31.8)
Weight loss	53 (49.5)
Pruritus	38 (35.5)
Ascites	4 (3.7)
AST (mean [SD])	85.8 (120.5)
ALT (mean [SD])	111.6 (144.5)
ALP (mean [SD])	668.8 (589.5)
Findings on MRI/MRCP (*n* [SD])	
Neoplasm	33 (30.8)
CBD stone	33 (30.8)
Other benign pathologies*	34 (31.8)
Normal	7 (6.5)

AST Aspartate aminotransferase; *ALT* Alanine aminotransferase; *ALP* Alkaline phosphatase; *CBD* Common bile duct

* GB stone alone, sphincter of Oddi dysfunction, chronic pancreatitis and congenital biliary cyst, Klatskin's tumor

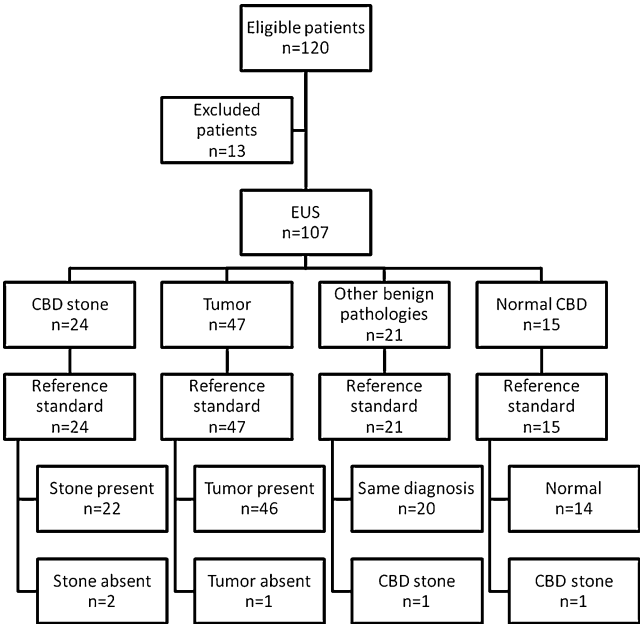

Fig. 1 Flow diagram of the study participants. *CBD* Common bile duct; *EUS* Endosonography

Discussion

This study showed the usefulness of EUS in patients with inconclusive MRI/MRCP in pancreatobiliary abnormalities especially in patients with periampullary neoplasms.

MRI/MRCP is a non-invasive option for the diagnosis of biliary obstruction. In addition, MRI/MRCP is as accurate as ERCP for detecting CBD stone (sensitivity 80% to 100%, specificity 85% to 100%) [6–13]. However, MRI/MRCP have limitations. Stones larger than 4 mm are readily seen but cannot be differentiated from filling defects such as blood clots, neoplasm, sludge, flow artifacts, biliary air or parasites [14]. There is difficulty in the diagnosis of small bile duct stones [15, 16], especially in the setting of non dilated ducts [17].

Table 2 Final diagnoses of endosonography (EUS) by the reference standard

EUS Reference standard	CBD stone	Neoplasms	Other benign pathologies[a]	Normal CBD[b]
CBD stone	22	0	1	1
Neoplasms	0	46	0	0
Others[a]	2	1	20	0
Normal CBD	0	0	0	14

CBD Common bile duct

[a] GB stone alone, sphincter of Oddi dysfunction, pancreatic cyst, congenital biliary cyst

[b] Completely normal, or gallbladder stones with normal CBD

Table 3 Estimates of diagnostic accuracy of EUS for recognizing causes of biliary obstruction

Statistic	Value (%)	95% CI[a]
Diagnosis of the neoplastic bile duct obstruction		
Sensitivity	100	92.3–100[b]
Specificity	98.4	91.2–99.9
Positive predictive value	97.9	88.7–99.9
Negative predictive value	100	94.0–100[b]
Accuracy	99.1	94.9–99.9
Diagnosis of common bile duct stone		
Sensitivity	91.7	73.0–99.0
Specificity	97.6	91.6–99.7
Positive predictive value	91.7	73.0–99.0
Negative predictive value	97.6	91.6–99.7
Accuracy	96.3	90.7–99.0
Correct diagnosis of any cause of obstruction[c]		
Sensitivity	98.9	93.9–99.9
Specificity	77.8	52.4–93.6
Positive predictive value	95.7	89.2–98.8
Negative predictive value	93.3	68.1–99.8
Accuracy	95.3	89.4–98.5

[a] 95% confidence intervals; [b] one-sided, 97.5% confidence interval; [c] estimates were calculated for any abnormality in the CBD (stone, neoplasm or other benign pathology) versus normal CBD

A number of studies have compared the accuracy of EUS to transabdominal ultrasonography, ERCP, CT, and MRI/MRCP for detecting CBD stones [18–22]. In most reports, the sensitivity of EUS ranged from 88% to 97% with a specificity of 96% to 100%, which is comparable to that of ERCP. In our study, the sensitivity and specificity of EUS for detection of CBD stone in patients with inconclusive diagnosis of CBD stone at MRI/MRCP was 91.7%, and 97.6%, respectively.

Two of the 24 cases with CBD stone diagnosed by EUS showed no stone in ERCP. The reason may be the lag time between doing ERCP and EUS. ERCP was done 1–5 days after EUS. During this time period the stones might have passed from CBD through the papilla. Results of another study also confirmed these results [23].

ERCP found CBD stones in 70.8% of patients initially diagnosed as CBD stone by MRI/MRCP. This shows that ERCP may be the next step in the management of patients with an inconclusive MRI/MRCP with the diagnosis of CBD stone.

After EUS, 47 patients (43.9%) did not require ERCP; these patients were found to have normal CBD with or without GB stone or resectable periampullary neoplasm, and were referred for surgery. A normal EUS might obviate the need for ERCP in a substantial number of patients with borderline indications for ERCP. This is especially true in patients with low or intermediate risk for having CBD stone [24]. Thus, EUS before ERCP could identify the cases that could benefit from therapeutic ERCP. In this study 56.1% needed therapeutic ERCP for CBD stone extraction or biliary stenting because of unresectable pancreatobiliary neoplasms. Also EUS determined the staging of the tumor in 47 patients with neoplasms and showed that 34 patients (79.1%) were unresectable (advanced stage).

MRI/MRCP often shows an unexplained dilated bile duct; this finding is interpreted as "cannot exclude peri-ampullary pathology/neoplasia" [6, 25]. Moreover even if MRI/MRCP could determine the probable neoplastic causes of biliary obstruction, it is not reliable for locoregional staging of the neoplasm.

The main question in the patients with malignant biliary obstructions is whether or not these neoplastic processes are resectable. In the present study, MRI did not report staging and resectability of the probable neoplasm in any of the cases. In pancreatic cancer, MRI/MRCP do not offer significant advantages over CT, because of movement artifacts, intestinal gas opacities and a resolution inferior to helical CT [26].

In ampullary and distal CBD neoplasms, both ERCP and MRI/MRCP have similar imaging findings (dilation of biliary tract) without reliable staging of the neoplasms. Although MRI/MRCP are comparable with ERCP in terms of imaging capabilities, its diagnostic accuracy is not superior to that of ERCP. There remains a need for other imaging tests (e.g. EUS) or tests that provide histology confirmation (biopsy from ampullary neoplasm or brush cytology for biliary neoplasms by ERCP or EUS/CT-guided aspiration-biopsy) [27].

There is enough evidence that EUS is the most accurate modality available to assess the T-stage of peri-ampullary neoplasms, which is critical for planning surgical intervention [25, 28–35]. It has been shown in a tertiary referral center that the percentage of patients requiring MRI/MRCP before ERCP is relatively small [36].

In conclusion, our study showed that patients with a doubtful MRI/MRCP diagnosis of CBD stone benefit from ERCP. We recommend EUS in cases of inconclusive MRI/MRCP indicating other pancreatobiliary disorders. Further studies are clearly needed to identify the optimal combination of imaging tests for various pancreaticobiliary indications.

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