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Clinical Impact of Endoscopic Ultrasonography in Pancreaticobiliary and Upper Gastrointestinal Diseases

Knut Johnsen[1*,3], **Rolv-Ole Lindsetmo**[2] **and Jon Florholmen**[1,3]

[1]*Department of Gastroenterology, Institute of Clinical Medicine, University of Tromsø, Norway*

[2]*Department of Gastrointestinal Surgery, University Hospital of North Norway, Norway*

[3]*Research Group of Gastroenterology and Nutrition, Institute of Clinical Medicine, University of Tromsø, Norway*

[*]**Corresponding author:** Knut Johnsen, Department of Gastroenterology, Research Group of Gastroenterology and Nutrition, Institute of Clinical Medicine, University of Tromsø, Norway, E-mail: knut.johnsen@finnmarkssykehuset.no

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Abstract

Objective: Endoscopic ultrasonography (EUS) is one of the most significant advances for imaging the gastrointestinal tract wall and contiguous organs in the past 20 years. This method has been extensively evaluated, with special emphasis on specificity and sensitivity. However, there are few publications on the clinical impact of EUS. The objective of the study was to evaluate the sensitivity (Se), specificity (Sp), positive and negative predictive values (PPV and NPV) and the accuracy (AC) of endoscopic ultrasonography (EUS) in a clinical setting and study the clinical impact of EUS in pancreaticobiliary and upper gastrointestinal diseases.

Materials and methods: EUS was performed in 197 patients with clinical signs indicating pancreaticobiliary or upper gastrointestinal diseases. Both radial and linear multifrequency scanners were available. Parallel examinations were performed by external ultrasonography, gastroduodenoscopy, endoscopic retrograde pancreatography, computed tomography and body magnetic resonance imaging. To evaluate the clinical impact of EUS, two clinicians (specialities in medical and surgical gastroenterology) analysed the data, with an observation time of at least 6 months after the clinical event.

Results: The overall accuracy, sensitivity and NPV of EUS were 100%, 95% and 100%. The overall clinical impact was 35%. After the EUS examination, the diagnoses were down-graded in 12% of cases and up-graded in 23%. The NPV was 100%.

Conclusions: EUS appears to have a high clinical impact and exhibits a high NPV. These observations justify using EUS as a first-line tool in the diagnosis of pancreaticobiliary and upper gastrointestinal diseases.

Keywords: Endoscopic ultrasonography; EUS; Clinical impact; Test performance

Introduction

Endoscopic ultrasonography (EUS) has become a widely used diagnostic method in gastrointestinal diseases in the last 20 years. EUS is one of the most powerful imaging methods for upper gastrointestinal diseases, with high sensitivity (SE), specificity (SP) and diagnostic accuracy (AC) compared with other diagnostic methods, e.g., spiral computed tomography (CT) and magnetic resonance imaging (MR) [1]. EUS is also the only clinically used method that permits the visualisation of the gut wall in detail with high accuracy [1,2]. In addition, sectorial linear EUS allows for the guided fine-needle aspiration (EUS-FNA) of lymph nodes, mediastinal masses, anastomotic relapses and pancreatic tumours. According to the literature, the global sensitivity of this technique varies between 76% and 91%, the specificity varies from 84% to 100%, and the accuracy varies from 78-94% [1,3].

Based on these reports, guidelines for the appropriate use of EUS in upper gastrointestinal diseases are now available [1]. Despite the recommendations, few studies have evaluated the clinical impact of EUS on pancreaticobiliary and upper gastrointestinal diseases [4].

The availability of EUS in different countries varies greatly. In Scandinavia, EUS is limited to only a few centres. At our hospital, the University Hospital of Northern Norway (UNN), we have performed EUS to assess upper gastrointestinal diseases since 2002.

The aims of this prospective study were to compare EUS with other diagnostic methods, such as helical CT, MR and endoscopic retrograde cholangiopancreatography (ERCP), for different upper gastrointestinal diseases and assess the SE, SP, PPV, NPV and AC.

Methods

Patients referred to the Gastrosurgical and Gastromedical Departments of the University Hospital of Northern Norway (UNN), Tromsø, Norway, from August 2002 to February 2003 were included in the study. The patients had various upper abdominal complaints and were referred for gastroduodenoscopy and/or further imaging diagnostics (external ultrasound examination (US), CT, MR and ERCP). The indications for EUS are listed in Table 1. Fifty patients had malignancy in the upper gastrointestinal tract or pancreas, and EUS was performed for both diagnostic and staging purposes (Table 2).

EUS examination was performed prospectively but as an open study. The study was planned as an evaluation of a new diagnostic method in a prospective open design. EUS was performed in addition to well-established methods, such as US, CT, MR, ERCP, external ultrasound biopsies, laparoscopy and laparotomy, and all examinations were performed for well-established clinical indications.

Indication for EUS
Upper abdominal pain and/or weight loss
Cholestasis of unknown reason
Control of suspicious findings by other methods
Staging of known cancer

Table 1: Indications for EUS.

Diagnoses in groups			
Diagnosis	**Female N (%)**	**Male N (5)**	**Total N (%)**
OGDs	16 (41)	23 (59)	39 (21)
CLT	17 (57)	13 (43)	30 (16)
CP	9 (41)	13 (59)	22 (12)
PBM	10 (50)	10 (50)	20 (11)
OD*	32 (59)	22 (41)	54 (29)
N	12 (55)	10 (45)	22 (12)
Total	96 (51)	91 (49)	187 (100)

OGDs: Oesophageal, gastric and duodenal diagnoses (Oesophageal cancer n: 21, gastric cancer n: 9);

CLT: Cholelithiasis (CBD stones n: 18, cholecystolithiasis n: 12); CP: Chronic pancreatitis;

PBM: Pancreaticobiliary malignancy; OD: Other diagnosis; N: Normal

*Included the following diagnoses: Peptic structures, lymphadenopathies, including lymphomas and metastasis, gastric folds, cystic lesions, polyps, and extraintestinal impressions

Table 2: EUS for diagnostic and staging purposes.

The Pentax EG-363O UR radial echo endoscope was used. This study was carried out at the gastroenterological laboratory at UNN. The examination was performed under moderate intravenous sedation with midazolam and often in combination with pethidine hydrochloride. A gastroenterologist (KJ) who was moderately skilled in EUS performed the examinations. He had performed approximately 200 EUS examinations at the start of the study, most with guidance and/or controlled with other imaging methods or laparotomies. However he was very skilled in external ultrasound, with over 10 years experience.

All US, EUS, CT, MR and ERCP diagnoses were registered separately as initially described. The final diagnosis (gold standard diagnosis) was independently made by a gastrointestinal surgeon (ROL) and a gastrointestinal internist (JF) after the evaluation of all available clinical information (patient data files, endoscopy, US, CT, MR, ERCP, operation files, etc.) and after a follow-up observation period from 8-12 months. When the final diagnoses of the two clinicians disagreed, a consensus was made after re-evaluation of the data. Based on the final diagnosis, the test performance (i.e., the SE, SP, PPV, NPV and AC) of EUS and CT was calculated and compared.

Finally, the clinical impact was individually assessed by the two clinicians in the following manner. 1. Down-grading: EUS excluded suspected diagnoses (false-positive findings with other test methods). 2. Up-grading: EUS confirmed the final diagnoses (gold standard) with false-negative findings with other tests. 3. Negative impact: incorrect diagnosis due to false-positive or false-negative EUS. Twenty-two (11%) patients with EUS-defined chronic pancreatitis were initially excluded from the study due to the lack of a gold standard, and these patients were re-evaluated 10 years later. Follow-up data were collected from the hospital records to obtain a complete overview of all chronic pancreatitis subjects.

Statistics

Descriptive statistics were used to describe differences between various parameters. Test performance analyses were performed using standard 2 × 2 tables. The confidence interval (CI) was computed for the test performance.

Results

In total, 197 patients were included in the study. Ten EUS examinations were unsuccessful (5%). Twenty-two (11%) patients with EUS-defined chronic pancreatitis were excluded from the initial study. The remaining 165 patients were evaluated according to the protocol and included 87 women (53%) and 78 men (47%), with a mean age of 58 years (range 17-88 years).

Ninety-five (48%) patients were examined with CT. Only 26 (13%) patients were examined with MR. The rest of the patients were examined by US, gastroscopy or ERCP or were surgically treated. One complication (0.5%), an oesophageal perforation, was observed in an 82-year-old woman with a large oesophageal hernia. The final diagnoses in the groups (gold standard diagnosis) are summarised in Table 2. The test performance was calculated for EUS for the total sample (N: 165) and the 95 patients examined with CT (Table 3). The test performance was not calculated for MR due to the small number of evaluated patients. The SE, NPV and AC for EUS were 100%, 100% and 95% compared with 56%, 52% and 67% for CT, respectively. Table 4 provides a summary of the clinical impact (impact down-grade, impact up-grade and negative clinical impact) in the entire study according to the group diagnoses. The overall positive clinical impact was 35%, and impact down-grade and impact up-grade were observed in 12% and 23% of cases, respectively. The same table also shows the impact results for the different diagnostic subgroups. The highest clinical impacts were obtained for cholelithiasis (CLT) and oesophageal, gastric and duodenal diagnoses (OGDs), with 57% and 49%, respectively. The clinical impact on pancreaticobiliary malignancy (PMT) was only 25%. Table 5 summarises all the reasons for the negative clinical impacts (false-positive EUS). EUS found CBD stones in three patients, but this diagnosis was disproved by ERCP performed 7-40 days after the EUS examination. The 10-year clinical follow-up revealed that 3 of these 22 chronic pancreatitis patients had died, but none of these deaths were due to chronic pancreatitis. Three patients with moderate and severe chronic pancreatitis had not worsened, and the remaining 16 patients initially diagnosed as light chronic pancreatitis were not examined for chronic pancreatitis.

Summary of results		
	EUS %, (N: 165)	CT %, (N: 91)
Sensitivity	100 (CI: 95-100)	56 (CI: 41-67)
Specificity	87 (CI: 78-93)	88 (CI: 73-97)
Positive predictive value	90 (CI: 82-93)	89 (75-97)
Negative predictive value	100 (94-100)	52 (38-65)
Accuracy	94 (87-97)	67 (56-76)

Table 3: Summary of results.

Results: Clinical impact (N: 165)					
Clinical diagnoses	No impact (%)	Impact down-grade (%)	Impact up-grade (%)	Negative clinical impact (%)	Total (n; %)
OGDs	18 (46)	3 (8)	16 (41)	2 (5)	39 (24)
PBM	13 (65)	1 (5)	4 (20)	2 (10)	20 (12)
CLT	10 (33)	0	17 (57)	3 (10)	30 (18)
OD	43 (80)	10 (18)	0	1 (2)	54 (33)
N	15 (68)	7 (32)	0	0	22 (13)
Total	99 (60)	20 (12)	38 (23)	8 (5)	165
OGDs: Oesophageal, gastric and duodenal diagnoses (Oesophageal cancer n: 21, gastric cancer n: 9);					
CLT: Cholelithiasis (CBD stones n: 18, cholecystolithiasis n: 12);					
CP: Chronic pancreatitis;					
PBM: Pancreaticobiliary malignancy; OD: Other diagnosis;					
N: Normal					

Table 4: Clinical impact.

Reasons for false-positive EUS		
EUS diagnosis	Final diagnosis	Patients (N: 8)
Common bile duct stone	No common bile duct stone n: 3	3
Pancreatic cancer	Chronic pancreatitis n: 2	2
Oesophageal cancer	Inflammatory stricture n: 3	3

Table 5: Reasons for false-positive EUS.

Discussion

EUS has been evaluated in several studies with calculations of test performance and clinical impact analyses, both with great variation in study design [1,3,5]. Thus, comparison between different studies is not easy [4]. In our study, we defined the clinical impact of EUS confirmation of the final diagnoses for false-negative findings by other test methods or false-positive findings by other test methods, termed up-grade and down-grade, respectively. When EUS was false positive or negative, the clinical impact was defined as a negative clinical impact. However, in this study, we did not have any false-negative EUS results.

Our study showed a total clinical impact of 35%, with impact down-grade in 12% of cases and impact up-grade in 23%, indicating that diagnoses were changed in 35% of cases based on the EUS results. The clinical impact of EUS in our study is much lower than in the majority of other studies. Ainsworth et al. [3] and Nickl et al. [6] showed a clinical impact (changed treatment plan) of about 75%. However, two single-centre studies reported nearly the same impact results as our study [5,7]. The negative impact in this study was 5% due to false-positive EUS. Common bile duct stones were over-diagnosed in three cases, as shown by ERCP, which was performed 3 to 40 days after the EUS examination. These false positives in our study could be due to the spontaneous migration of bile duct stones, which has been reported in 21% of cases within one month [8]. A French study [9] showed spontaneous migration in 18% of cases when EUS was performed 6 hours to 3 days after symptom onset, which increased to 36% at 3-27 days. Two cases with focal chronic pancreatitis were misinterpreted as pancreatic tumours. Follow-up excluded malignancy. Differentiating pancreatitis from cancer is difficult using not only EUS imaging alone but also EUS fine-needle aspiration (FNA) [10]. Three cases with severe esophagitis with strictures were suspected as malignant cases. Surface biopsies were normal, but the slow healing rate suggested malignancy, which was excluded during follow-up.

The relatively low clinical impact in our study can be due to the study design. In the beginning we had wide indications for EUS to get lot of experience on short time. Stronger indications had surely increased the clinical impact.

In this study, we documented significantly better accuracy, sensitivity and NPV of EUS compared with CT in the diagnosis of upper gastrointestinal tract and pancreatic diseases, which is comparable with other studies [1]. Our study revealed a 100% NPV for the entire study. EUS has been shown to have high diagnostic accuracy for diagnosis groups, as in this study [1]. Several studies have shown NPVs for EUS up to 100% in the diagnosis and staging of pancreatic cancer [11-13]. In our opinion, EUS is particularly suitable for excluding false-positive pathological findings shown by other tests. Both the SE and NPV for all diagnoses in this study were high, and they were higher than those reported in another comparable study [3]. This finding could be due to the size of the study and because of test review bias, i.e., the EUS investigator was not systematically blinded to the results from other examinations, thus possibly influencing the categorisation of false negatives as test positives and false positives as test negatives, resulting in the overestimation of Se and Sp. The test performances are high in our study probably due to relatively small number of patients included and due to the fact that all patients with chronic pancreatitis were excluded from the further study.

All patients with EUS-defined chronic pancreatitis were initially excluded from the study due to lack of a gold standard, but these patients were re-evaluated 10 years later to evaluate the progression rate for suspected chronic pancreatitis by EUS. None of these chronic pancreatitis clients diagnosed by EUS had progressed clinically in 10 years. The diagnosis of definite chronic pancreatitis is made if, among other signs, there are proven changes in the duct system by ERCP. Comparative studies between EUS and ERCP have been performed in patients with the suspicion of chronic pancreatitis, revealing good correlation within normal and severe pancreatitis [14,15]. However, diagnosis is difficult when EUS shows parenchymal changes but ERCP is normal. For this group, the clinical significance of EUS is unknown.

In our study, the progression rate for EUS-suspected chronic pancreatitis was not clinically traceable, which is comparable to another study that had a shorter follow-up period [16]. The rate of serious complications after EUS in our study was 0.5%, which is comparable to other studies [3,6].

This study was conducted in a relatively short period after the introduction of EUS at our hospital to evaluate our skills. In the beginning, we performed relatively few EUS-FNAs. By contrast, EUS-FNA examinations currently comprise a significant number of our EUS examinations. We are now planning a new EUS impact study after 12 years' experience with EUS to evaluate the position of EUS among the available gastrointestinal diagnostic modalities.

In summary, this survey demonstrates that EUS appears to have a high clinical impact in the diagnosis of pancreaticobiliary and upper gastrointestinal diseases. Furthermore, the survey reveals a high sensitivity and NPV for EUS. This justifies EUS as a particularly suitable tool for excluding the suspicious findings of other examinations.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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