

Does the Advent of Endoscopic Ultrasound (EUS) Sound the Death Knell for Endoscopic Retrograde Cholangiopancreatography (ERCP)?

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Abstract

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has been the premier diagnostic and therapeutic endoscopic procedure in the management of pancreatic and biliary diseases (PBD). The use of endoscopic ultrasound (EUS), including EUS-guided fine needle aspiration (FNA), of pancreatic and biliary tumours has become more widely available in the last decade and has gradually replaced diagnostic ERCP. Together with EUS, other imaging modalities like magnetic resonance cholangiopancreatography (MRCP) have resulted in a decrease in the number of ERCPs. With the advent of interventional EUS, ERCP is at risk of being completely eclipsed. **Methods:** A search of all relevant articles on EUS and ERCP from Medline and peer-reviewed journals. **Results:** This review article examines the exact place of ERCP and EUS and their relative contributions in the management algorithm of PBD. **Conclusion:** Although diagnostic EUS, including EUS-guided FNA, is well established in the evaluation of PBD, interventional EUS is still in its infancy and its true potential is unknown. Therefore, therapeutic ERCP still has a vital, albeit smaller role to play in the treatment of pancreatic and biliary diseases.

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has been the primary method of diagnosing and treating many pancreatic and biliary diseases (PBD) over the last 3 decades. The development of endoscopic ultrasound (EUS) since its introduction in the early 1980s has added a new dimension to the treatment of PBD.

EUS has progressed from a solely imaging modality to one that can provide a tissue diagnosis by fine needle aspiration (FNA) and also be able to perform interventional techniques. EUS is now performing the role that was once filled by diagnostic ERCP. After many years of being limited to academic centres, EUS is now practised more widely. Therefore, training issues and the availability of EUS facilities need to be addressed.

We attempt to review the current literature on EUS and ERCP and answer whether EUS can fully replace ERCP, essentially to address the concern that ERCP may be dead.

Is There a Role for Diagnostic ERCP?

There has been a steady decrease in diagnostic ERCP in the previous decade. The use of ERCP in PBD imaging has evolved from a purely diagnostic procedure in the early 1970s to a largely therapeutic one in 2005. In the past, many patients were subjected to ERCP with marginal indications, despite the fact that diagnostic ERCP carried the risk of morbidity in 1.4% to 3.2% and the potential of mortality.^{1,2}

With newer and safer modalities to evaluate the pancreaticobiliary system, like helical (spiral) computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP) and EUS, the indiscriminate use of diagnostic ERCP would be tantamount to courting malpractice litigation.

However, diagnostic ERCP would probably not disappear completely as it still provides an extremely accurate delineation of the pancreaticobiliary system. Two previous studies clearly show that the substitution of EUS for

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diagnostic ERCP is entirely feasible and provides a much safer alternative.^{3,4}

In an era of evidence-based medicine, we have begun to look at the risk-benefit data of procedures like ERCP. Clearly, to avoid or at least reduce complications, especially pancreatitis, one must avoid high risk/low yield procedures [example, biliary manometry in presumed sphincter of Oddi dysfunction (SOD) Type III]⁵ and concentrate on low risk/high yield procedures like removal of common bile duct (CBD) stones.

Therefore, the rate of diagnostic ERCP should be lower than 10% of ERCP procedures performed due to the availability of EUS and MRCP.^{6,7}

The Potential for Substitution of EUS for ERCP

EUS has developed a niche for itself in the evaluation of pancreaticobiliary diseases (PBD) such as choledocholithiasis, pancreatic and biliary cancers, and cystic lesions of the pancreas.

EUS has evolved from a pure research tool or mere laboratory curiosity to a clinically useful procedure with a major impact on patient management. In studies, referring physicians have found the information provided by EUS to be useful in 55% to 65% and resulted in a change in management in 6% to 75%.⁸⁻¹⁰ Clearly, referring physicians appreciate the impact of EUS and the information provided by the procedure in a differing manner. This could be due to an incomplete understanding of the indications and the true potential of EUS.

Choledocholithiasis

ERCP has long been considered the most accurate method to detect CBD stones. Several studies have confirmed that EUS and ERCP have very similar accuracy rates for detecting CBD stones (over 90% accuracy).¹¹⁻¹³

Based on clinical and biochemical criteria together with transabdominal ultrasound findings, patients can be classified into low, intermediate and high risk for choledocholithiasis. If one is confronted with the problem of possible choledocholithiasis in clinical practice, patients at high risk for bile duct stones (recent episode of acute cholangitis or acute pancreatitis jaundice or significantly abnormal liver function tests for example, serum alkaline phosphatase more than 2 times normal, dilated CBD of >10mm on transabdominal ultrasonography) would benefit most from ERCP.

Patients with an intermediate risk for choledocholithiasis (a previous history of cholangitis or pancreatitis, slightly abnormal liver function tests, e.g., a raised serum alkaline phosphatase less than twice normal, and dilated CBD of between 8 and 10 mm on transabdominal ultrasound)

should have a prior EUS before further intervention is considered.

A low-risk individual should proceed directly to a laparoscopic cholecystectomy without further evaluation.^{11,14} However, even patients classified as being high risk for choledocholithiasis pre-ERCP were found to eventually have CBD stones in only 66% to 70%.^{11,14,15} Therefore, potentially a third of patients even having undergone rigorous selection criteria were receiving unnecessary ERCPs. This has led some authors¹³ to advocate the more liberal use of EUS in the evaluation of patients with suspected choledocholithiasis, as it offers considerable clinical and economic advantages by preventing inappropriate and more invasive evaluation of the bile duct.

EUS has been compared directly to MRCP, and has been found to be more accurate than MRCP. The sensitivity of both modalities was 100% but EUS had a specificity of 95% and MRCP only 73%.¹² EUS is more accurate when choledocholithiasis occurs in the presence of an undilated bile duct.

A prospective study showed that the use of an extraductal catheter probe EUS (EDUS) as an adjunct to ERCP could reliably detect bile duct stones.¹⁶ EDUS detected 33 of 34 bile duct stones and all papillary adenomas (16 patients). The advantage of EDUS over a conventional echo-endoscope, is that it obviates the need to change endoscopic instruments as the catheter probe is introduced through a normal side-viewing therapeutic duodenoscope, and avoids cannulation of the bile duct.

Acute Pancreatitis

Patients with severe acute biliary pancreatitis, especially those with signs and symptoms of biliary obstruction should undergo emergency ERCP and endoscopic sphincterotomy (ES) if bile duct calculi are present.^{17,18} However, emergency ERCP carries the risk of pancreatic duct filling and worsening of pancreatitis.

Recent studies have examined the role of EUS in acute biliary pancreatitis¹⁹⁻²¹ and results suggest that EUS can determine which of these patients had choledocholithiasis and would benefit from early ERCP and stone extraction. However, pitfalls in the detection of CBD stones on EUS exist. This is seen more commonly in the Asian population because the nature of biliary stone disease is different from the West. In the local population, soft, pigmented stones causing acute biliary pancreatitis may not cast a shadow on EUS, and may be inadvertently missed. Hepatolithiasis more commonly seen in Asia, may not be picked up by EUS.²⁰

In such cases, ERCP with its superior ability to delineate the intra-hepatic biliary system would be complementary.

EUS can also determine important morphological features such as echogenicity and peripancreatic fluid collection, providing prognostic information in patients with acute pancreatitis. In a prospective study by Chak et al,¹⁹ there appeared to be a relationship between EUS findings of peripancreatic fluid and echogenicity of the pancreas and mean hospital stay.

EUS is also useful in determining the aetiology of patients with acute recurrent pancreatitis from microlithiasis²² or pancreas divisum.²³ The presence of microlithiasis of the gallbladder can be reliably detected using EUS with a better accuracy than microscopic bile examination.

Although the gold standard for diagnosing pancreas divisum remains ERCP, EUS can detect pancreas divisum with a sensitivity of 66% and a specificity of 83% using the 'stack sign' (when the main pancreatic duct lies parallel to the distal bile duct viewed from the duodenal bulb) as indicative of normal anatomy.

Despite all the merits of EUS in the evaluation of acute biliary pancreatitis, one would elect to perform an emergency ERCP in unstable patients if one has a high index of suspicion for an impacted distal biliary stone. As time is very often of the essence in such a situation.

Chronic Pancreatitis

EUS is a sensitive tool to diagnose chronic pancreatitis. A quantitative analysis with 9 possible criteria (hyperechoic foci, hyperechoic strands, lobularity, ductal dilation, ductal irregularity, hyperechoic duct margins, visible side branches, calcifications and cysts) showed that EUS is reliable only when it is clearly normal (<2 criteria) or clearly abnormal (>5 criteria).

By using the receiver operating curve (ROC) analysis, a threshold of 3 or 4 criteria offers the optimum compromise between sensitivity and specificity (70% each).²⁴

Given the inherent risks of ERCP and the difficulties of functional testing, EUS may be useful in diagnosing mild chronic pancreatitis when less sensitive tests such as CT and abdominal ultrasound are negative.

It is universally accepted that the role of ERCP would largely be restricted to therapy (removal of pancreatic duct stones or stenting of pancreatic or biliary strictures) in the management of chronic pancreatitis.

Pancreatic and Biliary Malignancies

EUS has a sensitivity of over 95% and is superior to several other imaging modalities including ERCP, angiography, MRI and helical CT for detecting lesions <2 to 3 cm.^{25,26} However, classifying the lesion as benign or malignant is more problematic. Once a pancreatic cancer has been diagnosed, one has to stage it.

In most studies, T-stage accuracy varies from 78% to 94% and N-stage accuracy ranges from 64% to 82%.^{27,28} However, the initial enthusiasm for the use of EUS in pancreatic cancer staging has been questioned. With improvements in imaging modalities like helical CT, the advantage of EUS in pancreatic cancer staging has reduced.

EUS would be unnecessary if the lesion is clearly demonstrated on helical CT.

Specificity of EUS for pancreatic cancers has been traditionally lower than the sensitivity. However, with EUS-guided FNA to sample pancreatic masses, a diagnostic accuracy reaching 90% can be achieved, especially if an experienced cytopathologist is in attendance.²⁹ The risk of tumour seeding is a rare occurrence with one case reported of tumour tract seeding into the gastric wall after EUS-FNA of a pancreatic tail carcinoma.³⁰

Tissue acquisition when performing biliary drainage at ERCP in patients with a suspected pancreato-biliary malignancy carries certain problems.

Despite combination sampling with brush cytology, FNA and forceps biopsy, the sensitivity of all 3 combined is only 62% with a negative predictive value of 39%.³¹

Multiple sampling requires considerable time and technical expertise with the risk of losing guidewire access across the biliary stricture. Finally, forceps biopsy requires a sphincterotomy, which carries a small risk of bleeding and perforation. Consequently, most endoscopists perform brush cytology alone which has a sensitivity of about 30%.³¹

However, tissue diagnosis is not required if the tumour is potentially resectable and the patient is desirous of surgery. Tissue sampling is only necessary if palliative chemotherapy is considered in irresectable cancers or the patient is insistent on a histological diagnosis before consenting to major surgery. EUS and intraductal EUS (IDUS) play useful roles in determining resectability in bile duct cancers. T staging is more accurate with IDUS, while N stage is better with conventional EUS.³²

Cystic Lesions of the Pancreas

Pancreatic cysts can be non-neoplastic (pseudocysts, simple cysts, duplication cysts) or neoplastic which could have a low malignant potential (serous cystadenoma) or have a high malignant potential (mucinous cystadenoma, mucinous cystadenocarcinoma, adenocarcinoma with cystic degeneration and intraductal papillary mucinous tumour).

EUS is capable of differentiating these lesions but there are limitations. Well-defined, simple uniloculated cysts are probably benign and complex cystic lesions with thick walls, septations with solid protrusions into the cyst lumen are likely malignant.³³ EUS-guided FNA can be used to

aspirate the cyst and send material for cytological analysis. A raised carcino-embryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 from the aspirate is suggestive of a malignant cyst.

A combination of fluid cytology, raised CEA levels and EUS features increases the sensitivity of EUS to diagnose malignant cysts to 89%.³⁴

The Cost-effectiveness of EUS in the Assessment of Pancreatic and Biliary Diseases

EUS is an expensive technology because of the price of the EUS equipment and the cost of the training programme. The price of the standard equipment with a radial echoendoscope is US\$180,000 and the cost rises if linear EUS, in order to perform interventional procedures, is added.

To justify acquisition of such specialised equipment, the centre must perform more than 200 procedures per year and it must serve an area of between 350,000 and 500,000 inhabitants.^{3,35}

Performing EUS with EUS-guided FNA has been shown to substantially reduce costs when it was the first endoscopic procedure used in patients suspected to have obstructive jaundice. This was largely due to the fact that the use of EUS obviated the need for about 50% of ERCPs and helped direct subsequent therapeutic ERCP.³⁶

The use of EUS in place of ERCP to stage pancreatic carcinoma has been shown to reduce overall costs because ERCP-related complications would be eliminated.³⁷

In the evaluation of CBD stones in patients with acute pancreatitis, using various imaging modalities [EUS, MRCP, ERCP and intraoperative cholangiography (IOC)], EUS was found to be the most cost-effective method if the pre-test probability of CBD stones was between 7% and 45% (intermediate risk). ERCP proved the most cost-effective method in the high-risk group (pre-test probability >45% of finding CBD stones).³⁸

Sahai et al³⁹ evaluated 4 treatment strategies (ERCP, IOC, EUS and expectant management in patients with suspected CBD stones) prior to laparoscopic cholecystectomy and found EUS to be the most cost-effective in the intermediate-risk group (pre-test probability 11% to 55%), expectant management best in the low-risk group, and ERCP optimal in the high-risk group (pre-test probability >55%).

Various factors affect the cost savings when EUS is employed, and vary amongst different healthcare systems. These factors include the diagnostic accuracy of EUS and/or EUS-guided FNA in a particular institution, efficiency of the healthcare provider, remuneration for various procedures (example, ERCP, EUS), overall hospital costs

(example, drugs, hospitalisation charges) and complication costs.

What is the Current Role of ERCP in the Management of Pancreaticobiliary Diseases?

ERCP should be performed only in cases with therapeutic intent. The probability that a patient has a CBD stone is a key factor in determining diagnostic and treatment strategies. Risk factors for CBD stones include a history of biliary colic with jaundice, abnormal liver chemistries, recent acute pancreatitis and dilatation of the biliary system and/or suspicion of choledocholithiasis on transabdominal ultrasound or CT.

Those with 3 or more criteria were classified as high risk for CBD stones.¹³ Such patients and those presenting with acute cholangitis require ERCP and sphincterotomy with stone removal. As mentioned previously, a third of such patients may eventually have no choledocholithiasis.

ERCP remains the procedure of choice in palliating inoperable pancreaticobiliary malignancies by draining an obstructed biliary system with stent placement. Metal stents are preferable in patients expected to survive longer than 6 months. Preoperative stent placement confers no measurable advantage unless there is a significant delay (more than 6 weeks) till surgery or there is concomitant cholangitis.⁴⁰

Reports of treatment of chronic pancreatitis with ERCP by removal/destruction of stones, placement of stents and dilation of strictures suggest that both immediate and long-term pain relief is possible.

ERCP with sphincter of Oddi (SOM) manometry can be considered in a very select group of patients.

Interventional EUS

The number of therapeutic procedures being attempted under EUS is rapidly growing.

Patients with irresectable pancreatic cancers often have intractable abdominal pain. Injection of bupivacaine and alcohol into the celiac ganglia has led to a significant reduction in pain and reduction in the need for narcotics in 88% of patients.⁴¹ The role of celiac plexus block in chronic pancreatitis is less encouraging.⁴²

EUS has augmented the endoscopic management of pancreatic pseudocysts⁴³ and avoided the complications of blind endoscopic cystenterostomy.⁴⁴ The entire procedure including stent placement is performed under EUS guidance.

ERCP is not always successful in accessing the pancreaticobiliary tree for a variety of reasons such as with Roux-en-Y reconstructions or luminal obstruction by tumour. Two small case series^{45,46} have shown that EUS-guided cholangio-drainage is a potential alternative to

percutaneous transhepatic biliary drainage in patients with unsuccessful ERCP.

An area of ongoing research is the injection of anticancer drugs directly into advanced pancreatic tumours using EUS techniques.⁴⁷

Although endosonographers continue to find novel therapeutic ways that EUS can be of use, ERCP still remains the best method for cannulation of the CBD. The place of ERCP in the removal of CBD stones and stenting of biliary strictures is unchallenged.

However, there are limitations to EUS which include the high cost of establishing the service and a long learning curve for the procedure.

The Learning Curve and Training in EUS

EUS has a steep learning curve comparable to therapeutic ERCP. To become competent in EUS, the trainee should spend at least 6 months training in a centre performing a minimum of 300 procedures per year.⁴⁸

To achieve competence in all fields of EUS, the American Society for Gastrointestinal Endoscopy (ASGE) recommended a minimum of 150 supervised cases, of which 75 should be pancreaticobiliary procedures and 50 should be EUS-guided FNA cases.⁴⁹

A survey was conducted amongst worldwide endosonographers addressing issues of EUS practice and training.⁵⁰ In general, half of the respondents were in academic practice and only 35% had undergone formal EUS training. Non-formal training was more prevalent amongst non-United States respondents as compared to endosonographers in the US. Sixty-five per cent of the endosonographers reported they trained other physicians, which is a definite increase since the last survey of ASGE members in 1999, where only 40% of the respondents were trainers.⁵¹ However, these 2 studies emphasise the dire need for formalised EUS training in accredited institutions. With the increasing number of EUS trainers, it is likely that some of these teachers may not have adequate training themselves which makes it essential that practical and effective guidelines be established and implemented to ensure the quality of EUS training.

Studies have also highlighted the importance of the learning curve and EUS accuracy. A study investigating the effect of formal supervised training on EUS-guided FNA accuracy for pancreatic masses showed a marked improvement in accuracy (33% to 91%) after 2 months of formal training.⁵²

With the emergence of EUS, the current role of ERCP is directed towards fewer but more complex therapeutic procedures. The impact on ERCP is undeniable.

EUS and ERCP require significantly different technical

skills and spatial appreciation. With more gastroenterology trainees interested in training in advanced endoscopic procedures, EUS and ERCP should have separate and distinct training pathways.

Conclusion

EUS is now firmly established in the management of PBD. With significantly lower morbidity, EUS has essentially replaced diagnostic ERCP, which should not exceed 10% of all ERCPs performed in any institution.

MRCP which has certain limitations, is costly and not readily available. It is in direct competition with diagnostic ERCP and EUS. Whether MRCP will supersede EUS is open to debate.

EUS has evolved in the last decade from a purely diagnostic tool to an interventional procedure with an increasing array of possibilities. As technical advances are made with scope design, accessory devices, and probes, it is likely that many potential therapeutic applications will become routine procedures.

It is, however, unlikely that EUS, even interventional EUS will completely replace therapeutic ERCP which is a long established procedure to access the biliary tree and in experienced hands and with proper patient selection, quite safe. Interventional EUS is still in its infancy and it is uncertain how far it can be developed.

The future of EUS would require significant investment in training programmes and service development. With well-trained endosonographers to complement competent ERCP practitioners, pancreaticobiliary disorders can be managed optimally.

Alternatively, interventional endosonographers with the capability to perform therapeutic ERCP may be the best choice but in practical terms, not always possible.

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Magnification: x420 (Philips SEM 515)
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The Ants and the Grasshopper

The ants were spending a fine winter's day sifting and drying grain collected in the summertime. A Grasshopper, perishing with famine, passed by and earnestly begged for a little food. The Ants inquired of him, "Why did you not treasure up food in the summer?" He replied, "I had not leisure enough. I passed the days in singing, drinking aphid juice, and mating. The Ants then chorused in derision: "If you were foolish enough to indulge yourself all the summer, you must dance supperless to bed in the winter. 'Tis thrifty to prepare today for the wants of tomorrow."