

Comparing the Roles of EUS, ERCP and MRCP in Idiopathic Acute Recurrent Pancreatitis

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ABSTRACT: Acute recurrent pancreatitis (ARP) is defined as more than two attacks of acute pancreatitis with complete or almost complete resolution of symptoms and signs of pancreatitis between episodes. The initial evaluation fails to detect the cause of ARP in 10%–30% of patients, whose condition is classified as idiopathic ARP. Endoscopic ultrasound (EUS) has gained increasing attention as a useful imaging modality for the pancreas and the extrahepatic biliary tree. The close proximity of the pancreas to the digestive tract allows EUS to obtain detailed images of this organ. This review aims to record pancreaticobiliary endoscopic ultrasound (EUS) and other imaging modalities in the clinical management of patients with idiopathic ARP.

KEYWORDS: idiopathic acute recurrent pancreatitis, endoscopic ultrasound

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Introduction

Acute recurrent pancreatitis (ARP) generally refers to a clinical entity characterized by two or more discrete episodes of acute pancreatitis with complete or relative-complete resolution of symptoms between episodes. Studies suggest that about 30% of patients with acute pancreatitis may experience recurrence after an initial episode.^{1,2}

The condition can present a diagnostic challenge. Major contributors to ARP are alcohol abuse and gallstone disease, accounting for 70% of cases.³ In initial evaluation, ARP in 10%–30% of patients has no obvious cause, and the condition in these patients is classified as idiopathic ARP (IARP). Further evaluation is indicated in these patients to disclose evidence of potential etiology, such as unrecognized gallstone disease, common bile duct (CBD) stone or chronic pancreatitis.⁴ Therefore a more extensive assessment including specialized lab testing, endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound, or magnetic resonance cholangiopancreatography (MRCP) are options for the evaluation of these patients^{3,4} (Fig. 1).

The expanding spectrum of EUS indications has provided a less invasive, highly accurate imaging modality for studying the pancreas and the biliary tree.¹ This review aims to compare pancreaticobiliary endoscopic ultrasound (EUS) and the role of other imaging modalities in the clinical management of patients with idiopathic acute recurrent pancreatitis.

Endoscopic Ultrasound (EUS)

Endoscopic ultrasound (EUS) combines a high-frequency ultrasound probe with an endoscope, and it is now considered

an integral part of the management of a variety of gastrointestinal conditions.^{5,6} EUS has been in use since the early 1980s, and is proposed as a safe diagnostic procedure in patients with ARP.^{1,5} The safety and complications of EUS have been evaluated in many studies. In most of the literature, this imaging modality has been shown to be safe with extremely low rates of complications.⁵

EUS is increasingly being performed to evaluate patients with IARP because of high diagnostic accuracy.^{3,7} In a prospective study published in 2000, Liu et al studied 89 consecutive patients with idiopathic acute pancreatitis, and EUS detected cholelithiasis in a large number of patients classified as having idiopathic pancreatitis. The authors concluded that EUS is a valuable diagnostic modality in the management of patients with acute pancreatitis.⁸ In addition, published data on the sensitivity of EUS to detect microlithiasis and sludge suggested that this imaging modality has equal or superior sensitivity to other commonly used tests.^{9,10} EUS is a reliable diagnostic method to detect pancreas divisum,^{11,12} occult ampullary mass lesions¹³ and pancreatic tumors.¹⁴ Finally, EUS is a useful diagnostic technique to detect the presence of chronic pancreatitis in patients initially diagnosed with idiopathic ARP.¹⁰ This imaging modality is one of the most promising techniques for diagnosis of extension and resectability of pancreatic tumors.¹⁵ It is the most appropriate technique for the assessment of malignancies of the gastrointestinal tract and nearby organs.

The most fascinating modification in the field of EUS was the idea of a biopsy needle, which first emerged in 1992. Since then, EUS utilizations have expanded from diagnostic

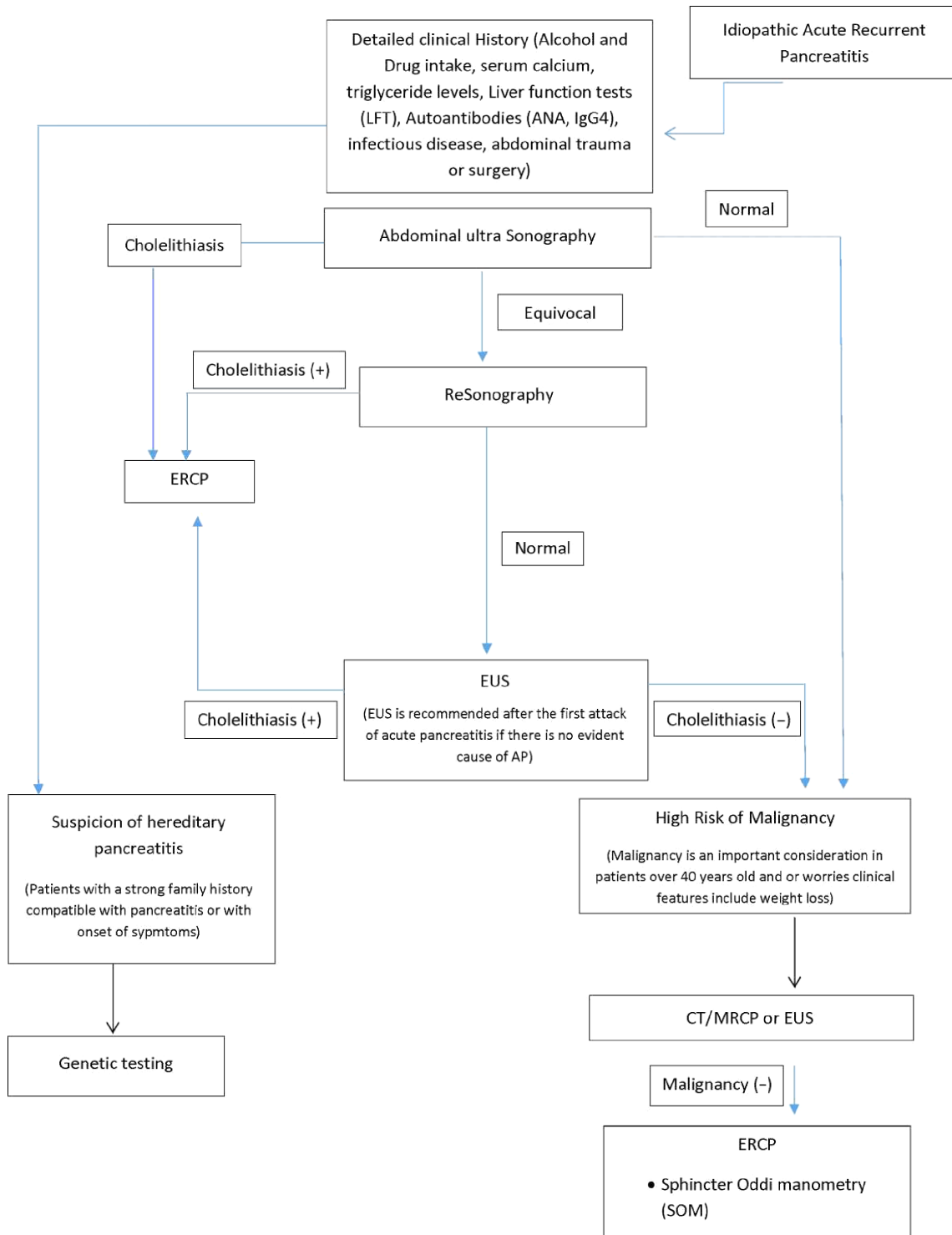


Figure 1. Algorithms for evaluation of patients with idiopathic acute recurrent pancreatitis.

Abbreviations: EUS, endoscopic ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; SOM, sphincter of Oddi manometry; CT, computed tomography; SOD, sphincter of Oddi dysfunction.

processes to therapeutic procedures.⁵ Since that date, a wide range of clinical indications for EUS have been found. The main therapeutic purposes of EUS procedure include EUS-guided celiac plexus block, celiac plexus neurolysis, pancreatic tumor ablation, pancreatic pseudocyst drainage and even gallstone extraction.¹⁶

Endoscopic Retrograde Cholangiopancreatography (ERCP)

ERCP can be used for diagnosis and treatment of a variety of pancreatic disorders.¹⁷ It was first used in 1968,¹⁸ and was soon accepted as a diagnostic technique; in the past decade, it has become exclusively a therapeutic procedure.¹⁷



There is a documented risk of ERCP-related complications including pancreatitis (1.3%–6.7%), infection (0.6%–5.0%), hemorrhage (0.3%–2.0%), and perforation (0.1%–1.1%) in a prospective series of unselected patients,¹⁹ therefore ERCP should be performed only for limited indications.²⁰

Because of the complications of ERCP, many believe that this technique is not indicated after the first episode of pancreatitis for any age groups.³ By contrast, ERCP has been indicated to evaluate patients with repeated attacks of pancreatitis.²¹

However, ERCP offers some advantages compared with EUS such as potential therapeutic maneuvers, sphincterotomy (either biliary or pancreatic), and the ability to inspect the ampulla, brush and biopsy tissues, aspirate bile fluid or insert a stent.^{1,3}

Magnetic Resonance Cholangiopancreatography (MRCP)

MRCP is a non-invasive exploration,²² which produces detailed images of the hepatobiliary and pancreatic systems. The appearance of MRCP images is considered to be similar to those obtained by ERCP or other invasive methods.²³ Since 1991, MRCP has played an important part in the diagnosis of pancreaticobiliary diseases because of its accuracy, safety and availability.²³ Because MRCP does not require administration of intravenous contrast or ionizing radiation, it is a useful adjunctive tool in almost all patients including infants or those with allergies to iodine-based contrast materials.^{23–26}

MRCP, which has been referred to as “the pancreatogram”,²⁷ can be used for selecting patients for preoperative ERCP.²⁶ The diagnostic accuracy of MRCP is considered to be equivalent to that of contrast-enhanced CT in predicting the severity of pancreatitis and identifying pancreatic necrosis.²⁶ Furthermore, MRCP and ultrasonography have similar sensitivity for detection of gallstones and gallbladder inflammation.²⁶ MRCP can evaluate pancreatic and peripancreatic cysts,²³ and it is less operator-dependent than ultrasonography or ERCP.²⁶ On the other hand, unlike ERCP, MRCP does not enable therapeutic maneuvers and it is known to miss gallstones smaller than 4 mm, small ampullary lesions, and ductal strictures.^{23,27,28} MRCP is indicated to diagnose pancreas divisum, choledochocoele, anomalous pancreatobiliary junction, or annular pancreas in patients with IARP.³

Comparison of Diagnostic Evaluation: EUS vs ERCP vs MRCP

Idiopathic recurrent pancreatitis has been diagnosed by ERCP for decades.¹ Over the years, EUS has been used instead of ERCP because of its sensitivity, safety and lower risk of complications.¹ At present, MRCP is gaining wider use as a non-invasive alternative to ERCP to detect the cause of acute pancreatitis in patients with IARP.²²

EUS has been documented to have a negative predictive value of 95.4% for the diagnosis of CBD stones,²⁹ and

sensitivity of 96% for diagnosing microliths.³⁰ Several trials have addressed the question of whether EUS is a reliable substitute for ERCP in cases of pancreas divisum. The sensitivity and specificity of EUS need further evaluation in cases of pancreas divisum.^{1,2} Many believe, however, that EUS is an accurate, minimally invasive investigational method for the diagnosis of pancreas divisum.^{11,12,31}

In 2002, Coyle et al studied 162 patients with pancreatitis to compare the diagnostic utility of ERCP with sphincter of Oddi manometry (SOM), bile analysis, and endoscopic ultrasound. The research showed that EUS is a useful technique to identify the etiology of unexplained acute pancreatitis and tumors. Furthermore, in nine patients suffering from chronic pancreatitis, the condition was detected by EUS but not by ERCP. However, none of the patients with Sphincter of Oddi dysfunction (SOD) was diagnosed by EUS.³ A similar study by Frossard et al in 2000 reached concordant conclusions. They evaluated 168 patients with idiopathic pancreatitis to compare the usefulness of endoscopic ultrasonography with endoscopic cholangiopancreatography and bile crystal analysis and medical follow-up. In 92% of patients, EUS was able to determine the etiology of idiopathic pancreatitis. The authors stated that EUS can correctly determine the cause of acute pancreatitis in patients initially considered to have idiopathic pancreatitis.³² Another report by Tandon et al states that EUS can demonstrate the etiology in two-thirds of idiopathic acute pancreatitis cases, and thus can be a less invasive and highly accurate alternative to ERCP.⁷

To compare EUS and MRCP, Forsmark et al enrolled 49 patients initially diagnosed with idiopathic acute pancreatitis in a prospective study. The authors demonstrated that the diagnostic yield of EUS is higher than MRCP in the evaluation of these patients (51% vs 20%). MRCP identified additional features in only 6% of patients in whom EUS could not diagnose the etiology of AP. On the other hand, MRCP outperformed EUS in diagnosing patients who had undergone a cholecystectomy (11% vs 60%).³³ Thevenot et al performed a prospective study with 128 AP patients to compare EUS and MRCP for diagnosing idiopathic acute pancreatitis. The etiology of acute pancreatitis was not found in 41 patients in first line investigation. These patients underwent EUS or MRCP as second line investigation. The authors concluded that EUS had a higher diagnostic yield than MRCP (29% vs. 10.5%).³⁴

The diagnostic yield of ERCP in patients with idiopathic pancreatitis varies from 38% to 78%.⁴ It is not the preferred first line test for ARP to assess for underlying etiologies because of its associated risk of post-ERCP pancreatitis.⁴

Magnetic resonance cholangiopancreatography is a non-invasive radiographic tool that produces images comparable to those obtained by ERCP,²² but requires advanced interpretation skills and may not be widely available.¹ The diagnostic yield of MRCP in IARP patients is 22%.²²

Trying to evaluate the usefulness of a new modality to visualize the pancreatic duct in idiopathic ARP, Khalid et al

**Table 1.** Studies evaluating EUS, ERCP and MRCP diagnostic rate in patients with IARP.

METHOD	REFERENCES, YEAR	NO. OF PATIENTS	BILIARY TRACT DISEASE	PANCREAS DIVISUM	TUMOR	CP	IDIOPATHIC	OVERALL YIELD
EUS	Frossard 2000 [32]	168	103	0	4	16	37	78%
	Tandon 2001 [7]	31	5	2	1	14	10	68%
	Yussoff 2004 [37]	169	46	13	1	69	54	68%
	Rana 2012 [31]	40	20	1	1	0	18	55%
ERCP	Frossard 2000 [32]	168	8	0	0	16	19	29%
	Kaw 2002 [38]	126	8	9	2	0	27	79%
	Fischer 2010 [39]	1,241	37	233	ND	589	425	65.8%
MRCP	GN Y, 2014 [22]	50	8	1	0	2	39	22%

Abbreviations: EUS, endoscopic ultrasonography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; CP, chronic pancreatitis; ND, non determined.

studied ten patients who underwent secretin-stimulated magnetic resonance with subsequent endoscopic retrograde pancreatogram, with or without manometry. They concluded that secretin-stimulated magnetic resonance provides high quality pancreatic duct images and has high specificity but low sensitivity for diagnosing pancreatic duct outflow obstruction using manometric/clinical criteria.³⁵

In an effort to evaluate the diagnostic quality of MRCP compared to ERCP, Hatano et al studied 56 patients with pancreaticobiliary diseases. Considering ERCP as the gold standard, a different diagnosis was observed in 10 of 56 patients. Therefore, the authors claimed that ERCP was superior to MRCP as the first diagnostic tool in the diagnosis of biliary and pancreatic duct.³⁶ Studies evaluating EUS, ERCP and MRCP diagnostic rates in patients with IARP are shown in Table 1.

Conclusion

Idiopathic acute recurrent pancreatitis is a diagnostic challenge that may be caused by a number of disorders. Understanding the etiology of IARP can modify patient management and improve prognosis. Extensive evaluations including ERCP, endoscopic ultrasound, or MRCP are used to establish the correct diagnosis. The use of ERCP is associated with a substantial risk of inducing acute pancreatitis, use of contrast and radiation. EUS is increasingly considered to be the endoscopic procedure of choice for evaluating patients with IARP, because of its sensitivity and safety. EUS can be performed as an initial diagnostic test in patients with unexplained acute pancreatitis.

Author Contributions

Conceived and designed the experiments: AHMA. Analyzed the data: MTS. Wrote the first draft of the manuscript: MTS. Contributed to the writing of the manuscript: MTS. Agree with manuscript results and conclusions: MTS. Jointly developed the structure and arguments for the paper: AHMA. Made critical revisions and approved final version: MBM, SE,

SS, and AHMA. All authors reviewed and approved of the final manuscript.

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