

Prospective evaluation of yield of endoscopic ultrasonography in the etiological diagnosis of “idiopathic” acute pancreatitis

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Abstract

Background: Etiology of acute pancreatitis (AP) remains idiopathic in 30% of patients. Endoscopic ultrasound (EUS) has been shown to increase the diagnostic yield in patients with idiopathic AP (IAP). **Aim:** The aim of this study was to evaluate the role of EUS in achieving etiological diagnosis in patients with IAP. **Materials and Methods:** Consecutive 192 patients with IAP were evaluated prospectively with EUS over a period of 2 years. Patients who had no etiological diagnosis for AP after detailed history, clinical examination, laboratory investigations, and magnetic resonance cholangiopancreatography were included in the study. **Results:** The mean age of patients was 34.6 ± 12 and male:female ratio was 2.1:1. Of these, 135 patients had gallbladder intact (Group A) and 57 patients had undergone cholecystectomy (Group B). In Group A, EUS identified a possible cause in 79 (58.5%) patients; microlithiasis ($n = 48$), chronic pancreatitis (CP) ($n = 23$), common bile duct (CBD) and gallbladder stone ($n = 3$), pancreatic divisum ($n = 3$), small pancreatic tumor ($n = 1$), and anomalous pancreaticobiliary junction ($n = 1$). In Group B, EUS yielded diagnosis in 28 (49.1%) patients; CP ($n = 22$), ascariasis ($n = 3$), CBD stone ($n = 2$), and pancreatic divisum ($n = 1$). Overall EUS helped in achieving etiological diagnosis in 107 (55.1%) of patients with IAP. The presence of intact gallbladder showed a tendency for increased diagnostic yield ($P = 0.06$). **Conclusion:** EUS is a useful modality to establish the diagnosis in IAP and this technique should be incorporated in the evaluation of IAP.

Key words

Endoscopic ultrasound, idiopathic acute pancreatitis, microlithiasis

Introduction

Common causes of acute pancreatitis (AP) include biliary stones, alcohol, hypercalcemia, hypertriglyceridemia, drugs, and trauma. The etiology of AP remains undetected in

10%–30% of patients after history, laboratory, and noninvasive imaging studies.^[1] Etiological evaluation is critical to optimize the treatment strategy and to prevent recurrence that may occur in 10%–30% of patients and has a risk of mortality.^[2,3] Endoscopic ultrasound (EUS) has emerged as an important procedure to identify the etiology of idiopathic AP (IAP).^[4-9] Microlithiasis is a major cause of an unexplained attack of AP in patients with gallbladder *in situ*, whereas chronic

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pancreatitis (CP) is common in those with recurrent attacks who have previously undergone cholecystectomy.^[10] Microscopic examination of bile,^[10,11] endoscopic retrograde cholangiopancreatography (ERCP),^[11,12] and magnetic resonance cholangiopancreatography (MRCP)^[13] have been used to find etiology in these cases; however, ERCP has some chances of complications and MRCP is inferior to EUS in detecting <5 mm stones.^[14,15] EUS offers several advantages over these modalities; it provides better resolution to diagnose small stones/tumors^[1] and CP.^[16] Most of the studies reported from India regarding acute idiopathic pancreatitis were before routine use of EUS. We evaluated the role of EUS for etiological diagnosis in a large group of patients with AIP.

Materials and Methods

The study was conducted over a period of 2 years at a Tertiary Care Centre in North India. Informed consent was taken from all the patients and study had the Institute's Ethical Committee approval. The study included 192 patients above 12 years of age, with one or more documented attacks of unexplained AP. AP was defined by the presence of characteristic abdominal pain and raised serum amylase or lipase levels to ≥ 3 times the upper limit of normal or imaging features suggestive of AP. The episode(s) of AP were considered as idiopathic when no cause could be identified after biochemical investigations and imaging. Patients with AP within the past 6 weeks, history of significant alcohol intake, deranged calcium or triglyceride levels, diagnosed biliary stone disease, CP, pancreas divisum were excluded.

Methods

Before EUS study, the following information was collected: age, sex smoking, alcohol consumption, number of previous episodes of AP, and the time interval from the last attack. History of abdominal trauma, infection, and relevant drug intake were also collected. Investigations including lipid profile, fasting blood sugar, liver function tests, autoimmune markers, and calcium levels were done before inclusion. All patients had a transabdominal ultrasound and either or both of a helical computed tomography (CT) scan and magnetic resonance imaging done before the EUS study.

Endoscopic ultrasound protocol

Informed consent was obtained from all the patients before the study. The study was approved by the Institutional Review Board of our hospital, and ICMR guidelines for conducting a study were followed. The instruments used were echoendoscopes (FG 34 UX; Pentax, Japan, and GF-UCT140 AL5; Olympus, Japan) with a longitudinal convex ultrasound transducer with an adjustable ultrasonic frequency of 5, 7.5, or 10 MHz, in combination with an Ultrasound Scanner (EUB 6500; Hitachi, Tokyo, Japan).

Study definitions

Both parenchymal and ductal features were recorded, and CP was defined as per Rosemont consensus [Figure 1].^[17] EUS

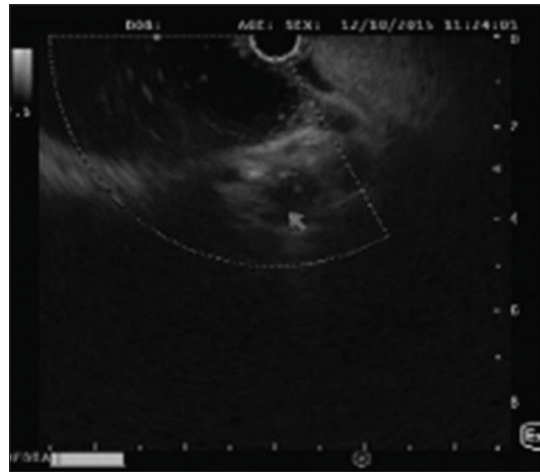


Figure 1: Gallbladder sludge and small calculi

findings were considered suggestive of pancreas divisum if the course of the pancreatic duct could not be followed from the ampulla of Vater through the ventral part to the dorsal pancreas or if the duct could not be visualized within the ventral pancreas. Anomalous pancreaticobiliary junction (APBJ) was defined as abnormally long (>15 mm) common pancreaticobiliary channel. Stones <3 mm in diameter were labeled as microlithiasis as shown in Figure 2.

Results

We studied 192 patients with acute idiopathic pancreatitis. The mean age of patients was 34.6 ± 12 years and male:female ratio was 2.1:1. Of these, 135 patients had gallbladder intact (Group A) and 57 patients had undergone cholecystectomy (Group B). One hundred and two patients had recurrent idiopathic pancreatitis, and ninety patients had only one episode. The mean duration after the last episode of AP when patients were enrolled in the present study was 9.6 ± 2.2 weeks.

In Group A (patients with intact gall bladder), EUS identified a possible cause in 79 (58.5%) patients; microlithiasis ($n = 48$), CP ($n = 23$), common bile duct (CBD) with gallbladder stone ($n = 3$), pancreatic divisum ($n = 2$), pancreatic tumor ($n = 2$, branch duct IPMN and pancreatic carcinoma), and anomalous pancreaticobiliary junction ($n = 1$). In Group B, EUS yielded diagnosis in 28 (49.1%) patients; CP ($n = 22$), ascariasis ($n = 3$), CBD stone ($n = 2$), and pancreatic divisum ($n = 1$). Overall EUS helped in achieving etiological diagnosis in 107 (55.7%) of patients with IAP. Overall, 58.5% of patients with gallbladder intact and 47.5% of postcholecystectomy patients had a positive finding in EUS; comparison of these two groups is shown in Table 1. Microlithiasis was the most common diagnosis achieved (25%), followed by CP (23.4%).

Patients who had a diagnosis of pancreas divisum on EUS underwent MRCP, and the findings were confirmed. Of the 85 patients who did not have any diagnosis after EUS, all

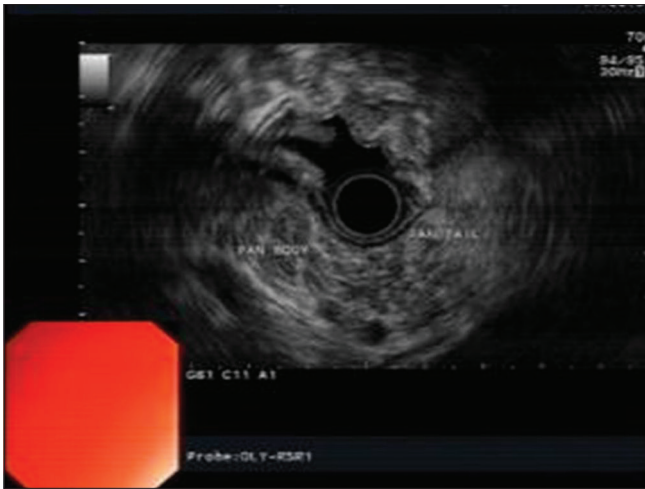


Figure 2: Representative image of early chronic pancreatitis

of them underwent MRCP; it identified APBJ in one and pancreas divisum in two patients. On follow-up, all patients underwent repeat EUS at 3 months, 6 months, and 1 year. Of the 45 patients with EUS diagnosis of CP, 32 had definite criteria for CP and 13 had probable CP (in the follow-up, 2 patients developed features of definite CP at 6 months and another 4 developed features of CP at 12 months on repeat EUS). Comparison of patients where EUS identified etiology of AP to the patients where EUS was not able to make a diagnosis is shown in Table 2; there was no difference in these groups regarding age, sex, number of AP episodes (single vs. multiple), and history of cholecystectomy.

Discussion

In this study of 192 patients with IAP, EUS identified an etiology in 55.7% of patients. The most common etiology identified in this group was gallbladder sludge/microlithiasis and CP, respectively.

Several studies have shown the utility of EUS to diagnose etiology in cases of IAP. A biliary pathology including cholelithiasis, biliary sludge, or CBD stones are the most EUS findings in various studies; it represented 25% of EUS findings observed in 192 patients in our series. A small series of 40 patients by Rana *et al.*^[18] showed that occult biliary pathology was the predominant cause of IAP and half of the cases without identified etiology already had an underlying CP, while another series of 51 patients by Govil *et al.*^[19] revealed that CP and biliary lithiasis were the common causes of IAP. Endoscopic ultrasonography allows us to visualize microlithiasis and small amount of biliary sludge that is not visible with other imaging techniques including MRCP. The elimination of biliary sludge results in a decrease in the recurrence of new episodes of pancreatitis.^[10] The current clinical practice in these cases is to consider biliary sludge and microlithiasis as etiological factors and recommend cholecystectomy in those patients with an acceptable surgical risk. ERCP offers a therapeutic

Table 1: Comparison between two groups of patients with gallbladder *in situ* and gallbladder removed and the endoscopic ultrasound diagnosis

Parameter	Group A (with GB <i>in situ</i>), n (%)	Group B (GB surgery earlier), n (%)	P
Number of patients	135	57	
Recurrent AP	61 (45.1)	29 (50.9)	0.62
EUS able to make diagnosis	79 (58.5)	28 (49.1)	0.62
Microlithiasis	48 (35.5)	0	<0.01
Chronic pancreatitis	23 (17.0)	22 (38.6)	<0.01
CBD stones	3 (2.2)	2 (3.5)	0.30
Pancreas divisum	2 (1.49)	1 (1.75)	0.44
Pancreatic tumor	2 (1.49)	0	0.18
Abnormal PB junction	1 (0.7)	0	0.26
Ascariasis	0	3 (5.3)	0.02

EUS=Endoscopic ultrasound, PB=Pancreaticobiliary, CBD=Common bile duct, AP=Acute pancreatitis, GB=Gallbladder

Table 2: Comparison of patients with endoscopic ultrasound diagnosis and without endoscopic ultrasound diagnosis

Parameter	Etiological diagnosis with EUS (n=107)	No etiological diagnosis (n=87)	P
Age			
>65 years (51)	29 (56.9)	22 (43.1)	0.81
<65 years (141)	79 (56.0)	62 (44)	
Male sex	74 (56.5)	57 (43.5)	0.64
Number of AP episodes			
Single	55 (53.9)	47 (46.1)	0.59
Recurrent	52 (57.8)	38 (42.2)	
History of cholecystectomy			
Yes (57)	28 (49.1)	25 (50.9)	0.06
No (135)	79 (58.5)	60 (41.5)	

AP=Acute pancreatitis, EUS=Endoscopic ultrasound

advantage in addition to diagnosis in biliary cases; however, EUS is associated with less risk of complications, and it may provide an alternate diagnosis (e.g., CP, small space occupying lesion in the pancreas). EUS provides a diagnosis in 60%–80% of cases and is associated with fewer complications.^[4-9,20] As compared to microscopic bile aspiration, EUS has similar^[21] or better results^[22] for diagnosis of microlithiasis and may provide an alternate diagnosis in up to 25% of cases.^[22] In patients who underwent cholecystectomy earlier, biliary causes are uncommon, and EUS may be considered the first-line approach to find cause for IAP. EUS is considered as an accurate imaging modality for diagnosis of CP, it has sensitivity, specificity, positive and negative predictive values of >85%, and has good correlation with ERCP for moderate or severe cases.^[16,23] EUS can diagnose small tumors not picked up by CT, and negative predictive value of EUS is close to 100% for such cases to exclude a tumor.^[24] Our study emphasizes the importance of EUS in patients with IAP irrespective of the number of episodes of AP. EUS is particularly useful in patients with intact gallbladder. Our study did not compare the utility of EUS against MRCP/ERCP. Similar studies including

larger number of patients with a follow-up to evaluate the sustainability of diagnosis will help us understand the exact role of EUS in idiopathic pancreatitis.

To conclude, we present a large series of idiopathic acute pancreatitis where EUS helped in making a probable diagnosis in 55% of patients.

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Conflicts of interest

There are no conflicts of interest.

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