



Place of Echo Endoscopy in Unexplained Acute Pancreatitis: A Retrospective Study

A. Benhamdane ^{a*}, I. El Koti ^a, S. Mrabti ^a, T. Addajou ^a,
R. Berraida ^a, F. Rouibaa ^a and H. Seddik ^a

^a Department of Gastroenterology II, HMIMV- Rabat, Morocco.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Acute pancreatitis may escape etiological diagnosis after clinical, biological and morphological investigation in 10-30% of patients. Echo-endoscopy is promising and particularly effective in exploring the bilio-pancreatic region.

The aim of our study is to evaluate the contribution of echo-endoscopy in unexplained acute pancreatitis.

Materials and Methods: This is a retrospective descriptive study, including 89 patients who underwent echoendoscopy for unexplained acute pancreatitis between January 2008 and December 2022.

Results: The mean age of our patients was 55 ± 16.3 years, with extremes ranging from 17 to 89 years. The sex ratio (M/F) was 0.81, with a slight female predominance of 55.1%.

A history of previous acute pancreatitis was found in 31.9% of cases, and 16.3% of patients had undergone cholecystectomy.

The diagnostic yield in our study was 68% of patients. Biliary origin was retained in 40.4% (n=36) of patients; 19 of whom benefited from complementary ERCP at the same anesthetic time. A tumor pathology was found in 32.5% of cases (n=30) and chronic pancreatitis in 22.4% of patients (n=20).

*Corresponding author: Email: ahlame.benhamdane@gmail.com;

We also found two cases of pancreas divisum, one case of sphincter of Oddi dysfunction and one case of choledochocoele.

Echo-endoscopy was normal in the remaining 32% of cases, with no cause found.

Conclusion: Echo-endoscopy is currently an indispensable tool in the etiological investigation of unexplained acute pancreatitis. In our study, the diagnostic yield was 68%.

Keywords: Echo endoscopy; unexplained pancreatitis; bilio-pancreatic; idiopathic pancreatitis.

1. INTRODUCTION

Acute pancreatitis may escape etiological diagnosis after clinical, biological and morphological investigation in 10-30% of patients [1].

Idiopathic acute pancreatitis (IAP) can be challenging to diagnose for clinicians, as little is known about the interaction between genetic, environmental, anatomical and other factors contributing to the disease. Hence the interest of identifying the cause of pancreatitis and initiate appropriate treatment, that may prevent recurrence in up to 70% depending on the cause [2].

The management of biliopancreatic diseases has been revolutionized over the last 20 years by advances in imaging, with less invasive and more effective examinations.

Echo-endoscopy is one of the most recent advances in gastrointestinal endoscopy, and has radically changed the management of biliopancreatic diseases. It is an endoscopic examination combining conventional endoscopy with ultrasound. Its benefits are twofold: diagnostic and therapeutic.

Endoscopic ultrasound was developed for high-resolution imaging of the upper gastrointestinal tract and adjacent organs, such as pancreas and bile ducts. It is well suited to pancreas assessment, thanks to its high resolution and the proximity of the transducer to the pancreas, avoiding air in the intestine. Its concept is to reduce the distance between the ultrasound source and the organs to be explored.

The aim of our study is to evaluate the role of endoscopic ultrasound and determine its usefulness in the etiological diagnosis of unexplained acute pancreatitis.

2. MATERIALS AND METHODS

2.1 Study Design and Participants

This is a retrospective descriptive study of 89 cases, who presented with unexplained acute

pancreatitis hospitalized in the gastroenterology II department of the Mohammed V Military Hospital in Rabat during the period between January 2008 and December 2022.

2.2 Methods

1- Inclusion criteria:

All patients over 18 years with AP of undetermined origin after clinical, biological and morphological investigation.

2- Exclusion criteria:

- Patients under 18 years
- Acute pancreatitis whose cause was determined by other imaging means.

3- Equipment used:

The equipment used was an Olympus radial or linear echo-endoscope coupled to the Aloka Prosound α 5 SV ultrasound scanner or a PENTAX echo-endoscope:

The carrier endoscope was a video endoscope with a 100° field of view. It is equipped with a radial ultrasound transducer with variable frequencies (from 5 to 10MHz), offering a good ratio between image resolution and depth of field.

The radial probe had enabled 360° circular images to be produced. It is in fact of the video-electronic type, as is the Doppler function.

Linear probes are mainly used for procedures such as biopsy. Its image is parallel to the probe axis, enabling real-time tracking of the puncture needle path. The ultrasound field of our linear device was 180°.

4- Examination procedure:

To ensure good examination conditions, patients were fasted for 12 hours prior to the examination. Patients were admitted to a day hospital with a blood crase test requested beforehand.

The examination lasted a minimum of 45 minutes. The echo-endoscopy was transgastric and transbulbar in our study.

During the echo-endoscopic examination, we always tried to specify the state of the pancreatic parenchyma, the state of the Wirsung (dilated or not), the presence or absence of calcification and the search for malformations of the bilio-pancreatic ducts. We also tried to determine whether the bile ducts were dilated or not, and the nature of the obstruction.

We have always tried to specify certain essential data in line with international recommendations, depending on the pathology (benign or malignant) and the segment of the digestive tract explored.

When necessary, echo endoscopy was combined with endoscopic biliary sphincterotomy for biliary drainage or biopsy for anatomopathological study.

5- Data collection:

Each of our patients was the subject of a well-established data sheet, enabling us to collect the various demographic (age and sex), clinical and morphological data from the patient's medical records. Endoscopic data were collected from the operator's interventional endoscopy logbook.

6- Statistical analysis:

All data were entered and analyzed on a JAMOV program database.

Qualitative variables were represented by headcounts and percentages, while quantitative variables were expressed using measures of central tendency and dispersion: mean and standard deviation.

3. RESULTS

3.1 Demographic Characteristics

The mean age of our patients was 55 +/- 16.3 years, with extremes ranging from 17 to 89 years. The predominant age range was 50 to 59 years.

Our series was characterized by a 55.1% female predominance, giving a sex ratio (M/F) of 0.81.

31.9% of our patients had a history of previous acute pancreatitis, and 16.3% had undergone cholecystectomy.

All our patients had pancreatic-type epigastralgia. 10.1% had associated hepatic colic and 5.6% had cholestatic jaundice.

Table 1. Clinical characteristics of the study population

Characteristics	Values (n=89)
Age (years) [°]	55 +/- 16,3
Gender *	
Male	39 (44,9)
Female	50(55,1)
Past history *	
Acute pancreatitis	28 (31,9)
Cholecystectomy	14 (16,3)
Clinical symptoms*	
Pancreatic-type epigastralgia	89 (100)
Hepatic colic	9 (10,1)
Cholestatic jaundice	5 (5,6)

[°]Expressed as mean +/- standard deviation

*Expressed as headcount (percentage)

3.2 Endoscopic Findings

The CBD was of normal caliber in 68.6% of cases (n=59), dilated in 16.3% (n=14) and disparate in caliber (in 15.1% of cases (n=13). VBP median was 6 mm (5-7.8).

The VB was lithiasic in 27.9% (n=24) of our patients, non-lithiasic in 55.8% (n=48) and cholecystectomized in 14 (16.3%).

The Wirsung was thin in 81.8% (72 patients), dilated in 15.9% (14 patients) and not visible in 2.3% (n=2).

The echostructure of the papilla was normal in the majority of cases (n=72).

EES enabled us to analyze the echostructure and echo anatomy of the head of the pancreas in order to orient ourselves towards the various pathologies of the organ. In our study, we obtained the following results:

Normal in 74.3%, heterogeneous in 8.1%, hypoechoic in 5.4%, hyperechoic in 4.1%, areolar honeycomb with hyperechoic spots in 5.4% and enlarged in 1.4%.

Analysis of the results revealed:

- Lithiasis in 40.4% of patients (n=36), 19 of whom underwent ERCP at the same time as anesthesia.
- Tumor pathology in 32.5% of patients (n=30): 18.2% pancreatic head cancer, 6.3% ampulloma and 1.3% biliary papillomatosis.
- Chronic pancreatitis in 22.4% of patients (n=20)
- 2 cases of pancreas divisum
- One case of sphincter of Oddi dysfunction.
- One case of choledocele

The diagnostic yield in our study was 68%.

Bilio-pancreatic SEA was normal in the remaining 32% of cases, with no cause found. (Table 2).

Table 2. Etiologies of acute pancreatitis diagnosed by endoscopic ultrasound

Diagnosis	N=89	%
Lithiasis	36	40,4
Tumor pathology	29	32,5
Chronic pancreatitis	20	22,4
Pancreas divisum	2	2,2
Sphincter of Oddi dysfunction	1	0,89
Choledocele	1	0,89

4. DISCUSSION

In use since the early 1980s, echo endoscopy is a safe, minimally invasive diagnostic procedure for patients with acute idiopathic pancreatitis.

Its advantages include the proximity of the probe to the pancreas, the availability of high-frequency probes for obtaining high-resolution images, and the absence of intestinal gas interference with image acquisition. Endoscopic ultrasound also has few complications [3,4].

The diagnostic yield of echo endoscopy varies, depending on the study, from 29% to 80%. In our study, the diagnostic yield of endoscopic ultrasound was 68%.

Various studies report that echo endoscopy has a higher sensitivity than other commonly used imaging techniques such as ultrasound, CT or cholangio pancreato MRI [3-9]. It is a reliable diagnostic method for detecting pancreas divisum [10,11], biliary and pancreatic tumours, with diagnostic accuracy superior to that of CT,

particularly for tumours less than 2.5 cm in diameter [12]. It is highly specific in the diagnosis of pancreatic cancer, with a negative predictive value of 100% [13].

Endoscopic ultrasound can detect solid and cystic pancreatic tumours at an early stage, before they are identified by ultrasound or CT, which can lead to early management and a better prognosis [14]. It is a useful technique for diagnosing chronic pancreatitis [15].

In a systematic review by Smith et al, of 13 studies evaluating the role of echo endoscopy in idiopathic acute pancreatitis, the most frequent etiology was biliary origin (stones, mini-lithiasis and sludge) missed by other imaging modalities. In these 13 studies, pancreatic diseases such as chronic pancreatitis, pancreas divisum and periampullary tumours were identified in 22.1% of patients. Overall, endoscopic ultrasound was diagnostic in 61% of patients with idiopathic acute pancreatitis, 41% of whom had biliary disease [6].

In a recent study conducted in 2022, biliary acute pancreatitis was the most frequent etiology in 52% of idiopathic acute pancreatitis cases.

In a systematic review of 28 studies including 1850 patients with idiopathic acute pancreatitis who underwent echo endoscopy, a biliary etiology (mini lithiasis or choledocholithiasis) was the most common and was found in 37% of cases [16].

It has been suggested that it is the small stones that have a transient impact on the ampulla of Vater and cause pancreatitis [17]. In some studies, mini-lithiasis is the main cause of idiopathic pancreatitis [9] and has been observed in 75% of cases of idiopathic pancreatitis in patients with a gallbladder [18]. Among IAPs, 20-50% present with mini calculi and tend to recur with high morbidity and mortality rates [19].

Echo-endoscopy is considered the best technique for diagnosing gallbladder mini-lithiasis, but biliary tract mini-lithiasis has rarely been detected or may not have a pathogenic role in acute pancreatitis in cholecystectomy patients [20].

In our study, biliary origin was the main cause of IAP frequency, accounting for 40.4% (n=36).

Some recurrent IAPs are secondary to genuine chronic pancreatitis (CP), not yet diagnosed by

standard morphological examinations. EE can show ductal abnormalities (intraductal calculi, dilated and irregular Wirsung, hyperechoic Wirsung wall) and parenchymal abnormalities (areolar appearance, hyperechoic spots, micro-calcifications, calcifications) in favour of the diagnosis of CP [21,22].

In our series, chronic pancreatitis was observed in 22.4% of cases.

In a 2019 study, chronic pancreatitis and associated pancreatic duct abnormalities (duct dilatation or stenosis) were reported in 21% of cases [16].

In a study by Yusoff et al, EE findings consistent with CP were reported as the most frequent findings in patients with PAI [14].

A smaller but significant number of pancreatic tumors (32.5%) were detected by EE in our study. The sensitivity of EE in the diagnosis of pancreatic tumours is 85.5%; specificity is 100%. In a retrospective study of 43 patients with pancreatic cancer revealed by AP, the diagnosis of cancer was made in all cases by standard morphological examinations [23].

In the study by Yussof et al [14], carried out on more than 370 patients with PAI, cancer was found in 0.8% of cases (3 patients). For these 3 patients, only EE allowed the diagnosis of pancreatic cancer.

In a systematic review, pancreatic neoplasms were found in 6% of patients [16].

Benign or malignant ampullary tumors are rare causes of recurrent IAP [24]. In our study, we found 5 cases of vaterial ampullomas that escaped other imaging modalities. It is sometimes difficult to diagnose a small intraductal ampulloma responsible for IPA.

In the study by Defrain et al. [25], EE with puncture aspiration had a sensitivity, specificity and negative predictive value of 82%, 100% and 80% respectively for the diagnosis of ampulloma. As ampulloma is a rare cause of IAP (probably <1%), EE with puncture aspiration is the reference test for the diagnosis of ampulloma when it has no obvious endoscopic translation on duodenoscopy.

Patients with recurrent IAP are more likely to present with pancreas divisum (10-25% of cases) than the general population [26]. Pancreas divisum is therefore considered a possible cause of recurrent IAP [26]. In our study, there was one case of pancreas divisum. Pancreas divisum is thought to be responsible for 10% of recurrent IPAs, and is therefore a diagnosis of elimination.

In a study by Rana et al. [10], the sensitivity, specificity, positive predictive value and negative predictive value of EE for the diagnosis of pancreas divisum were 100%, 96%, 80%, 100% and 96% respectively.

In a recent retrospective cohort study of 45 consecutive patients diagnosed with pancreas divisum, the diagnostic accuracy of EE was compared with that of CT and CP-MRI. The sensitivity of EE was 86.7%, significantly higher than that of CT (15.5%) or CP-MRI (60%). It was concluded that EE is a sensitive test for the diagnosis of pancreas divisum and is superior to CT and CP-MRI [27].

Finally, EE plays an indispensable role in the etiological assessment of IAP. Diagnostic cost-effectiveness in IAP ranges from 60 to 88% [17] (Table 3), meaning that for around 8 out of 10 patients presenting with IAP, EE enables the cause to be diagnosed.

The British Society Working Party determined that no more than 20% of patients with acute pancreatitis should be labelled idiopathic [28].

Table 3. Diagnostic cost-effectiveness of EE in the etiological investigation of IAPs

REVUE	No. of patients	Diagnostic efficiency (%)
(3) Frossard et al.	168	78
(17) Norton et al.	44	73
(7) Liu et al.	18	78
(9) Tandon et Topazian.	17	88
(14) Yussof et al.	169	84
Our study	89	68

The diagnostic cost-effectiveness of EE is the same whether it is a first attack or a recurrence [14]. If the EE was not performed immediately after the first flare, or if it is non-contributory, it should be performed again 4 weeks after the acute episode [14]. In case of negativity of the second EE, a cholangio-IRM is discussed in order to search for a bilio-pancreatic malformation (pancreas divisum or annulus) often difficult to demonstrate in EE [29].

This has been confirmed by the IAP /APA guidelines, which suggest that EE is the initial examination in PAI, and in the event of a negative result, to proceed with an MRI [30].

5. CONCLUSION

Echo endoscopy is currently an indispensable tool in the etiological investigation of unexplained acute pancreatitis. In our study, the diagnostic efficiency was around 68%. It is an indispensable diagnostic and therapeutic tool in many pathologies of the digestive tract, pancreas and biliary tract.

The etiology of acute pancreatitis remains uncertain in around 20% of cases, despite a complete clinical, biological and morphological work-up. Whether it's a first attack of AP or recurrent acute pancreatitis, specialized tests such as endoscopic ultrasound are required before we can speak of "unexplained" acute pancreatitis (IAP). In our study, the most frequent etiology was biliary.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Steinberg W, Tenner S. Acute Pancreatitis. *N Engl J Med.* 1994; 330:1198-1210. DOI: 10.1056/NEJM199404283301706N
2. Bank S, Indaram A. Causes of acute and recurrent pancreatitis. *Gastroenterol Clin North Am.* sept 1999;28(3):571-89. DOI: 10.1016/S0889-8553(05)70074-1
3. Frossard JL, SosaValencia L, Amouyal G, et al. Usefulness of endoscopic ultrasonography in patients with "idiopathic" acute pancreatitis. *Am J Med.* 2000; 109:196200. PMID: 10974181 DOI: 10.1016/S00029343(00)004782
4. Rana SS, Bhasin DK, Rao C, et al. Role of endoscopic ultrasound in idiopathic acute pancreatitis with negative ultrasound, computed tomography, and magnetic resonance cholangiopancreatography. *Ann Gastroenterol.* 2012; 25:133137 [PMID: 24714266]
5. Wilcox CM, Seay T, Kim H, et al. Prospective endoscopic ultrasound-based approach to the evaluation of idiopathic pancreatitis: Causes, response to therapy, and long term outcome. *Am J Gastroenterol.* 2016; 111:13391348. PMID: 27325219. DOI: 10.1038/ajg.2016.240
6. Smith I, Ramesh J, Kabir Baig KR, et al. Emerging role of endoscopic ultrasound in the diagnostic evaluation of idiopathic pancreatitis. *Am J Med Sci.* 2015;350:229-234. PMID: 26252794. DOI: 10.1097/MAJ.0000000000000054.
7. Liu CL, Lo CM, Chan JK, et al. EUS for detection of occult cholelithiasis in patients with idiopathic pancreatitis. *Gastrointest Endosc.* 2000;51:2832. PMID: 10625791. DOI: 10.1016/S00165107(00)703828
8. Vila JJ, Vicuña M, Irisarri R, et al. Diagnostic yield and reliability of endoscopic ultrasonography in patients with idiopathic acute pancreatitis. *Scand J Gastroenterol.* 2010;45:375381. PMID: 20034361. DOI: 10.3109/00365520903508894.
9. Tandon M, Topazian M. Endoscopic ultrasound in idiopathic acute pancreatitis. *Am J Gastroenterol.* 2001; 96: 705709. PMID: 11280538. DOI: 10.1111/j.15720241.2001.03609.x
10. Rana SS, Gonen C, Vilmann P. Endoscopic ultrasound and pancreas divisum. *JOP.* 2012; 13:252257. PMID: 22572127.
11. Sharma M, Pathak A, Rameshbabu CS, et al. Imaging of pancreas divisum by linear-array endoscopic ultrasonography. *Endosc Ultrasound.* 2016; 5:2129. PMID: 26879163. DOI: 10.4103/23039027.175878

12. DeWitt J, Devereaux B, Chriswell M, et al. Comparison of endoscopic ultrasonography and multidetector computed tomography for detecting and staging pancreatic cancer. *Ann Intern Med.* 2004;141:753763. PMID: 15545675. DOI: 10.7326/0003481914110200411160-00006
13. Klapman JB, Chang KJ, Lee JG, et al. Negative predictive value of endoscopic ultrasound in a large series of patients with a clinical suspicion of pancreatic cancer. *Am J Gastroenterol.* 2005;100:26582661. PMID: 16393216. DOI: 10.1111/j.15720241.2005.00315.x.
14. Yusoff IF, Raymond G, Sahai AV. A prospective comparison of the yield of EUS in primary vs. recurrent idiopathic acute pancreatitis. *Gastrointest Endosc.* 2004;60:673678. PMID: 15557941. DOI: 10.1016/S00165107(04)020188
15. Teshima CW, Sandha GS. Endoscopic ultrasound in the diagnosis and treatment of pancreatic disease. *World J Gastroenterol.* 2014;20:99769989. PMID: 25110426. DOI: 10.3748/wjg.v20.i29.9976
16. Pereira R, Eslick G, Cox M, Endoscopic ultrasound for routine assessment in idiopathic acute pancreatitis. *Journal of Gastrointestinal Surgery.* DOI: 0.1007/s11605-019-04272-3
17. Norton SA, Alderson D. Endoscopic ultrasonography in the evaluation of idiopathic acute pancreatitis. *Br J Surg.* 2000;87:1650–5. PMID: 11122178. DOI: 10.1046/j.1365-2168.2000.01587.x
18. Wilcox CM, Varadarajulu S, Eloubeidi M. Role of endoscopic evaluation in idiopathic pancreatitis: a systematic review. *Gastrointest Endosc.* 2006;63:1037–45. PMID: 16733122. DOI: 10.1016/j.gie.2006.02.024
19. Ardengh JC, Malheiros CA, Rahal F, et al. Microlithiasis of the gallbladder: Role of endoscopic ultrasonography in patients with idiopathic acute pancreatitis. *Rev Assoc Med Bras.* 2010;56:27–31. PMID: 20339782. DOI: 10.1590/s0104-42302010000100011
20. Elta GH. Sphincter of Oddi dysfunction and bile duct microlithiasis in acute idiopathic pancreatitis. *World J Gastroenterol.* 2008;14:1023–6. PMID: 18286682. DOI: 10.3748/wjg.14.1023
21. Catalano MF, Geenen JE. Diagnosis of chronic pancreatitis by endoscopic ultrasonography. *endoscopy.* Août. 1998;30(S 1):A 111-A 115. PMID: 9765100. DOI: 10.1055/s-2007-1001489
22. Wiersema MJ. Endosonography-guided cystoduodenostomy with a therapeutic ultrasound endoscope. *Gastrointest Endosc.* 1996;44(5):614-7. PMID: 8934175. DOI: 10.1016/s0016-5107(96)70022-6
23. Mujica VR, Barkin JS, Go VLW, Participants SG. Acute pancreatitis secondary to pancreatic carcinoma. *Pancreas.* 2000;21(4):329-32. PMID: 11075985. DOI: 10.1097/00006676-200011000-00001
24. Guzzardo G, Kleinman MS, Krackov JH, et al. Recurrent acute pancreatitis caused by Ampullary Villous Adenoma. *J Clin Gastroenterol.* avr 1990;12(2):200-2. PMID: 2182707. DOI: 10.1097/00004836-199004000-00020
25. DeFrain C, Chang CY, Srikureja W, et al. Cytologic features and diagnostic pitfalls of primary ampullary tumors by endoscopic ultrasound-guided fine-needle aspiration biopsy. *Cancer.* 2005;105(5):289-97. PMID: 15986397. DOI: 10.1002/cncr.21306
26. Sahel J, Cros RC, Bourry J, et al. Clinico-Pathological conditions associated with pancreas divisum. *Digestion.* 1982;23(1):1-8. PMID: 7084565. DOI: 10.1159/000198689
27. Kushnir VM, Wani SB, Fowler K, et al. Sensitivity of endoscopic ultrasound, multidetector computed tomography, and magnetic resonance cholangiopancreatography in the diagnosis of pancreas divisum: a tertiary center experience. *Pancreas.* 2013;42:436441. PMID: 23211370. DOI: 10.1097/MPA.0b013e31826c711a
28. Working Party of the British Society of G, Association of Surgeons of Great B, Ireland, Pancreatic Society of Great B, Ireland, Association of Upper GISoGB, et al. UK guidelines for the management of acute pancreatitis. *Gut.* 2005;54 Suppl 3:iii1-9. PMID: 15831893.

- DOI: 10.1136/gut.2004.057026
29. Lee SP, Nicholls JF, Park HZ. Biliary sludge as a cause of acute pancreatitis. N Engl J Med. 1992;326(9):589-93. PMID: 1734248.
DOI: 10.1056/NEJM199202273260902
30. Working Group IAPAPAAPG. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13(4 Suppl 2):e1-15. PMID: 24054878.
DOI: 10.1016/j.pan.2013.07.063

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