An investigation into the sensitivity of endoscopic ultrasound in the diagnosis of malignant bile duct in patients with idiopathic acute pancreatitis

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ABSTRACT

Introduction and Objective: Acute pancreatitis (AP) is an inflammatory process of the pancreas characterized by abdominal pain and increased pancreatic enzymes. This disease is diagnosed clinically. Endoscopic ultrasound (EUS), which is a technique with high sensitivity and specificity, is used to diagnose biliary disease. This study aimed to determine the sensitivity of EUS in the diagnosis of malignant bile duct in patients with idiopathic AP.

Methods: This descriptive study was performed on 146 patients with pancreatitis hospitalized in the gastrointestinal tract section of the Imam Khomeini Hospital of Ahwaz Jundishapur University of Medical Sciences. The collected data were analyzed by the SPSS 22.0 and the significance level of the test was <0.05.

Results: According to the results, 79 (54%) out of the 146 patients were female and 67 (46%) were male. The mean and standard deviation of the patients’ age were 52.5 and 19.6 years, respectively. The findings showed that the sensitivity and specificity of the EUS were 33% and 99%, respectively. Compared to the endoscopic retrograde cholangiopancreatography (ERCP), the sensitivity and specificity of the abdominal ultrasound were 62% and 62.5%, respectively. Compared to the ERCP, the sensitivity and specificity of EUS were 92% and 50%, respectively.

Conclusion: The findings of this study showed that the sensitivity and specificity of EUS were higher than those of abdominal ultrasound. Moreover, EUS was the preferred method to detect common bile duct stones (CBDS).

Keywords: Bile duct stones, endoscopic ultrasound, idiopathic acute pancreatitis

Introduction

Acute pancreatitis (AP) is an inflammatory process of the pancreas characterized by abdominal pain and increased pancreatic enzymes. Several clinical conditions are known as the causes of AP, the most common of which are gallstones and alcohol consumption.

The annual prevalence of AP is estimated to be 5–35 people per 100,000, while the mortality rate of AP is 5%.[1] Gallstones (including microlithiasis) are the most common causes of AP in 35–40% of cases.[1] Only 4–7% of those with gallstones have AP.[2] The gender of the patient and the size of the stone are known as risk factors for stone-induced pancreatitis. The risk of developing pancreatitis is higher in males. However, owing to the increased prevalence of bile duct stones in women, the prevalence of pancreatitis is higher in women.[3]

Abdominal ultrasound should be performed to detect bile duct stones in all patients with the first occurrence of AP.[7]
Ultrasound is not considered as an appropriate method for diagnosing and classifying the severity of pancreatitis. It is more commonly used to diagnose the presence of gallstone.\[9\]

The sensitivity of ultrasound for common bile duct stones (CBDs) in dilated and non-dilated cases is 75% and 50%, respectively.\[9\] The sensitivity and specificity of ultrasound for gallstones are 84% and 99%, respectively.\[10\] It should be pointed out that ultrasound does not have the ability to detect stones <3 mm.\[11\]

Endoscopic ultrasound (EUS) is a technique with high sensitivity and specificity that can be used to detect biliary disease.\[11\] Meta-analyses have shown that in contrast to endoscopic retrograde cholangiopancreatography (ERCP) and intraoperative cholangiography, EUS has a sensitivity and specificity of 89% and 94%, respectively, for the diagnosis of common bile duct stones (CBDS).\[12,13\]

The sensitivity of the EUS for the detection of CBDS is 100%, compared to the sensitivity of ultrasound that is 84%.\[14,15\] Compared to abdominal ultrasound, one of the most important advantages of EUS is that images of the biliary system are more clearly seen without the effects of abdominal fat and gases in the digestive system. Although EUS has great diagnostic capabilities, the aggressive nature and inability to perform therapeutic measures are regarded as deficiencies that do not allow the EUS to be known as the primary diagnostic tool for bile duct stones.\[16\] In 60–70% of cases, EUS can detect the main cause of AP. Studies have shown that the diagnostic capabilities of EUS are higher than magnetic resonance cholangiopancreatography (MRCP) for the diagnosis of small bile duct stones.\[17\] On the other hand, studies suggest that EUS performs as well as ERCP for the diagnosis of bile duct stones in the duodenum.\[16,18\]

Given the fact that the diagnosis of idiopathic AP can be performed by EUS and ERCP after ruling out the most common cause of pancreatitis (bile duct stones and gallbladder), EUS is of great importance. If patients are dismissed without definitive diagnosis of empiric therapy, the likelihood of a recurrence or subsequent complications will increase. Further studies are needed to investigate the diagnostic role of EUS in cases such as idiopathic AP. Owing to the fact that this has not been studied in Khuzestan and the great number of patients with pancreatitis, the present study aimed to determine the sensitivity of abdominal EUS and EUS in the diagnosis of malignant bile duct stones in patients with idiopathic AP.

### Materials and Methods

This descriptive study was performed on 146 patients with pancreatitis hospitalized in the Imam Khomeini Hospital in Ahwaz Jundishapur University of Medical Sciences. The study was approved by the ethics committee of the Ahvaz University of Medical Sciences, and written consent was obtained in accordance with the Helsinki Treaty. The demographic data of all participants were recorded. Those participants who were not excluded from the study underwent EUS during the first week of admission. Microlithiasis with a size of 0.5–3 mm was considered as the diagnostic level.

### Exclusion criteria

1. History of trauma in the abdomen,
2. History of chronic pancreatitis,
3. Pregnancy,
4. Long-term malnutrition,
5. History of chemotherapy, azathioprine, thiazide diuretic, OCP,
6. Alcohol consumption (>20 g per day),
7. Hypercalcemia,
8. Hypertriglyceridemia, and
9. Stones >3 mm in ultrasound.

The EUS device (EPM-3500 Hitachi Eub-5500) was provided by Pentax.

### Data analysis

The quantitative variables were mean, standard deviation, minimum, and maximum, while the qualitative variables included numbers (percentage). The normality of quantitative variables was investigated using the Shapiro–Wilk test. In order to examine the relationship between qualitative variables, the Chi-square test (or Fisher's exact test) was used. Accordingly, independent t-test and Mann–Whitney test were used to compare the quantitative variables. The significance level of the above tests was <0.05. Data analysis was performed using the SPSS 22.0.

### Results

According to the results, out of the 146 patients, 79 (54%) were female and 67 (46%) were male. The mean and standard deviation of the patients were 52.5 and 19.6 years, respectively.

Table 1 shows the frequency and percentage of gall bladder in ultrasound. In general, 55 patients (38%) were diagnosed without stones and sludge. Accordingly, 31 patients (21%) were reported to have sludge containing stones. Stones and sludge were detected in 40 patients (27%). The results of the Chi-square test showed that there was no significant difference between men and women in the gallstone report ($P = 0.19$). Of the 146 patients studied, 142 (97%) patients had bile duct stones and 3 (4%) had malignant bile duct stones.

| Variable                        | Female | Male | All patients | P      |
|---------------------------------|--------|------|--------------|--------|
|                                | n      | %    | n            | %      |
| Report of bile duct in ultrasound |        |      |              |        |
| Without stone or sludge         | 28     | 19   | 55           | 38     | 0.191 |
| With sludge                     | 14     | 17   | 31           | 21     |       |
| With stone                      | 15     | 5    | 20           | 14     |       |
| With stone and sludge           | 22     | 18   | 40           | 27     |       |
| Total                           | 79     | 100  | 146          | 100    |       |
Determining the sensitivity of abdominal ultrasound in the diagnosis of bile duct stones in comparison with EUS

Table 2 shows the sensitivity, specificity, positive and negative predictive value, and accuracy of abdominal ultrasound in the diagnosis of bile duct stones.

According to this table, abdominal ultrasound detects 125 patients as negative (no diagnosis of bile duct stones) and 17 patients as positive (diagnosis of bile duct stones).

The sensitivity of ultrasound was 0.33, which means that abdominal ultrasound was able to detect the bile duct stones correctly (33%). The specificity of abdominal ultrasound was 99%. The abdominal ultrasound was able to detect the absence of bile duct stones accurately (99%). The positive predictive value of abdominal ultrasound was 94.0. In fact, positive predictive value was a part of cases in which patients actually had bile duct stones. The negative predictive value of abdominal ultrasound was 74.0. In fact, negative predictive value showed that the participants were actually healthy. Overall, the accuracy of abdominal ultrasound was 0.66. In fact, the capability of abdominal ultrasound in the correct differentiation between healthy subjects and patients was 66%.

Determining the sensitivity of abdominal ultrasound in the diagnosis of malignancy

Table 3 shows the sensitivity, specificity, positive and negative predictive value, and accuracy of abdominal ultrasound in the diagnosis of malignancy.

According to Table 3, out of four cases of malignancy, abdominal ultrasound has not been able to detect any negative (detecting the absence of malignancy) or positive cases (detecting the malignancy). While abdominal ultrasound has detected three patients as false positive (misdiagnosis of malignancy) and one false negative (misdiagnosis of the absence of malignancy). Owing to the small sample size of patients with malignancy and the lack of true positive and negative diagnosis by abdominal ultrasound, it was concluded that the sensitivity, specificity, positive and negative predictive value, and accuracy of abdominal ultrasound were zero in the diagnosis of malignancy [Diagram 1].

Determining the sensitivity of EUS in diagnosis of bile duct stones in comparison with ERCP

Table 4 shows the sensitivity, specificity, positive and negative predictive value, and accuracy of EUS in the diagnosis of bile duct stones [Diagram 2].

According to Table 4, EUS has detected 6 negative cases (no bile duct stones) and 27 positive cases (with bile duct stones). The sensitivity of EUS was 0.92, meaning that it was able to detect the presence of bile duct stones correctly in 92% of the cases. The specificity of EUS was 0.5. It means that the capability of EUS to detect the absence of bile duct stones correctly was 50%.

The positive predictive value of EUS was 0.85. In fact, the positive predictive value shows that the patients actually have bile duct stones. The negative predictive value of EUS was 0.67. In fact, the negative predictive value shows that the subjects are healthy. Overall, the accuracy of EUS was 0.71. In fact, the
capability of abdominal ultrasound in differentiating healthy subjects from patients was 71%.

Discussion and Conclusion

AP is an inflammatory process of the pancreas characterized by abdominal pain and increased pancreatic enzymes. This disease is diagnosed clinically. Several clinical conditions are known as the causes of AP, with the most common of which being gallstones and alcohol consumption. There are several methods to diagnose bile duct stones. In this study, three diagnostic and therapeutic methods (abdominal ultrasound, EUS, and ERCP) were compared. The findings showed that the sensitivity of abdominal ultrasound was 33%. In contrast to ERCP, the sensitivity and specificity of abdominal ultrasound were 62% and 62.5%, respectively. Accordingly, EUS and ERCP were compared with one another. The sensitivity and specificity of the EUS were 92% and 50%, respectively.

Ardengh et al. investigated the sensitivity and specificity of EUS. They performed surgical and histological studies and concluded that the sensitivity and specificity of EUS were 92.6% and 55.6%, respectively. The present study obtained similar results and confirmed their study. Taha Ahmed et al. examined the sensitivity and specificity of abdominal ultrasound and EUS in comparison with ERCP. They showed that the sensitivity and specificity of abdominal ultrasound were 52% and 21%, respectively. Accordingly, the sensitivity and specificity of EUS were 62% and 36%, respectively. In the present study, the sensitivity and specificity of EUS were higher than abdominal ultrasound, but the sensitivity and specificity of EUS were higher than what the Taha Ahmed et al. reported. This can be attributed to the old generation endoscope used in the study.

In several studies, researchers evaluated patients for the sensitivity and specificity of abdominal ultrasound and EUS. The results showed that the sensitivity of ultrasound was 15–56% and the sensitivity of EUS in the detection of CBDS was 88–97%. The extensive sensitivity of the abdominal ultrasound in different studies can be attributed to the dependence of ultrasound on the person who undergoes it.

Conclusion

The findings of this study that were similar to those of previous studies showed that the sensitivity and specificity of EUS were higher than abdominal ultrasound, and EUS was the preferred method to detect the CBDS.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sarles H. Pancreatitis Symposium. Basel SK, Marseille; 1963.
2. Sarles H. Revised classification of pancreatitis—Marseille 1984. Dig Dis Sci 1985;30:573-4.
3. Cavallini G, Frulloni L, Bassi C, Gabbrielli A, Castoldi L, Costamagna G, et al. Prospective multicentre survey on acute pancreatitis in Italy (ProInf-AISP): Results on 1005 patients. Dig Liver Dis 2004;36:205-11.
4. Riela A, Zinsmeister AR, Melton LJ, DiMagno EP. Etiology, incidence, and survival of acute pancreatitis in Olmsted County, Minnesota. Gastroenterology 1991;100:A296.
5. Forsmark CE, Baillie J, AGA Institute Clinical Practice and Economics Committee, AGA Institute Governing Board. AGA Institute technical review on acute pancreatitis. Gastroenterology 2007;132:2022-44.
6. Moreau JA, Zinsmeister AR, Melton LJ 3rd, DiMagno EP. Gallstone pancreatitis and the effect of cholecystectomy: A population-based cohort study. Mayo Clin Proc 1988;63:466-73.
7. Sharma VK, Howden CW. Metaanalysis of randomized controlled trials of endoscopic retrograde cholangiography and endoscopic sphincterotomy for the treatment of acute biliary pancreatitis. Am J Gastroenterol 1999;94:3211-4.
8. Dervenis C, Johnson CD, Bassi C, Bradley E, Imrie CW, McMahon MJ, et al. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini consensus conference. Int J Pancreatol 1999;25:195-210.
9. Chak A, Hawes RH, Cooper GS, Hoffman B, Catalano MF,
Parsi, et al.: The sensitivity of endoscopic ultrasound in the diagnosis of malignant bile duct

10. Shea JA, Berlin JA, Escarce JJ, Clarke JR, Kinosian BP, Cabana MD, et al. Revised estimates of diagnostic test sensitivity and specificity in suspected biliary tract disease. Arch Intern Med 1994;154:2573-81.

11. Sgouros SN, Bergel C. Endoscopic ultrasonography versus other diagnostic modalities in the diagnosis of choledocholithiasis. Dig Dis Sci 2006;51:2280-6.

12. Garrow D, Miller S, Sinha D, Conway J, Hoffman BJ, Hawes RH, et al. Endoscopic ultrasound: A meta-analysis of test performance in suspected biliary obstruction. Clin Gastroenterol Hepatol 2007;5:616-23.

13. Tse F, Liu L, Barkun AN, Armstrong D, Moayyedi P, et al. EUS: A meta-analysis of test performance in suspected choledocholithiasis. Gastrointest Endosc 2008;67:235-44.

14. Dill JE, Hill S, Callis J, Berkhouse L, Evans P, Martin D, et al. Combined endoscopic ultrasound and stimulated biliary drainage in cholecystitis and microlithiasis–diagnoses and outcomes. Endoscopy 1995;27:424-7.

15. Frossard JL, Sosa-Valencia L, Amouyal G, Marty O, Hadengue A, Amouyal P. Usefulness of endoscopic ultrasonography in patients with “idiopathic” acute pancreatitis. Am J Med 2000;109:196-200.

16. Verma D, Kapadia A, Eisen GM, Adler DG. EUS vs MRCP for detection of choledocholithiasis. Gastrointest Endosc 2006;64:248-54.

17. Ortega AR, Gómez-Rodriguez R, Romero M, Fernández-Zapardiel S, Céspedes Mdel M, Carrobles JM. Prospective comparison of endoscopic ultrasonography and magnetic resonance cholangiopancreatography in the etiological diagnosis of “idiopathic” acute pancreatitis. Pancreas 2011;40:289-94.

18. Kohut M, Nowakowska-Dulawa E, Marek T, Kaczor R, Nowak A. Accuracy of linear endoscopic ultrasonography in the evaluation of patients with suspected common bile duct stones. Endoscopy 2002;34:299-303.

19. Ardengh JC, Malheiros CA, Rahal F, Pereira V, Ganc AJ. Microlithiasis of the gallbladder: Role of endoscopic ultrasonography in patients with idiopathic acute pancreatitis. Rev Assoc Med Bras 2010;56:27-31.

20. Buscarini E, Tansini P, Vallisa D, Zambelli A, Buscarini L. EUS for suspected choledocholithiasis: Do benefits outweigh costs a prospective, controlled study. Gastrointest Endosc 2003;57:510-8.

21. Amouyal P, Amouyal G, Levy P, Tuzet S, Palazzo L, Vilgrain V. Diagnosis of choledocholithiasis by endoscopic ultrasonography. Gastroenterology 1994;106:1062-7.

22. Sugiyama M, Atomi, Y. Endoscopic ultrasonography for diagnosing anomalous pancreaticobiliary junction. Gastrointest Endosc 1997;45:261-7.

23. Dancygier H, Nattermann C. The role of endoscopic ultrasonography in biliary tract disease: Obstructive jaundice. Endoscopy 1994;26:800-2.

24. Songur Y, Temucin G, Sahin B. Endoscopic ultrasonography in the evaluation of dilated common bile duct. J Clin Gastroenterol 2001;33:302-5.