

CLINICAL STUDY

The role of endoscopic ultrasound in patients with acute pancreatitis

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ABSTRACT

OBJECTIVES: Acute biliary pancreatitis is the most common form of acute pancreatitis worldwide.

Endoscopic ultrasound (EUS) may be helpful in detecting common bile duct stones and in indicating more invasive endoscopic retrograde cholangiopancreatography (ERCP) examinations or determining rarer aetiologies of acute pancreatitis.

METHODS: Over a period of six years, we prospectively collected 131 patients with acute biliary pancreatitis and observed the need for endoscopic examination alongside with a decrease in the number of necessary ERCP examinations as a result of negative EUS results (no bile duct stones detected). We compared groups of patients given different endoscopic treatments in relation to their hospital mortality relative to the incidence of severe acute pancreatitis.

RESULTS: As many as 68 % of primarily indicated EUS examinations had a negative result (no common bile duct stones detected) and this result saved the patients from needing to undergo an invasive ERCP procedure. Both the incidence of the severe form of acute pancreatitis and the hospital mortality rate were lower among patients who underwent only EUS or ERCP after EUS as compared to patients who underwent ERCP straight away.

CONCLUSION: The use of EUS in patients with acute pancreatitis is very helpful in determining the treatment strategy (ERCP indication) and may reduce hospital mortality (Tab. 2, Ref. 14). Text in PDF www.elis.sk

KEY WORDS: acute pancreatitis, endoscopic ultrasound, common bile duct stones.

Introduction

Acute pancreatitis is an acute inflammatory disease of the pancreas with an annual incidence of 5 to 80 cases per 100,000 population and varying severity (from a mild form to a severe, fatal form with possible local or organ complications). In many countries, acute pancreatitis is one of the most frequent gastrointestinal causes of hospital admission. Gallstones (biliary form) and alcohol are the most common causes of acute pancreatitis worldwide; in 5–10 % of cases the aetiology of the disease is idiopathic (1).

Endoscopic ultrasound (EUS) is a non-invasive imaging technique used to investigate the organs of the gastrointestinal tract and the organs and tissue next to the digestive tract, such as those

in the pancreaticobiliary area, including the pancreas and the extrahepatic biliary tree, which can be visualized from the stomach and duodenum. This method even enables tissue sampling by EUS-guided fine needle aspiration (EUS-FNA) (2).

The role of the pancreato-biliary endoscopic ultrasound has extended during the last 40 years, and it is now routinely used worldwide. A systematic review of the use of EUS in pancreato-biliary disease while examining its performance and outcomes, was published by Fusaroli et al in 2012. That review examined 1,089 papers, but only 40 of them discussed the role of EUS in acute pancreatitis and only 6 looked at the role of EUS in detecting common bile duct stones (3).

In this paper we demonstrate the key role EUS can play in detecting common bile duct stones in patients with acute biliary pancreatitis. EUS enables the treatment strategy to be altered for such patients, in particular as concerns the indication of endoscopic retrograde cholangiopancreatography (ERCP). This paper will also show how accurate EUS is in establishing the aetiology of pancreatitis, including cases with unclear history, laboratory tests, abdominal ultrasound or CT scan. Last but not least, we compare the morbidity and mortality rates between patients who did not undergo any endoscopic examination, patients who were treated straight away using ERCP, and patients who were first examined via EUS.

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What we know about EUS in biliary and idiopathic acute pancreatitis

Studies carried out in the past decades (Chak et al, Sugiyama et al) have shown that EUS is a very sensitive tool in the diagnosis of gallstones (including microlithiasis), as well as in differentiating between acute and chronic pancreatitis, pancreatic tumors, intraductal papillary mucinous neoplasm (IPMN), ampuloma and other causes of acute pancreatitis that may not be conclusively diagnosed by other imaging methods (4, 5).

Four studies included in the review by Fusaroli et al investigated the presence of common bile duct stones during the course of acute pancreatitis and showed that EUS was able to detect such stones with a sensitivity of 91 % to 100 % and specificity of 85 % to 100 %. EUS was more sensitive than ERCP in detecting stones smaller than 4 mm in the common bile duct (90 % vs 23 %) (3).

Sugiyama et al report that there is no significant difference between EUS and magnetic resonance cholangiopancreatography (MRCP) for the detection of common bile duct stones; however, the sensitivity of MRCP seems to decrease for the detection of small (< 6 mm) stones, while EUS remains highly sensitive (5).

EUS can be used to diagnose rare causes of acute pancreatitis and is more sensitive than ultrasound (US) and computer tomography (CT) in diagnosing causes of biliary obstruction, including malignant obstruction (97 % vs 49 % or 66 %). The diagnosis of ampullary neoplasms and their local staging is more accurate by EUS than via CT or MRI (EUS 78 %, CT 24 %, MRI 46 %) (4, 5). EUS and MRCP are able to diagnose IPMN with better sensitivity than a CT scan, even though IPMN is overall a rare cause of acute pancreatitis (approximately 1 % of all cases) (6, 7).

ERCP indication in acute biliary pancreatitis

The biliary form is the most common form of acute pancreatitis worldwide; ERCP is thus often used in the treatment of the disease. The indication and timing of ERCP in acute biliary pancreatitis has recently been changing; current recommendations approve ERCP if clinical signs of acute cholangitis are present, otherwise conservative treatment is recommended (8–10). EUS may be very helpful in decreasing the number of ERCP indications by confirming or excluding the presence of stones in the bile duct (8–11).

ERCP is an invasive procedure that may lead to some complications. The most common of these is post-ERCP acute pancreatitis (PEP) with an incidence of 3–10 %. The risk factors for PEP comprise the history of PEP or recurrent pancreatitis, female sex, age below 40 years, normal level of bilirubin, difficult cannulation of the papilla, repeated cannulation of the pancreatic duct, endoscopic papillosphincterotomy and endoscopic papillary balloon dilation. Serious haemorrhage may be a complication of endoscopic papillosphincterotomy (0.3–2 %), mostly in patients with coagulopathy (spontaneous or drug-induced) or thrombocytopenia. Acute post-ERCP cholangitis or cholecystitis have

an incidence of 0.5–3 % and usually require treatment with antibiotics. Finally, a very serious potential complication of ERCP is the perforation (of the duodenum, papilla or common bile duct after cannulation), with a low incidence of 0.08 % to 0.6 % but high morbidity and mortality rates (9–14).

Methods

Over a period of six years, between 1.1.2014 and 31.12.2019, 248 patients with acute pancreatitis (AP) were hospitalized at the Department of Internal Medicine. We collected data on these patients prospectively during their hospitalisation and follow-up as part of outpatient care provided to patients with intermediate or severe forms of AP. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent (approved by the Institutional Ethics Committee) was obtained from each patient in the study. We collected the data in order to assess the epidemiology of AP at our hospital, analyse the use of CT scans and endoscopic examinations in patients with AP, recognize potential new risk factors for intermediate or severe AP at the time of hospital admission in comparison with established global scoring systems, and to compare the morbidity and mortality among patients who undergo different types of endoscopic treatment. We excluded patients with an exacerbation of chronic pancreatitis (based on the patient's history or findings on US or CT scan or via endoscopy) from the statistical analysis.

Statistical analysis

Comparisons of continuous variables were made using t-tests or Mann–Whitney tests, as appropriate. Comparisons of categorical variables were made using chi-square tests or Fischer tests, as appropriate. All computations were performed using STATISTICA 13.5 software.

Results

Acute biliary pancreatitis (ABP) was the most common form of acute pancreatitis in our group, occurring in 52 % of all AP patients (131/248 patients). We established this diagnosis in 64 men and 67 women.

Among the 64 men with ABP, 43, 9 and 12 had a mild, moderate and severe form, respectively; while 5 men died. Among the 67 women, 54, 8 and 5 had a mild, moderate and severe form, respectively, while 3 women died. The overall mortality of the patients with acute biliary pancreatitis was 6 % (7.8 % in men, 4.4 % in women) (Tab. 1).

During the six-year observation period, we treated 131 patients with ABP. As many as 32 of these patients did not undergo any

Tab. 1. Characteristics of patients and their AP courses.

	Total n (%)	Median age	Mild form n (%)	Moderate form n (%)	Severe form n (%)	Mortality n (%)
Men	64 (48.8)	62.5	43 (67.2)	9 (14)	12 (18.8)	5 (7.8)
Women	67 (51.1)	66.1	54 (80.6)	8 (11.9)	5 (7.4)	3 (4.4)

endoscopic examination (18 men and 14 women), because repeated abdominal ultrasound examinations or CT scans revealed a common bile duct of normal size and their cholestatic liver tests showed normal levels. In this group of patients without endoscopic examination, 59.4 %, 15.6 % and 25 % of patients had a mild (19/32), moderate (5/32) and severe (8/32) form of ABP, respectively. In this group, the incidence of severe ABP was higher than in the other groups of observed patients ($p = 0.023$) while the incidence of mild ABP was lower ($p = 0.050$). Three patients died while hospitalised, so the hospital mortality in this group was 9.4 %.

In 24 of our observed patients, we indicated ERCP straight away (due to symptoms of acute cholangitis in the acute phase, or common bile duct stones or evident dilatation of the common bile duct (CBD) visible via ultrasound, or lasting elevation of cholestatic liver tests, or endoscopic papillosphincterotomy as a therapeutic aim in patients not indicated for cholecystectomy). In this group, 70.8 %, 8.3 % and 20.8 % of patients had a mild (17/24), moderate (2/24) and severe (5/24) form of ABP, respectively. Three of these patients died, so the hospital mortality in this group was the highest, namely 12.5 % (3/24, $p = 0.026$).

In 75 of our observed patients (34 men and 41 women) we indicated EUS to exclude or to confirm the presence of stones in the CBD, mostly on the 3rd–5th day of the course of the disease. As a result of using EUS we were able to exclude the presence of CBD stones in 51 of these patients (22 men and 29 women). In other words, EUS helped us to exclude choledocholithiasis in 68 % of the indicated patients so that they did not need to undergo ERCP. In the group of patients who underwent only EUS, 86.3 %, 9.8 % and 3.9 % of patients had a mild (44/51), moderate (5/51) and severe (2/51) form of ABP. Only 1 patient died (mortality was 1.96 %).

Following EUS, we indicated ERCP in 24 patients; 18 of those ERCP examinations confirmed CBD stones, while in 6 cases no CBD stones were found, although in 2 of these patients a deformation of the papilla or terminal stenosis of the CBD was described, meaning that a passage of a stone was very possible (10–12). We did not make both endoscopic examinations in one day; the period between EUS and ERCP was mostly 1 day, while in the 4 cases of ERCP not confirming the CBD stones, the period between EUS and ERCP was longer, particularly between 2 and 7 days (mean period 4 days). This may be also the reason behind the differences between the results of the EUS and ERCP in these cases. In the group of patients treated in 2 steps, with ERCP after CBD stones had been found using EUS, 75 %, 16.7 % and 8.3 % of patients had a mild (18/24), moderate (4/24) and severe (2/24) form of ABP. Only 1 patient died (mortality was 4.1 %) (Tab. 2).

In 11 patients, we indicated EUS because the cause of the disease was unknown (based on patient history, laboratory tests and abdominal ultrasound or CT scan). In 4 of these patients, EUS confirmed the cause of the pancreatitis (IPMN in 3 patients, *pancreas divisum* in 1 patient). In 7 patients, the EUS did not reveal the cause and after repeated revision of the history and all results, we

Tab. 2. Various types of endoscopy examinations.

	Total n (%)	Mild form n (%)	Moderate form n (%)	Severe form n (%)	Mortality n (%)
No Endoscopy	32 (24.4)	19 (59.4)	5 (15.6)	8 (25)	3 (9.4)
Only ERCP	24 (18.5)	17 (70.8)	2 (8.3)	5 (20.8)	3 (12.5)
Only EUS	51 (39.2)	44 (86.3)	5 (9.8)	2 (3.9)	1 (2)
EUS + ERCP	24 (18.5)	18 (75)	4 (16.7)	2 (8.3)	1 (4.1)

treated 3 of these cases as alcoholic pancreatitis (even though the patients did not concede regular alcohol abuse), 2 cases as being likely drug-induced and 2 cases as being idiopathic – 1 with mild ABP and 1 with a moderate form of the disease with a huge acute fluid collection followed by a spontaneous regression without any need for endoscopic treatment (drainage) or surgery.

Discussion

Endoscopic ultrasound is a simple, non-invasive examination, which should be considered absolutely essential in the diagnosis and treatment of acute biliary and idiopathic pancreatitis.

In our group of 131 patients with ABP, we indicated EUS in 75 patients. EUS helped us to determine whether to indicate ERCP. As many as 68 % (51 of 75 patients) did not have to undergo ERCP because the EUS had already excluded the presence of CBD stones. With the help of EUS we therefore reduced the use of invasive ERCP examinations while saving patients from the potential complications that come with ERCP. During the 6-year period in question, we had only 1 case of fatal post-ERCP complication at our clinic, in which a patient with ABP suffered a severe arterial haemorrhage after an endoscopic papillosphincterotomy and died of haemorrhagic shock 5 days later. Our study therefore confirmed that making use of EUS for ABP patients in line with current recommendations and guidelines reduces the need for ERCP and in turn reduces the potential for severe post-ERCP complications (8–10).

One of our secondary aims in this study was to compare the hospital mortality rate and morbidity (the incidence of severe AP) between groups of patients treated using different endoscopic strategies. The hospital mortality was higher in 2 groups, namely in patients who did not undergo any endoscopic examination (mortality rate 9.4 %) and patients who underwent ERCP only (mortality rate 12.5 %). The mortality rate in the group of patients who underwent EUS only was 2 %, and the mortality rate among the patients who underwent ERCP after the EUS had confirmed the diagnosis of CBD stones was 4.1 %. The incidence of severe AP was also higher among the patients who did not undergo any endoscopic examination (25 %) or underwent only ERCP (20.8 %) than among the patients examined by EUS only or with ERCP after EUS. Hence, our study's results suggest that by making use of EUS in this way we could decrease both the morbidity of acute biliary pancreatitis and hospital mortality rate among patients with this disease.

Last but not least, making use of endoscopic ultrasound during the period of observation also helped us to identify a causal diagnosis in 36 % of cases (4 out of 11 patients) of apparently

idiopathic pancreatitis. We indicated EUS after the first attack of AP for all 11 of these patients; in 4 of these cases, EUS revealed the reason for AP (IPMN in 3 cases, and *pancreas divisum* in 1 case). All 4 of these patients then underwent MRCP and the diagnosis of IPMN or *pancreas divisum* was confirmed. The patients were provided with follow-up outpatient care. All 3 patients with IPMN were over the age of 80 years, so they did not undergo surgery; the patient with *pancreas divisum* was 50 years old at the time of his first attack of acute pancreatitis and has not suffered any relapse to date.

The authors of the manuscript are aware, that there is a limited number of patients in the present study while recognising the need of investigating a larger number of patients with acute pancreatitis to have more accurate and convincing data. The authors also agree that magnetic resonance cholangiopancreatography (MRCP) as a noninvasive examination for detecting CBD stones could be an alternative, but in many hospital acute MRCP is unattainable, or with a very long waiting period.

Conclusion

At our clinic, we have excellent experience of using endoscopic ultrasound in the diagnosis of patients with ABP. Our study shows that routine use of EUS by an experienced endoscopist helps to determine the need for ERCP and may decrease the number of non-indicated ERCP examinations performed, thereby also decreasing the occurrence of post-ERCP complications. The use of EUS may also decrease the mortality rate among AP patients and can reveal the aetiology of AP.

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