Role of endoscopic ultrasound during hospitalization for acute pancreatitis

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Abstract
Endoscopic ultrasound (EUS) is often used to detect the cause of acute pancreatitis (AP) after the acute attack has subsided. The limited data on its role during hospitalization for AP are reviewed here. The ability of EUS to visualize the pancreas and bile duct, the sonographic appearance of the pancreas, correlation of such appearance to clinical outcomes and the impact on AP management are analyzed from studies. The most important indication for EUS appears to be for detection of suspected common bile duct and/or gall bladder stones and microlithiasis. Such an approach might avoid diagnostic endoscopic retrograde cholangio-pancreatography with its known complications. The use of EUS during hospitalization for AP still appears to be infrequent but may become more frequent in future.

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Key words: Acute pancreatitis; Endoscopic ultrasound; Acute biliary pancreatitis; Endoscopic retrograde cholangio-pancreatography; Idiopathic pancreatitis

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INTRODUCTION
In recent years endoscopic ultrasound (EUS) has emerged as a very useful diagnostic modality in the evaluation of patients with acute pancreatitis (AP). Studies have shown EUS to be highly accurate in the diagnosis of gallstone disease (including microlithiasis), chronic pancreatitis, pancreatic tumors and other causes of AP which have negative or inconclusive results as assessed by other imaging methods. However, most of these studies have been carried out after the acute attack has subsided.

There are very limited data regarding the role of EUS during AP. We have reviewed the literature as to the role of EUS during an episode of acute pancreatitis and attempted to find out its utility in terms of making a diagnosis, finding an etiology and predicting the severity and outcomes in AP.

We could find only 8 studies (7 published and 1 in abstract form) so far which have investigated EUS during an episode of AP. Of these, only one study looked specifically at the diagnostic usefulness of EUS in AP and another looked at its prognostic value. Most of the other studies looked at the role of EUS in evaluation of gallstone pancreatitis and compared it to other diagnostic modalities such as transabdominal US and endoscopic retrograde cholangio-pancreatography (ERCP). We reviewed these studies in an attempt to answer the following questions with regard to AP: (1) how good is EUS in visualizing the pancreas and bile duct? (2) what are the findings...
on EUS? (3) whether these findings correlate with the clinical outcomes and (4) what is the role of EUS in suspected biliary pancreatitis?

VISUALIZATION OF THE PANCREAS AND THE BILE DUCT BY EUS DURING ACUTE PANCREATITIS

During acute pancreatitis, edema of the duodenal wall, pancreatic necrosis and inflammation or fluid collection around the pancreas can potentially hinder the visualization of the pancreas, gallbladder or bile duct by EUS. There are only two prospective studies (with 23 and 35 patients, respectively) which have commented about visualization of the pancreas during AP, and the entire pancreas could be visualized in all patients in both of the studies\(^\text{[5,7]}\). While there are four studies (with a total of 228 patients) which have shown complete visualization of the gallbladder and bile duct in all patients during AP\(^\text{[5-7,10]}\), this was not possible in three studies\(^\text{[8-10]}\). In one study, the gallbladder could not be visualized in three out of 28 patients (10.7%)\(^\text{[10]}\). One out of the 3 patients had situs inversus, and in two the gall bladder was located abnormally. In the same study, visualization of the common bile duct (CBD) was complete in 32 patients (88.8%), partial in 3 (8.3%) and unsuccessful in 1 patient (2.7%). Prat et al\(^\text{[11]}\) in their study of 123 patients, found that EUS imaging of the CBD was unsatisfactory in three out of 123 patients (2.4%), two with Billroth II gastrectomy and one who underwent transcystic drainage. In another study, CBD could not be visualized in one out of 38 patients (2.6%) due to severe pancreatic necrosis\(^\text{[11]}\).

These observations suggest that even though EUS can visualize the entire pancreas, gallbladder and bile duct in acute pancreatitis in most patients, there may be occasional difficulties encountered in patients with severe pancreatic necrosis, unusual location of gallbladder or altered gastroduodenal anatomy.

We would like to stress here that while the entire pancreas can be visualized in AP, changes of chronic pancreatitis and small tumors can be missed and hence EUS for these indications should be avoided during an episode of AP. Another question that needs to be addressed is, how well can the pancreatic duct be imaged by EUS during AP? This has been mentioned in only one study of 23 patients, out of which the main pancreatic duct was seen in 78% of patients\(^\text{[11]}\). There are no data concerning sensitivity and specificity of EUS in detecting pancreatic duct disruptions and strictures during the course of AP.

EUS FINDINGS OF THE Pancreas IN ACUTE PANCREATITIS

There are 4 studies\(^\text{[5-8,10]}\) that looked prospectively at the EUS findings in AP early in the disease course. In 3 of the studies\(^\text{[5-7,10]}\), EUS was performed within 72 h of admission and in the other it was done within the 1st week\(^\text{[5]}\). In two prospective studies by Sugiyama et al\(^\text{[5,7]}\), EUS showed a normal or diffusely enlarged pancreas with a normal or diffusely low internal echo pattern in all patients with edematous pancreatitis. The details of these findings were given in only one out of the 2 studies, involving 23 patients\(^\text{[10]}\). In this study, the pancreas was normal in size in 37.5% of patients with edematous pancreatitis. The echogenicity was normal in 25% and the remaining 75% had diffusely hypoechoic pancreas. However, in another study by Chak et al\(^\text{[10]}\), the pancreas appeared normal in size in 63.8% of patients. Only eight out of 36 patients (22.2%) with edematous pancreatitis had a hypoechoic pattern on EUS. Four patients (11.1%) had hyperechoic pattern and the remaining 24 (66.6%) had a mixed pattern. Based on these findings, it appears that in edematous pancreatitis, EUS can show a normal-sized or enlarged pancreas, while hyperechoic pattern may be quite common. In our experience, in some patients the only findings on EUS suggestive of AP can be peripancreatic inflammation/ fluid collection (unpublished data). Table 1 shows the salient EUS features of acute edematous pancreatitis. In the studies carried out by Sugiyama et al\(^\text{[5,7]}\), EUS also demonstrated extrapancreatic inflammatory spread as a hypoechoic area. When results of these two studies were combined, EUS correctly identified fluid in the lesser sac in all 18 patients (100%) while fluid in the retroperitoneum was identified in 20 out of 25 patients (80%).

Sugiyama et al\(^\text{[7]}\) also found that all patients with necrotizing pancreatitis (n = 6) had focal hypoechoic areas with or without interspersed hyperechoic spots. The location and size of focal hypoechoic regions on EUS corresponded to those of avascular pancreatic necrosis on contrast-enhanced CT. Schoefer et al\(^\text{[8]}\) in their abstract commented that EUS was able to detect pancreatic necrosis early in 3 patients. However, the number of patients with necrotizing pancreatitis in these studies was very small and therefore these results cannot be extrapolated to all patients with acute necrotizing pancreatitis.

CORRELATION OF EUS FINDINGS WITH CLINICAL OUTCOMES IN AP

Chak et al\(^\text{[10]}\), in their study of 36 patients, found that in patients with peripancreatic fluid collection on EUS, there was a trend toward longer duration of hospital stay but it was not statistically significant (9.2 d vs 5.7 d, P < 0.1). They also found that patients whose pancreas had a coarse echotexture (n = 6) had a significantly shorter hospitalization (2.6 d) as compared to those with fine (n = 19) or grainy (n = 11) echotexture (6.6 and 8.2 d, respectively). However, size of the inflamed gland, parenchymal heterogeneity, parenchymal echogenicity and gastroduodenal wall edema did not correlate with the duration of hospital stay.

Schoefer et al\(^\text{[8]}\), in a prospective study of 31 patients, developed an EUS score from 1-30 based on findings such as organ size, aspect of outer margin, echogenicity, location and degree of peripancreatic fluid. The score was correlated with clinical course and CT severity index. EUS score correlated significantly with duration of hospital stay (P < 0.0001), number of days with fever (P < 0.001),
days spent in ICU ($P < 0.0001$) and CT severity index ($P = 0.0004$). However, this study was published only in abstract form and therefore requires further validation.

### ROLE OF EUS IN SUSPECTED ACUTE BILIARY PANCREATITIS

There are many studies which have looked at the utility of EUS in the diagnosis of CBD stones. However, only 4 studies have so far investigated this during the course of AP\cite{7,8,10,12}. These studies showed that EUS had a sensitivity of 91% to 100% and specificity of 85% to 100% to detect CBD stones (Table 2). It is generally believed that in patients with acute pancreatitis and intermediate probability of CBD stones, EUS can be done safely and may avoid diagnostic ERCP, with its attendant complications. A recent meta-analysis based on 4 randomized controlled trials performed by Petrov et al\cite{7} showed that use of EUS for the selection of patients who need therapeutic ERCP results in significantly lower risk of complications in comparison with the use of ERCP for both diagnosis and treatment of choledocholithiasis. However, it should be noted that only one of these 4 RCTs was carried out in the setting of AP\cite{10}. In this trial, 140 patients with first episode of suspected biliary AP were randomized to EUS or ERCP, within 24 h of admission. In the EUS group, therapeutic ERCP with endoscopic sphincterotomy (ES) and stone extraction was performed if EUS detected choledocholithiasis; otherwise the patients were managed conservatively. None of the patients with negative EUS for CBD stones had recurrent pancreatitis or symptoms suggestive of biliary stones during a median follow up of 26 mo. The only statistically significant difference between the two groups was that EUS could be performed in 100% of patients, while successful cannulation of the CBD in the ERCP group was possible in 86% ($P = 0.001$).

While there were no complications related to EUS, four patients in the ERCP arm had post-ES bleeding. However, there was no significant difference in morbidity or mortality between the 2 groups.

### CAN EUS REPLACE CT OR TRANSABDOMINAL ULTRASOUND?

Sugiyama et al\cite{7} pointed out that EUS did not have some of the drawbacks of CT such as radiation exposure and contrast load and therefore could be potentially used for both the diagnosis and detection of the cause of AP. However, in patients with edematous pancreatitis, EUS can show normal pancreas. Moreover, the findings on EUS are variable in edematous pancreatitis (hypoechoic, hyperechoic or mixed). Although there is a suggestion that EUS might be able to detect pancreatic necrosis, this is based on a small sample size and therefore larger studies are needed for its validation. Again, EUS cannot detect fluid collection in the retroperitoneal area very well. At the same time, patients with severe pancreatitis may require multiple CT scans to evaluate the dynamics of local complications. Whether EUS, an invasive test, will be feasible and cost effective under these circumstances is a question that needs to be addressed.

Chak et al\cite{5} recommended that if the patient would undergo EUS regardless of the transabdominal US findings, it made sense to forgo the expense of transabdominal US. However, in the same study there were 3 patients in whom the gallbladder was not seen on EUS but was seen only on conventional US and all 3 had gallstones.

Therefore, based on current evidence, one cannot propose that EUS can replace CT or transabdominal US. However, in certain situations such as patients with renal failure, contrast allergy or early pregnancy when CT scan cannot be carried out, EUS might have a role to play.

### CONCLUSION

The data regarding the role of EUS during AP are limited because its use in this situation is evolving. There is a wide variation in appearance of the pancreas on EUS during AP and it may even be normal in some patients. The finding of focal hypoechoic areas on EUS has been suggested to indicate pancreatic necrosis, but this finding needs to be validated with larger trials. Preliminary data

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Table 1  Endoscopic ultrasound features in acute edematous pancreatitis

| Study               | No. of patients | Normal-sized pancreas (%) | Normal echogenicity (%) | Hypoechoic (%) | Hyperechoic (%) | Mixed (%) |
|---------------------|-----------------|----------------------------|-------------------------|----------------|-----------------|-----------|
| Sugiyama et al\cite{7}, 1995 | 16              | 37.5                       | 25.0                    | 75.0           | None            | None      |
| Chak et al\cite{5}, 1999      | 36              | 63.8                       | None                    | 22.2           | 11.1            | 66.6      |

Table 2  Sensitivity, specificity, positive and negative predictive value of endoscopic ultrasound to detect common bile duct stones in acute pancreatitis

| Study               | No. of patients | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|---------------------|-----------------|-------------|-------------|---------------------------|---------------------------|
| Sugiyama et al\cite{7}, 1998 | 35              | 100         | 100         | -                         | -                         |
| Chak et al\cite{5}, 1999      | 36              | 91          | 100         | 100                       | 95                        |
| Liu et al\cite{8}, 2001       | 100             | 97          | 98          | -                         | -                         |
| Stabuc et al\cite{10}, 2008   | 48              | 96          | 85          | 92                        | 92                        |
have shown that some findings on EUS might be able to predict the severity of AP, but further studies are needed for confirmation. One of the important indications for performing EUS in AP is suspected acute biliary pancreatitis when transabdominal US and CT do not show biliary calculi. Although the EUS-guided ERCP approach has been shown to be beneficial in patients with suspected choledocholithiasis, data supporting this in the setting of acute pancreatitis are limited. Identifying other causes such as tumors during the acute stage, while possible, is often done after the resolution of the attack. EUS definitely has a role in the drainage of pancreatic fluid collection and in helping to obtain access to perform necrosectomy. Thus, at the present time, the role of EUS during the acute stage of AP is still limited.

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