Endoscopic assessment and treatment of biliary pancreatitis

Nora D.L. Hallensleben¹,², Nicolen J. Schepers¹,³, Marco J. Bruno¹ and Djuna L. Cahen¹,⁴ on behalf of the Dutch Pancreatitis Study Group

¹ Dept. of Gastroenterology and Hepatology, Erasmus University Medical Center, PO 2040, 3000 CA Rotterdam; the Netherlands, ² Dept. of Surgery, St. Antonius Hospital, PO 2500, 3430 EM Nieuwegein; the Netherlands, ³ Dept. of Gastroenterology and Hepatology, St. Antonius Hospital, PO 2500, 3430 EM Nieuwegein; the Netherlands, ⁴ Dept. of Gastroenterology and Hepatology, Amstelland Medical Center, PO 328, 1180 AH Amstelveen; the Netherlands

e-mail: n.hallensleben@pancreatitis.nl

Version 1.0, October 8, 2015 [DOI: 10.3998/panc.2015.40]

1. Introduction

Acute pancreatitis is the most common gastrointestinal cause for acute hospital admission in the United States and associated with substantial costs (20). The reported incidence varies from 5 to 73 per 100,000 persons in different populations (8, 37). The overall mortality rate is 4 to 8%, which increases to 33% in patients with infected necrosis (4, 12, 20, 32). As the incidence of acute pancreatitis is rising, the burden for patients and society will further increase (23, 37). An ageing population and abdominal obesity, with a concomitant increased risk of gallstone formation, is likely to play an important role (23, 27, 37).

‘Sludge’ or gallstones, particularly small common bile duct stones, are the cause of acute pancreatitis in approximately 32 to 40% of cases (9, 26, 33, 36). Although the pathogenesis of acute biliary pancreatitis is not fully understood, transient or persistent obstruction of the ampulla, compromising the outflow of pancreatic juices and bile, is thought to be the initiating event (1). Either an obstructing stone or mucosal edema after spontaneous gallstone passage can result in ampullary obstruction. The etiology of acute pancreatitis should be determined on admission, as biliary obstruction may require duct clearance in the early phase. This chapter gives an overview of the available diagnostic tests and imaging modalities. Subsequently, the role of endoscopic retrograde cholangiography (ERC) will be discussed.

2. Establishing a Biliary Etiology

Acute pancreatitis is diagnosed when two of the following three criteria are fulfilled: 1. typical abdominal pain, 2. more than three times elevated serum amylase/lipase and 3. signs of acute pancreatitis on imaging. Determination of the etiology is important for clinical decision-making. A history of gallstone disease or biliary colics points towards biliary etiology. In the early disease phase, biochemical markers can be helpful. In the absence of alcohol abuse, an alanine transaminase (ALAT) >150 IU/L has a predictive value of 88 to 100% in establishing biliary etiology (15, 17, 25). Other elevated biochemical markers, such as serum alkaline phosphatase, bilirubin, gamma glutamyl transferase and aspartate aminotransferase are also suggestive of a biliary origin. However, 15 to 20% of patients with acute biliary pancreatitis
have normal liver function tests at presentation (7).

Recent guidelines advocate abdominal ultrasonography on admission, to identify cholelithiasis, because of its high sensitivity of 92 to 95% (24, 35). However, in patients with acute pancreatitis, sensitivity is lower (67 to 87%), due to bowel distension, and in obese patients it decreases even further (11, 19). Nevertheless, the combination of cholelithiasis on abdominal ultrasonography and elevated liver biochemistry has a positive predictive value of 100% for biliary pancreatitis (2, 19). Predicting the severity of the disease course is desirable to determine whether intensive monitoring or early interventions are needed. Although several scoring systems exist, they lack accuracy and are generally cumbersome to use (18). Due to the simplicity, familiarity and comparable performance, recent IAP/APA guidelines recommend using persistent (lasting for more than 48 hours) systemic inflammatory response syndrome (SIRS) as a predictor for disease severity (35).

3. Endoscopic Ultrasonography (EUS) or Magnetic Resonance Cholangiopancreatography (MRCP)?

If the etiology of pancreatitis remains unclear, EUS or MRCP are the next step in the diagnostic pathway (Figure 1). Both modalities have a higher accuracy in detecting common bile duct (CBD) stones, compared to laboratory tests and transabdominal ultrasound (31).

---

**Fig 1.** Diagnosis and management in the early phase of acute (biliary) pancreatitis.
For EUS, a recent meta-analysis showed a sensitivity and specificity for detecting choledocholithiasis of 0.95 (95% CI 0.91 - 0.97) and 0.97 (95% CI 0.94 - 0.99), respectively (10). In patients with pancreatitis, data are limited, but the accuracy of EUS does not seem to drop, with a reported sensitivity of 91 to 100% and specificity of 85 to 100% (14).

An advantage of EUS over MRCP is the possibility of conversion to ERC, in case common bile duct (CBD) stones are detected, provided the procedures are done in the same setting and by investigations trained in both techniques. Thus, in the hands of a trained physician with access to the appropriate equipment, diagnosis and treatment can be combined into a single procedure, with minimal additional burden for the patient. In patients with a contraindication for MRCP (e.g. claustrophobia, metal implants or cardiac pacemaker), EUS is the only semi-invasive technique available, before intraoperative cholangiography or ERC.

The advantage of the MRCP over EUS is that it is not operator dependent and is non-invasive. Although small gallstones (<5mm) and sludge may be missed, the sensitivity and specificity of MRCP were 0.93 (95% CI 0.87 - 0.96) and 0.96 (95% CI 0.89 – 0.98), in a meta-analysis (10, 13, 21). Data regarding the accuracy of MRCP in the acute phase of pancreatitis are lacking.

In conclusion, the diagnostic accuracy of both EUS and MRCP is excellent and these modalities can prevent unnecessary invasive procedures, by preselecting patients for ERC (16). In clinical practice, factors such as availability, costs and experience will determine the choice between these two modalities (34).

4. Endoscopic Retrograde Cholangiography (ERC)

In biliary pancreatitis, ampullary obstruction results in pancreatic inflammation and complications. Accordingly, early biliary decompression, using endoscopic sphincterotomy and, if necessary, stone extraction, may ameliorate disease severity and prevent complications. On the other hand, CBD stones pass spontaneously in up to 80% of cases, in which case ERC might be redundant and even unhelpful (28). This is important, as ERC is associated with a complication rate of around 10% and a resultant mortality of 0.3 to 1% (3, 6). The most common complications are perforation and bleeding. Furthermore, contrast injection or cannulation of the pancreatic duct, may aggravate the disease course (30).

Recent guidelines state that in patients with acute biliary pancreatitis and concomitant cholangitis, emergency ERC is warranted (24, 35). Urgent biliary decompression has been proven to reduce mortality and complications (29). However, diagnosing cholangitis can be challenging in this group, as the clinical signs of cholangitis are often not easily differentiated from a SIRS reaction due to pancreatitis. Evidence based diagnostic criteria for cholangitis in patients with acute pancreatitis are currently not available.

In patients with predicted mild disease, the potential benefits of ERC do not outweigh the risks for complications. Therefore, ERC is not advocated in this group (24, 35). The indication for ERC in patients with an acute biliary pancreatitis and a predicted severe disease course is controversial. Recent international guidelines state that early ERC with sphincterotomy may be beneficial, but acknowledge the limited evidence (24, 35). A recent systematic review draws a similar conclusion; despite publication of multiple
randomized trials and systematic reviews on this subject, there is no consensus on the use of ERC in this group of patients (5). Heterogeneity of the studies is a possible source of contradiction. Some studies included patients with predicted mild disease or non-biliary etiology and different scoring systems for identifying patients at high risk for complications were used. Also, patients with cholangitis or signs of biliary obstruction were not analyzed separately in all studies. Furthermore, the pooled sample size of patients with a predicted severe disease course was too small and statistically underpowered to draw conclusions. Finally, the definition of ‘early’ ERC differed between trials and varied between 24 to 72 hours after onset of symptoms or after hospital admission. Timing may be important, as the duration of biliary obstruction seems to correlate with disease severity. Therefore, some suggest that ERC should be performed as early as possible (22).

Currently, an adequately powered, randomized multicenter superiority trial is being conducted by the Dutch Pancreatitis Study Group to study the role of early ERC with sphincterotomy in patients with predicted severe biliary pancreatitis without cholangitis. (APEC trial, Current Controlled Trials number, ISRCTN97372133).

5. Conclusion

Acute pancreatitis is a common and potentially fatal disease. Establishing its etiology on admission is paramount for adequate treatment. In about half of the cases, acute pancreatitis is caused by gallstones or ‘sludge’. The first steps in establishing a biliary origin is a detailed history, laboratory tests and an transabdominal ultrasound. In the acute phase, an elevated ALAT (>150 IU/L) is the most sensitive biomechanical marker. MRCP and EUS both have an excellent diagnostic accuracy in detecting choledocholithiasis and can be used as second line diagnostic tools. Early ERC, is only indicated in patients with proven biliary pancreatitis and concomitant cholangitis. It is not indicated in patients with a predicted mild disease course and in patients with with a predicted severe disease course, the role of ERC is currently under investigation. A flow sheet on diagnosis and management of acute biliary pancreatitis is provided in Figure 1.

Funding:
N.D.L. Hallensleben and N.J. Schepers are sponsored by The Netherlands Organisation for Health Research and Development (ZonMW, grant number 837002008) and the Foundation for Health Care Subsidies (Fonds NutsOhra, grant number 1203-052) to perform a clinical trial and acute pancreatitis.

6. References


