

The Effect of ERCP on Mortality and Morbidity in Acute Pancreatitis

Akut Pankreatitte ERCP'nin Mortalite ve Morbiditeye Etkisi

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Abstract

Background: Gallstones and biliary sludge are the most important causes of acute pancreatitis (AP) in our country. For many years, endoscopic retrograde cholangiopancreatography (ERCP) has been used to diagnose and treat acute biliary pancreatitis (ABP). The patient's treatment with acute biliary pancreatitis should be assessed in light of current international guidelines. This study aimed to analyze the patients who were admitted to our clinic with the diagnosis of acute biliary pancreatitis and underwent Endoscopic Retrograde Cholangiopancreatography (ERCP) for treatment, in the light of the literature.

Materials and Methods: The records of patients who underwent ERCP with a diagnosis of acute biliary pancreatitis in our general surgery endoscopy department between April 2020 and March 2021 were retrospectively reviewed.

Results: ERCP was performed in 131 patients with acute biliary pancreatitis. 60 (45.8%) of the patients were male, whereas 71 (54.2%) were female. ERCP was performed on 121 (92.36%) patients for common choledochal stones, 9 (6.87%) for periampullary/distal end of the choledochal tumor, and 1 (0.76%) for acute pancreatitis due to biliary tract rupture after hepatic cyst surgery. While 30 patients underwent ERCP, endoscopic sphincterotomy (ES), and the placement of a plastic stent in the common bile duct, 99 patients underwent ERCP, ES, and stone extraction from the common bile duct. There was no operative mortality.

Conclusions: Acute pancreatitis is a very heterogeneous disease, ranging from mild edematous pancreatitis to severe necrotizing pancreatitis with a mortality of 20%. There are still many controversial issues in the diagnosis and treatment of this disease. However, endoscopic retrograde cholangiopancreatography, a minimally invasive biliary pancreatitis procedure, should be at the forefront of diagnosis and treatment.

Keywords: Acute biliary pancreatitis, Endoscopic retrograde cholangiopancreatography, choledocholithiasis

Öz.

Amaç: Ülkemizde akut pankreatitin (AP) en önemli nedeni safra taşı ve safra çamurudur. Endoskopik retrograd kolanjiyopankreatografi (ERCP) uzun yıllardır akut biliyer pankreatitin (ABP) tanı ve tedavisinde kullanılmaktadır. Akut biliyer pankreatitli hastanın tedavisi; güncel uluslararası kılavuzlar eşliğinde değerlendirilmelidir. Bu çalışmada akut biliyer pankreatit tanısı ile kliniğimize yatırılan ve tedavi amacıyla Endoskopik Retrograde Kolanjiyo pankreatografi (ERCP) yapılan hastaları literatür eşliğinde analiz etmeyi amaçladık.

Materyal ve metod: Nisan 2020-Mart 2021 tarihleri arasında akut biliyer pankreatit tanısıyla Genel Cerrahi Endoskopi Ünitemizde ERCP yapılan hastaların kayıtları retrospektif olarak incelendi.

Bulgular: akut biliyer pankreatit tanısı alan 131 hastaya ERCP yapıldı. Hastaların 60'ı (%45,8) erkek, 71'i(%54,2) kadındı. Hastaların 121'i (%92,36) koledok taşı, 9'u(%6,87) periampuller/koledok distal uç tümörü, 1'i(%0,76) kist hadatik ameliyatı sonrası safra yollarına kist rüptürüne bağlı Akut Pankreatit nedeniyle ERCP' ye alınmışlardı. 30 hastaya ERCP, endoskopik sfinkterotomi (ES) ve koledoğa plastik stent yerleştirilmesi işlemi yapılırken 99 hastaya ERCP, ES ve koledoktan taş ekstraksiyonu işlemi yapıldı. Operatif mortalite olmadı.

Sonuç: Akut pankreatit; hafif ödematöz pankreatitten, %20 mortaliteye sahip şiddetli nekrotizan pankreatite kadar uzanan, oldukça heterojen dağılıma sahip bir hastalıktır; tanı ve tedavisinde halen birçok tartışmalı konu mevcuttur. Ancak biliyer pankreatitte minimal invaziv bir işlem olan Endoskopik retrogradkolanjiyopankreatografi tanı-teşhis ve tedavi sağlamlas bakımından ilk planda tutulmalıdır.

Anahtar Kelimeler: Akut biliyer pankreatit, Endoskopik retrogradkolanjiyopankreatografi, koledokolitiazis

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Introduction

Gallstones and biliary sludge are the most important causes of acute pancreatitis (AP). In developed countries, acute biliary pancreatitis (ABP) is associated with gallstones in 35-75% of cases. Only 3-7% of patients with gallstones develop pancreatitis. Acute pancreatitis occurs when the biliary and pancreatic ducts of the Ampulla of Vater open jointly, and a millimetric gallstone frequently obstructs the pancreatic duct (1). Small stones are often the cause of acute gallstone pancreatitis.

Compared to large stones, microscopic stones (<5 mm in diameter), as well as bile sludge and microlithiasis (2), can pass through the cystic duct and obstruct the ampulla. Pancreatitis is more common in women than males because cholelithiasis is more common in women (2).

Gallstone pancreatitis is caused by a stone blocking the pancreatic duct from the cystic duct. This obstruction increases the pressure in the pancreatic ducts and damages the duct and acinar cells. Severe pancreatitis frequently results in local inflammatory complications, a systemic inflammatory response, and even sepsis.

Despite modern diagnostic and treatment procedures, acute pancreatitis remains a disease with high morbidity and mortality. For many years, endoscopic retrograde cholangiopancreatography (ERCP) has been used to diagnose and treat ABP. When treating the patient with acute biliary pancreatitis, the patient should be assessed according to current international guidelines. This method should also be used to assess the appropriate timing of the ERCP operation for the patient (3). Acute pancreatitis (AP) is a clinical picture that can appear in different clinical situations, from interstitial edematous pancreatitis, a mild form of the disease, to acute necrotizing pancreatitis, a severe condition and has a variable prognosis. Pancreatitis, which develops in 80% of patients, is acute edematous pancreatitis that is self-limiting and mild, rarely develops local and systemic complications, and can be improved with general supportive care. The remaining 20% of patients present with acute necrotizing pancreatitis, severe organ failure, high morbidity, and mortality (4).

The presence of at least two of the following three criteria leads to the diagnosis of acute pancreatitis:

- 1) Abdominal pain consistent with the disease,
- 2) Biochemical evidence of pancreatitis (amylase and lipase above three times the upper limit),
- 3) Presence of characteristic findings on abdominal imaging.

Although the disease takes a mild course in 80-85% of patients, the physician needs to predict the remaining 20% who may take a mortal course (3). An Ultrasonography (USG) is recommended in the first application to clarify the etiology of acute pancreatitis. In most cases, computed tomography (CT) is not necessary for the initial diagnosis, although it may be performed if the diagnosis is in doubt. In cases where the etiology cannot be clarified, it is recommended that an investigation with USG followed

by Magnetic resonance cholangiopancreatography (MRCP) or endoscopic USG be performed to reveal occult choledocholithiasis (3). Although measurement of serum pancreatic enzymes (amylase, lipase) is the "gold standard" in the diagnosis of pancreatitis, both may elevate in non-pancreatitis, but lipase proved to be more specific. The cut-off value for diagnosis is the elevation of these enzymes by more than three times the upper limit of normal. Many markers have been studied to determine the severity of pancreatitis, but no early marker of severity AP has been found. However, a CRP level of ≥ 150 mg/l on the 3rd day can be used as a prognostic factor for severe AP (5th). Procalcitonin is the most sensitive marker for the presence of pancreatic infection, and low levels have a substantial negative predictive value for infected necrosis. Although acute pancreatitis has been recognized for over a century, the basic treatment approach has not changed significantly. After the clinical application of endoscopic retrograde cholangiopancreatography was introduced, the location and timing of endoscopic retrograde cholangiopancreatography in biliary pancreatitis were questioned. Few prospective randomized clinical studies have been conducted on this topic in the last 20 years, and it has been reported to be beneficial in severe pancreatitis in the early stages and concomitant cholangitis (5). In mild and temporary cases, it has been observed to provide no additional benefit. In light of recent data, it has been determined that it is more useful to evaluate many different parameters together, such as the duration of the biliopancreatic obstruction, the severity and course of the disease, and the availability of other diagnostic methods such as magnetic resonance cholangiopancreatography/endoscopic ultrasonography, and perform an analysis.

Based on the World Society of Emergency Surgery (WSES) resolutions held in Italy in 2018, the guideline states the indications for emergency ERCP as follows: Routine ERCP is not recommended for acute calculous pancreatitis. In the presence of cholangitis and acute calculous pancreatitis, as well as common bile duct obstruction and acute calculous pancreatitis, ERCP is indicated. Routine ERCP is not recommended only in predicting severe AP without cholangitis or obstruction of the common bile duct (3). The superiority of ERCP in treating biliary stones and cholangitis attacks in acute pancreatitis of biliary origin has been proven. This study aimed to retrospectively examine 131 patients who had undergone ERCP for acute pancreatitis in our clinic in the light of the literature.

Materials and Methods

The study was conducted with the decision of the Clinical Research Ethics Committee of Harran University dated 05.07.2021 and decision number:HRU/21.13.07. Acute pancreatitis was diagnosed in 256 patients at the General Surgery Clinic of Mehmet Akif Inan Training and Research

Hospital between April 2020 and March 2021 using physical examinations, laboratory tests, and imaging techniques. ERCP was performed in 131 patients with choledochal obstruction. The diagnosis of acute pancreatitis was established based on abdominal pain, a serum amylase level three times normal. All patients underwent diagnostic abdominal USG, MR cholangiography, and computed tomography. Demographic characteristics of patients, the severity of disease, complications after ERCP, mortality, and surgery were recorded. The Revised Atlanta Classification was used to classify the severity of acute pancreatitis. Informed consent for the procedure was obtained from all patients and their first-degree relatives. Prophylactic intravenous antibiotics (sulbactam sodium+cefoperazone sodium 1 g) were administered to each patient before the procedure. All patients were operated on under general anesthesia. The Olympus Exera II CV-180 and Fujifilm Processor VP-3500HD were used for the ERCP.

Results

60 (45.8%) of the patients were male, whereas 71 (54.2%) were female. The age range of patients was 18 to 96 years, and the mean age of all patients was 54.09 ± 20.55 years, 58.68 ± 19.15 years in men, and 50.21 ± 21.02 years in women. Table 1 displays demographic information about the patients. When the etiology of acute pancreatitis was studied, 131 (60.9%) patients had diseases obstructing the bile ducts, while other causes of acute pancreatitis were found in 125 (48.82%) patients (alcoholism, hyperlipidemia, pancreatic cancer, drug intake, and an undetectable cause).

Table 1. Demographic information about the patients

Demographic Data	
Age	(18-93)
Gender	Female: 71 (54,19%) Male: 60 (45.80%)
Etiology	Biliary obstruction: 131 (51,17%) No biliary obstruction:(48,82%)
Hospitalization Period	Average 9 days
Disease severity	Light: 85 (%33,20) Middle:158 (61,71) Severe:13 (5,07)

Of the patients who underwent ERCP for acute pancreatitis, 82% also had cholangitis. The diagnosis of cholangitis was made based on the cholangitis findings on MRCP along with leukocytosis, elevated bilirubin, laboratory findings with elevated liver function tests, clinical findings with fever, and abdominal pain.

Radiological examinations of patients who underwent ERCP revealed choledochal stones in 121 (92.36%), periampullary/choledochal distal end tumors in 9 (6.87%), and choledochal obstruction due to rupture of the bile ducts after cystic surgery in 1 (0.76%). All patients with choledochal stones also had stones in the gallbladder. At MR cholangiography, the mean diameter of the common

bile duct was 9.22 ± 2.57 mm (minimum 6.0, maximum 23 mm). Mean bilirubin levels were 4.02 ± 1.80 (min 1.0, max 9.0) mg/dl. 131 patients were taken for the ERCP procedure. Eight patients with choledochal stones could not be cannulated. All these patients were female and had a common bile duct diameter less than 9 mm and bilirubin levels less than 4. Endoscopic sphincterotomy (ES) was performed in all patients with choledochal stones. In 93 of these patients, stone extraction was performed with ES and balloon, and basket catheter. In 20 patients, a 10 French 12 cm plastic stent was inserted into the common bile duct following ES. In patients who underwent ERCP with the diagnosis of the distal common bile duct and papillary tumor, a plastic stent was placed after ES. After liver cyst surgery, ES was performed on a patient who had pancreatitis due to the cyst opening in the bile ducts, and a plastic stent was placed in the common bile duct. There was no during the process mortality. During the surgery, four patients experienced sphincterotomy-related bleeding. Bleeding was stopped with an adrenaline injection and balloon pressure. Postoperative blood transfusion was not required. Post ERCP, the patient's cholangitis did not regress, and he died of septic shock on day 2. The average hospital stay of patients was nine days.

Discussion

Acute pancreatitis presents a comprehensive clinical picture ranging from mild interstitial edema to severe hemorrhagic gangrene and necrosis. In addition to spontaneous recovery, a severe picture characterized by abdominal pain or hypotension, fluid sequestration, metabolic disorders, sepsis, and death may be observed clinically (4). Acute pancreatitis still has high morbidity and mortality today. Biliary factors are the most common etiologic factors causing acute pancreatitis. Gallstones are known to cause 35-75% of acute pancreatitis in developed countries (6-7).

The presence or absence of acute cholangitis with ABP is essential in deciding whether to perform ERCP. After antibiotic treatment and biliary decompression in the presence of acute cholangitis, mortality decreased from 100% to 9-40%. The concomitant occurrence of acute cholangitis in ABP is a condition requiring urgent ERCP (5). In randomized controlled studies, biliary sphincterotomy for acute biliary pancreatitis and early ERCP with stone removal has been shown to accelerate patient recovery (8).

ERCP can reveal papillary and ductal abnormalities

in patients with recurrent pancreatitis attacks whose etiology cannot

be detected by other methods (9).

In the literature, there are four extensive prospective randomized controlled studies and many meta-analyses that question the role of ERCP in the early setting at ABP and guide our clinical behavior. A prospective randomized

study conducted by Neoptolemos and his team from Leicester, England, investigating the role of early ERCP in ABP, published in *The Lancet* journal in 1988, was the first powerful study in the literature (10). 121 Patients with acute pancreatitis and gallstones on the USG were divided into a medical follow-up or ERCP emergency treatment within the first 72 hours. About half of the ERCP group was classified as severe pancreatitis. Choledochal stones were found in 63% of severe pancreatitis cases and 25% of mild pancreatitis cases. Endoscopic sphincterotomy (ES) was also performed on those who were found to have choledochal stones. A significant reduction in complications and mortality was observed in patients with severe pancreatitis who underwent ERCP and ES. In one study, the cases where endoscopic methods were prioritized for treatment were summarized as endoscopic retrograde cholangiopancreatography (ERCP) stone extraction for biliary pancreatitis and endoscopic sphincterotomy (EST) for AP due to sphincter Oddi dysfunction, and EST and/or stenting in the pancreas divisum (11).

Sphincterotomy with ERCP and surgery reduces recurrence by 30% within six weeks in biliary pancreatitis, AP, and cholangitis (12).

The precipitating factor in pancreatitis due to gallstones is permanent obstruction of the biliopancreatic duct or periampullary edema, which develops even when the stone leaves. With increasing duration of permanent obstruction of the biliopancreatic duct, the rate of worsening pancreatic damage increases (10,13). Therefore, early ERCP is essential.

One hypothesis is that small stones cause transient obstruction in the common bile duct and trigger mild pancreatitis if they pass into the duodenum and the event resolves spontaneously, whereas large stones cause intermittent obstruction and trigger severe pancreatitis if they are permanently lodged in the common bile duct. In our study, there was no meaningful correlation between the severity of pancreatitis and the size of the stone pushed by ERCP from the common bile duct to the duodenum.

Some experimental and clinical studies have also shown that the duration of biliopancreatic obstruction is more important and meaningful to explain this situation (10,13).

According to one study, the duration of biliopancreatic obstruction is more important than the severity of pancreatitis in the decision to perform early ERCP (14). Because pancreatitis resolves rapidly in transient obstructions, it was found more appropriate to evaluate patients for ERCP with imaging in cases of permanent obstruction (more than 48 hours). In acute cholangitis and permanent obstruction, ERCP should be performed; in other cases, medical treatment is sufficient.

Limited data are available to determine when non-urgent ERCP should be performed in patients with acute biliary AP with persistent obstruction and without cholangitis.

The Cochrane analysis concluded that ERCP should be performed within 72 hours (15).

According to the recommendation of the American Gastroenterology Society, it seems appropriate that the timing of the ERCP procedure should not be less than 24 hours to allow the stone obstructing to pass spontaneously and that it should not exceed 48 hours to prevent the formation of long-term biliary obstruction (16).

In our study, patients were taken to ERCP within an average of 48-72 hours after hospitalization. The cure rate of acute pancreatitis and the cause of cholangitis were crucial for the decision to use ERCP. An ERCP procedure was performed after antibiotic suppression of the septic picture due to patients' cholangitis, pancreatitis, and fluid replacement. High-volume fluid replacement before ERCP was found to be an independent protective factor against moderate to severe PEP and was associated with a shorter hospital stay in one study (17).

In this study, 48.82% of 256 patients diagnosed with APR had no choledochal stones or other cause of choledochal obstruction, and ERCP was indicated in 131 (51.17%). In 82% of APR patients brought for ERCP, cholangitis was also seen. All patients were administered intravenous antibiotics (sulbactam sodium+cefoperazone sodium 1 g, metronidazole 500 mg). In 1 patient, cholangitis did not regress after ERCP, and the patient died on the 2nd postoperative day. In other patients, acute pancreatitis and cholangitis regressed. Leukocytosis and liver function tests regressed from the first day after the procedure. Rapid improvement was observed from day 3 onward in those whose bilirubin levels were above ten before ERCP and from day 1 onward in those below 10.

In preprocedural MRCPs of patients undergoing ERCP for acute pancreatitis, the mean diameter of the common bile duct was 10 mm. The MR cholangiographic diagnoses made to confirm the diagnosis of acute pancreatitis were compatible with those made on ERCP. As described in the literature, stones of the common bile duct were visualized as filling defects in MRCP images in our study, whereas irregular strictures in the distal common bile duct were detected in common distal end tumors and papillary tumors.

Diagnostic and therapeutic ERCP is also performed in acute recurrent pancreatitis. In recurrent acute pancreatitis where the etiology cannot be understood with MRCP, EUS is evaluated with ERCP. Etiology includes, in particular, the study of causes such as microlithiasis and biliary sludge, pancreatic divisum, dysfunction of the sphincter of Oddi, parasitic diseases. The diagnostic value of ERCP in recurrent acute pancreatitis with negative imaging has been reported to be 38-79% in the literature (18). A biliary and/or pancreatic sphincterotomy is required if ERCP is to be performed for this reason. In our study, ERCP was performed in 8 patients diagnosed with acute recurrent pancreatitis. In these patients, MRCP revealed filling de-

fects in the common bile duct. ES was performed in 8 patients during ERCP, and millimeter-sized stones and bile sludge were removed. ERCP is an invasive method, and the risk of pancreatitis after ERCP is even higher in these patients. A stent can be placed in the pancreatic duct in high-risk patients, or rectal indomethacin can be used (19). If gallstones or gallstone sludge cannot be detected in idiopathic acute recurrent pancreatitis, if EUS and/or MRCP findings are normal, ERCP with Oddi sphincter manometry may be considered. Empirical sphincterotomy of the bile ducts and/or pancreas can be performed without performing sphincter manometry of Oddi, i.e., ERCP can be used for primary treatment as a method to move from treatment to diagnosis (20).

In a study we conducted in a monocentric manner in our clinic, our rate of post ERCP pancreatitis (PEP) was 8.1% in a series of 513 patients who underwent ERCP in 19 months (21).

Our PEP rate was 8.9% in this series of 131 patients who underwent ERCP with a diagnosis of acute pancreatitis, and no significant difference was found. Acute cholangitis is the most widely accepted parameter for the early diagnosis of biliopancreatic obstruction. After many different diagnostic approaches, a consensus for the diagnosis of acute cholangitis was reached in Tokyo in 2007 (22).

ERCP is useful in the diagnosis and treatment of biliary pancreatitis (23,24). However, since it is an invasive procedure in which various complications such as worsening of pancreatic inflammation, bleeding, respiratory failure, cholangitis, cholecystitis, lumbar osteitis may occur; many different parameters such as these complications, the experience of the endoscopist, comorbidities, and adequate hygienic infrastructure should be considered when deciding to perform ERCP (14,25). In this study, ERCP was performed in patients with pancreatitis due to obstruction of the common bile duct (e.g., stone, tumor, hydatid cyst). After ERCP, clinical and laboratory results improved in a short time.

Conclusion:

The most common indication for ERCP is the presence of stones in the common bile duct. Emergency ERCP and endoscopic sphincterotomy are the main treatment options for acute suppurative obstructive cholangitis due to stones.

Decompression with ERCP in patients with acute biliary pancreatitis and concomitant cholangitis reduces patient mortality and morbidity. If there is no indication of cholangitis, an early ERCP is ineffective in mild or severe acute biliary pancreatitis.

Consequently, after reviewing the literature data, ERCP and sphincterotomy are recommended in all cases of acute biliary pancreatitis with cholangitis and jaundice, enlargement of the bile ducts in the USG, or a severe form.

Ethical Approval: The study was conducted with the decision of the Clinical Research Ethics Committee of Harran University dated 05.07.2021 and decision number:HRU/21.13.07.

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