

## Endoscopic sphincterotomy in acute biliary pancreatitis: A question of anesthesiological risk

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### Abstract

Two consecutive surveys of acute pancreatitis in Italy, based on more than 1000 patients with acute pancreatitis, reported that the etiology of the disease indicates biliary origin in about 60% of the cases. The United Kingdom guidelines report that severe gallstone pancreatitis in the presence of increasingly deranged liver function tests and signs of cholangitis (fever, rigors, and positive blood cultures) requires an immediate and therapeutic endoscopic retrograde cholangiopancreatography (ERCP). These guidelines also recommend that patients with gallstone pancreatitis should undergo prompt cholecystectomy, possibly during the same hospitalization. However, a certain percentage of patients are unfit for cholecystectomy because advanced age and presence of comorbidity. We evaluated the early and long-term results of endoscopic intervention in relation to the anesthesiological risk for 87 patients with acute biliary pancreatitis. All patients underwent ERCP and were evaluated according to the American Society of Anesthesiology (ASA) criteria immediately before the operative procedure. The severity of acute pancreatitis was positively related to the anesthesiological grade. There was no significant relationship between the frequency of biliopancreatic complications during the follow-up and the ASA grade. The frequency of cholecystectomy

was inversely related to the ASA grade and multivariate analysis showed that the ASA grade and age were significantly related to survival. Finally, endoscopic treatment also appeared to be safe and effective in patients at high anesthesiological risk with acute pancreatitis. These results further support the hypothesis that endoscopic sphincterotomy might be considered a definitive treatment for patients with acute biliary pancreatitis and an elevated ASA grade.

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**Key words:** Acute biliary pancreatitis; Anesthesiological risk; Endoscopic retrograde cholangiopancreatography; Endoscopic sphincterotomy

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### INTRODUCTION

Two consecutive surveys of acute pancreatitis in Italy, based on more than 1000 patients with acute pancreatitis, reported that the etiology of the disease indicates biliary origin in about 60% of the cases<sup>[1,2]</sup>.

Why patients with gallstones, especially those with biliary sludge<sup>[3]</sup>, develop acute pancreatitis remains an open issue. Small gallstones, enlarged cystic ducts, impacted stones of normal dimensions, and a functioning

common channel have been demonstrated to be predisposing local etiologic factors in the development of gallstone pancreatitis<sup>[4]</sup>. McMahon and Shefta have<sup>[5]</sup> reported that numerous small stones having an irregular shape appeared to be more common in patients who had suffered acute pancreatitis, and might be a factor in the pathogenesis of the attack. Diehl *et al*<sup>[6]</sup> supported these findings, demonstrating that patients with at least one gallstone smaller than 5 mm in diameter have more than a four-fold increased risk of presenting with acute biliary pancreatitis. Why do patients with small gallstones develop acute pancreatitis? An answer to this question comes from a study carried out in The Netherlands<sup>[7]</sup>. The authors compared postprandial gallbladder motility using ultrasonography and, after subsequent cholecystectomy, numbers, sizes, and types of gallstones, gallbladder bile composition, and cholesterol crystallization in 21 gallstone patients with previous pancreatitis and 30 patients with uncomplicated symptomatic gallstones. The authors found that gallbladder motility was stronger in patients with pancreatitis than in patients with uncomplicated symptomatic gallstones. Patients with pancreatitis often had significantly more sludge, and a greater number of small gallstones than patients with symptomatic gallstones. Crystallization also occurred significantly faster in the bile of patients with pancreatitis, possibly because of higher mucin concentrations. No significant differences were found in type of gallstones, relative biliary lipid content, cholesterol saturation index, bile salt species composition, phospholipid class, total protein or immunoglobulin, haptoglobin, and  $\alpha$ -1 acid glycoprotein concentration. The conclusions drawn from this study are important because they have demonstrated that patients with small gallstones and/or preserved gallbladder motility are at increased risk of pancreatitis because the stones could more easily migrate from the gallbladder to the common bile duct, if gallbladder contraction is preserved.

## THERAPEUTIC APPROACH TO ACUTE BILIARY PANCREATITIS

In 1998 the United Kingdom guidelines reported that severe gallstone pancreatitis in the presence of increasingly deranged liver function tests and signs of cholangitis (fever, rigors, positive blood cultures) requires an immediate and therapeutic endoscopic retrograde cholangiopancreatography (ERCP)<sup>[8]</sup>. The same position was taken by the American Gastroenterological Association<sup>[9]</sup> and by the Italian Association for the Study of the Pancreas<sup>[10]</sup>. These societies also recommend that patients with gallstone pancreatitis should undergo prompt cholecystectomy, possibly during the same hospitalization. In fact, a study on the recurrent form of pancreatitis<sup>[11]</sup> found that of the 1068 patients with acute pancreatitis enrolled in five European countries, gallstones were the cause of recurrent pancreatitis in 25% of the cases. It is also important to emphasize that a substantial number of patients with 'idiopathic' pancreatitis might have small gallstones that were undetected by

abdominal ultrasound or computed tomography<sup>[12]</sup>. However, a certain percentage of patients are unfit for cholecystectomy because advanced age and presence of comorbidity<sup>[13,14]</sup>.

## THERAPEUTIC OPTIONS IN PATIENTS UNFIT FOR CHOLECYSTECTOMY

From a practical point of view, therapeutic solutions have been empirically proposed. Even if cholecystectomy is the main therapeutic option in patients with gallstones, some authors have proposed the use of urso-deoxycholic acid in order to prevent further attacks of acute pancreatitis having a biliary origin<sup>[15,16]</sup>; others have suggested that endoscopic sphincterotomy might be an option, especially in patients considered unfit for surgery<sup>[13,14,17]</sup>. In fact, it has been suggested that endoscopic sphincterotomy is the method of choice for treatment of lithiasis of the common bile duct, particularly in elderly patients or in patients at poor operative risk<sup>[18-20]</sup>. This therapeutic approach has also been proposed for the management of severe acute biliary pancreatitis as a definitive procedure to avoid recurrence of the disease in patients unfit for surgery because of age or comorbidities<sup>[13,21]</sup>. However, there was a lack of follow-up data for these patients after endoscopic procedures. The American Society of Anesthesiology (ASA) grading system<sup>[22]</sup> has been used for over 50 years as a predictor of risk for perioperative morbidity and mortality. The ASA grade has recently been proposed to stratify the risk of complications in patients who undergo endoscopic procedures<sup>[23]</sup>. Thus, we undertook a study to evaluate the early and long-term results, i.e., morbidity and mortality, of endoscopic intervention in relation to the anesthesiological risk in patients with mild and severe acute biliary pancreatitis<sup>[24]</sup>.

## ERCP AND ANESTHESIOLOGICAL RISK IN PATIENTS WITH MILD AND SEVERE ACUTE BILIARY PANCREATITIS

We studied all patients who underwent ERCP for acute biliary pancreatitis<sup>[24]</sup>; all the patients were evaluated according to the ASA criteria immediately before the operative procedure. Eighty-seven patients with acute biliary pancreatitis were enrolled (35 males and 52 females; median age, 72 years; range, 34-93). According to the Atlanta classification system, 57 of the 87 patients enrolled (65.5%) had mild acute pancreatitis, whereas 30 (34.5%) had a severe form of the disease (local and systemic complications in these latter 30 patients are reported in Table 1). All patients were treated conservatively.

According to the ASA criteria, the 87 patients' grades were distributed as follows: 49.4% of patients had ASA grade 2; 29.9% ASA grade 3; and 20.7% had ASA grade 4. The major medical diseases in patients having elevated anesthesiological grades are reported in Table 2. None of the patients enrolled in the study were of ASA grade 5.

**Table 1** Local and systemic complications in the 30 patients with severe acute pancreatitis

Complication	n (%)
Sterile necrosis	9 (63.3)
Infected necrosis	4 (13.3)
Respiratory insufficiency	17 (56.7)
Metabolic alterations	16 (53.3)
Multiorgan failure	3 (10.0)
Renal insufficiency	2 (6.7)
Heart failure	1 (3.3)

More than one complication might occur in the same patient.

Nonparametric statistical analyses (Kruskal-Wallis one-way ANOVA, Spearman rank correlation, Fisher exact test, and Mantel-Haenszel test for linear association) and multiple regression analysis were applied to the data. Stepwise multivariate survival analysis was performed by means of the Cox hazard model, and the odds ratios (ORs), with their 95% confidence intervals (95% CIs), were evaluated. The SPSS/PC+ package (SPSS, Chicago, IL, USA) and the BMDP package (University of California, Berkeley, CA, USA) were used to perform the nonparametric tests and survival analysis, respectively. A two-tailed *P* value less than 0.05 was considered statistically significant.

There were no significant differences in gender and frequency of previous cholecystectomy among the three groups of patients, whereas age and the severity of acute pancreatitis were positively related to the anesthesiological grade. Multivariate regression analysis showed that these latter two variables were independently related to the ASA grade. ERCP showed lithiasis of the common bile duct in 55 patients (63.2%) and biliary sludge in the remaining 32 patients (36.8%). Endoscopic sphincterotomy was performed successfully in 86 patients but was unsuccessful in one patient with biliary sludge. All 86 patients in whom endoscopic sphincterotomy was successfully performed had complete stone/sludge clearance of the common bile duct; four patients (4.6%) required two attempts to achieve clearance of the common bile duct, and two (2.3%) of them required extracorporeal shock-wave lithotripsy. In 10 patients (six with ASA grade 2, 3 with ASA grade 3, and one with ASA grade 4), deep cannulation of the common bile duct was achieved with precut sphincterotomy. None of the patients had cardiopulmonary complications related to the endoscopic procedure. Six of the 87 patients (6.9%) had complications related to the endoscopic procedure. Two patients (2.3%), one with ASA grade 2 and one with ASA grade 3, had clinically mild hemorrhage, requiring a red blood cell transfusion (2 units) in the former. Three patients (3.4%), one with ASA grade 2 and two with ASA grade 4, had retroperitoneal perforation, which was resolved with nasobiliary drainage and conservative treatment. One patient (1.1%) with ASA grade 3 had mild hemorrhage and a perforation. None of the patients with endoscopy-related complications underwent a surgical procedure,

**Table 2** Major chronic diseases in patients with ASA grade 3 and 4 (44 cases)

Disease	n (%)
Chronic myocardial ischemia	34 (77.3)
Arterial hypertension	18 (40.9)
Chronic obstructive pulmonary disease	9 (20.5)
Diabetes mellitus	7 (15.9)
Chronic atrial fibrillation	7 (15.9)
Chronic active hepatitis	2 (4.5)
Chronic renal insufficiency	2 (4.5)
Congestive cardiomyopathy	1 (2.3)
Severe mitral prolapse syndrome	1 (2.3)
Abdominal aortic aneurysm	1 (2.3)
Chronic obliterative arteriopathy	1 (2.3)
Hepatic cirrhosis	1 (2.3)
Active duodenal ulcer	1 (2.3)
Epilepsy	1 (2.3)
Chronic leukemia	1 (2.3)
Systemic lupus erythematosus	1 (2.3)

and there were no deaths. The frequencies of the complications related to the endoscopic procedure were equally distributed among the various ASA grades (4.7% in patients having ASA grade 2, 27.7% in those having ASA grade 3, and 11.1% in patients having ASA grade 4).

Three patients (3.4%) died of complications unrelated to the endoscopic procedure: one patient with ASA grade 4 died of irreversible heart failure and two (one with ASA grade 3 and one with ASA grade 4) died of multiorgan failure related to the severity of the acute pancreatitis. Pancreatic surgery was performed on two patients due to infection of the necrosis. All 84 patients discharged from the hospital were followed for a median of 12 mo (range, 1-84). The duration of the follow-up was not significantly different among the three groups of patients studied. Twenty-three patients (27.4%) had biliopancreatic complications: 11 were of ASA grade 2 (25.6%), eight of ASA grade 3 (32.0%), and four of ASA grade 4 (25.0%). There was no significant relationship between the frequency of complication and the ASA grade. Twenty-eight of the 76 patients who had not previously undergone cholecystectomy underwent cholecystectomy during the follow-up period. The frequency of cholecystectomy was inversely related to the ASA grade (*P* = 0.003). Seven patients (8.3%) died during the follow-up period: two with ASA grade 3 (8.0%) and five with ASA grade 4 (31.3%). The causes of death were as follows: heart failure in four, pulmonary embolism in one, chronic leukemia in one, and pulmonary sepsis in one. The death rate significantly increased with the increase in the ASA grade and the multivariate analysis showed that the ASA grade (OR = 10.9; 95% CI: 1.2-96.6) and age (OR = 1.1; 95% CI: 1.0-1.3) were significantly related to survival, whereas gender and the severity of pancreatitis had no bearing on survival.

## CONCLUSION

The data reported in this study indicated that patients at

elevated anesthesiological risk had a significantly higher rate of severe acute pancreatitis. Early complications after endoscopy were unrelated to age or comorbidities, even if the deaths occurred only among severely ill patients. Finally, endoscopic treatment also appeared to be safe and effective in patients at high anesthesiological risk with acute pancreatitis. After exclusion of age as a confounding factor, survival remained significantly related to ASA grade.

These results further support the hypothesis that endoscopic sphincterotomy might be considered a definitive treatment for patients with acute biliary pancreatitis and an elevated ASA grade. This finding might also reflect the reluctance on behalf of the surgeon to operate on patients at high anesthesiological risk.

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