ERCP in acute pancreatitis: What takes place in routine clinical practice?

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Abstract

AIM: To evaluate the data from a survey carried out in Italy regarding the endoscopic approach to acute pancreatitis in order to obtain a picture of what takes place after the release of an educational project on acute pancreatitis sponsored by the Italian Association for the Study of the Pancreas.

METHODS: Of the 1 173 patients enrolled in our survey, the most frequent etiological category was biliary forms (69.3%) and most patients had mild pancreatitis (85.8%).

RESULTS: 344/1 173 (29.3%) underwent endoscopic retrograde cholangiopancreatography (ERCP). The mean interval between the onset of symptoms and ERCP was 6.7 ± 5.0 d; only 89 examinations (25.9%) were performed within 72 h from the onset of symptoms. The main indications for ERCP were suspicion of common bile duct stones (90.3%), jaundice (44.5%), clinical worsening of acute pancreatitis (14.2%) and cholangitis (6.1%). Biliary and pancreatic ducts were visualized in 305 patients (88.7%) and in 93 patients (27.0%) respectively. The success rate in obtaining a cholangiogram was statistically higher (P = 0.003) in patients with mild acute pancreatitis (90.6%) than in patients with severe disease (72.2%). Biliary endoscopic sphincterotomy was performed in 295 of the 305 patients (96.7%) with no difference between mild and severe disease (P = 0.985). ERCP morbidity was 6.1% and mortality was 1.7%; the mortality was due to the complications of acute pancreatitis and not the endoscopic procedure.

CONCLUSION: The results of this survey, as with those carried out in other countries, indicate a lack of compliance with the guidelines for the indications for interventional endoscopy.

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Key words: Acute pancreatitis; Epidemiology, Endoscopic retrograde cholangiopancreatography; Data collection

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INTRODUCTION

The pathogenesis of acute biliary pancreatitis (ABP) is still unknown; several hypotheses have been made such as transient obstruction of both the common bile duct and the pancreatic duct, reflux of bile and duodenal content into the pancreatic duct and, finally, increase in the hydrostatic pressure in the pancreatic duct\[1,2\]. The severity of biliary pancreatitis probably depends on individual predisposition but the duration of bile duct obstruction seems to be the main factor contributing to the development of the severity of pancreatitis, as suggested by animal models and human studies\[3-6\]. The decision for the management of patients with predicted severe acute biliary pancreatitis is still a matter of debate; even if endoscopic treatment appears to be safe and effective and may be the definitive treatment in patients with acute pancreatitis with a high anesthesiological risk\[7\]. Several guidelines on acute pancreatitis recommend that urgent therapeutic endoscopic retrograde cholangiopancreatography (ERCP) be performed within 72 h of admission for all patients with predicted severe ABP, whether or not cholangitis is present\[8-10\]. However, two recent meta-analyses\[11,12\] suggested that early ERCP, with or without endoscopic sphincterotomy (ES), had no beneficial effect in patients with predicted mild or severe acute biliary pancreatitis without cholangitis or persistent biliary obstruction; this point of view has also been supported by two position papers\[10,13\]. However, what happens in clinical practice is not completely known. The majority of studies come from the United Kingdom; Mofidi et al\[14\] have reported that physicians complied with all the UK guidelines except for urgent ERCP for severe acute pancreatitis because only 48% of patients underwent ERCP within 72 h due to difficulties in transferring patients to specialized centers capable of performing and providing ERCP outside normal weekday working hours. The two above-mentioned factors may have contributed to these results and these results were also confirmed by another study carried out in England\[15\]. For this reason, we believe the data from an observational study on acute pancreatitis carried out in Italy to be of particular interest; the results on the diagnosis and treatment of acute pancreatitis were published in 2007\[16,17\]. Complete data on the endoscopic approach to the disease have never been reported; of importance, the study was carried out after the release of the recommendations of the Italian Association of the Study of the Pancreas (AISP) in 1999\[18\] and before the release of the new position statement of the same Society in 2008\[19\]. Thus, these data represent a picture of what takes place during the course of this educational project on acute pancreatitis sponsored by the AISP.

MATERIALS AND METHODS

The present study involved 56 Italian public hospitals, equally distributed throughout Italy and almost all of them had access to the same facilities. Ad hoc software including 530 items designed by the scientific committee of the study was furnished to each participating center. Of these 530 items, 64 (12%) regarded specific questions about endoscopic treatment. All cases of acute pancreatitis consecutively observed in the various centers during the period from December 2001 to November 2003 were included in the study.

The diagnosis of acute pancreatitis was based on clinical (onset of pancreatic-type pain), biochemical (a threefold increase of amylase and/or lipase) and radiological (ultrasonography, computer tomography scan, magnetic resonance) findings\[19\]. The disease was classified into mild and severe forms according to Atlanta criteria\[8\]. The etiological classification of the disease was made according to the United Kingdom guideline\[8\].

Data were collected and tabulated centrally; a careful monitoring process was carried out during the period of the study. At the end of the study, additional quality control regarding the completeness and congruence of each single chart was carried out in order to exclude cases with incomplete and/or inconsistent charts. One of the endpoints of the study was to evaluate, in detail, the endoscopic approach in patients with acute pancreatitis in Italy.

Statistical analysis

Data are presented as mean ± SD and frequencies. Statistical analysis was carried out using the chi-square test and Fisher’s exact test. Data were run on SPSS version 10. Differences with a P value of less than 0.05 were considered significant.

RESULTS

One thousand one hundred and seventy-three patients (581 females and 592 males; mean age ± SD: 62.0 ± 18.2 years) were considered for the present study. Biliary forms represented the most frequent etiology (813 cases, 69.3%) while alcoholic forms occurred in only 77 cases (6.6%); the remaining etiologies (post-surgical, post-endoscopic cholangiopancreatographic, traumatic, hyperlipemic, drug-induced and from pancreas divisum) accounted for 83 cases (7.1%). Two hundred cases (17.1%) remained without a definite etiological factor (idiopathic forms).

One thousand and six patients (85.8%) had mild pancreatitis and 167 (14.2%) had the severe form. The mean interval between the onset of pain and hospital admission was not statistically significant (P = 0.374) between patients with mild (14.9 ± 37.2 h) and those with severe pancreatitis (17.8 ± 39.1 h). Of the 1 173 patients, 344 (29.3%; males 140, females 204, mean age ± SD: 65.7 ±
16.2 years) underwent ERCP. The mean interval between the onset of symptoms and ERCP was 6.7 ± 5.0 d and the mean interval between hospital admission and ERCP procedure was 5.7 ± 5.0 d. Eighty-nine examinations (25.9%) were performed within 72 hours from the onset of symptoms.

Of the 344 patients, 320 (93.0%) patients had biliary pancreatitis (288, 90.0% had mild acute pancreatitis; 32, 10.0% had the severe form). As reported in Table 1, the main indication for ERCP was radiological and/or biochemical suspicion of common bile duct stones in 90.3% followed by jaundice (47.8%), clinical worsening of acute pancreatitis (14.1%) and cholangitis (6.6%). In 24 patients suffering from non-biliary pancreatitis (4 with severe disease), the indications for the procedure were suspicion of common bile duct stones in 17 patients, worsening of the disease in 4, disruption of the main pancreatic duct in 2 and suspicion of malignancy in the remaining one.

The endoscopic aspect of the papilla was reported in 303 of the 344 patients (88.1%) and appeared pathological in 62 cases (20.5%). In particular, in 41 patients (66.1%) there was an aspect of recent stone migration while, in the remaining 21 (33.9%), an impacted stone was found.

Biliary and pancreatic ducts were visualized in 305 of the 344 patients (88.1%) and appeared pathological in 62 cases (20.5%). In particular, in 41 patients (66.1%) there was an aspect of recent stone migration while, in the remaining 21 (33.9%), an impacted stone was found.

| Table 2 Distribution of different techniques used for biliary sphincterotomy according to the severity of the acute pancreatitis |
|---------------------------------------------------------------|
| Mild acute pancreatitis (N = 269) | Severe acute pancreatitis (N = 26) | P value |
|----------------------------------|----------------------------------|---------|
| Standard sphincterotomy          | 219                             | 23      | 0.531  |
| Precut                           | 21                              | 7       |        |
| Standard sphincterotomy + Precut | 29                              | 1       |        |

In the 93 patients in whom the main pancreatic duct was visualized, two patients had pancreas divisum and three had a disruption of the Wirsung duct associated with necrotizing pancreatitis while the majority of patients had a normal main pancreatic duct (88/93; 94.6%).

Biliary endoscopic sphincterotomy was performed in 295 of the 305 patients (96.7%) in whom the common bile duct was visualized: in 269 cases out of 279 (96.4%) with mild pancreatitis and in all 26 patients with severe disease (P = 0.985).

Biliary endoscopic sphincterotomy was performed for the following reasons (more than one indication may be present in the same patient): common bile duct stones in 168/295 patients (57.0%), biliary sludge in 173/295 (58.6%), cholangitis in 16/295 (5.4%) and high surgical risk in order to prevent further attacks of pancreatitis in 3/295 (1.0%).

The technique of biliary sphincterotomy was standard in 242/295 (82.0%), precut in 23/295 (7.8%) and precut associated with standard 30/295 (10.2%). The distribution of these different techniques did not differ (P = 0.531) in mild and severe pancreatitis (Table 2).

Complete clearance of the common bile duct was achieved in all 168 patients with biliary stones; in 161 of the 168 (95.9%), patient clearance was obtained at the first attempt. A nasobiliary drain was inserted in 28 of the 295 patients (9.5%) for retained stones or transient distal stenosis of the common bile duct due to pancreatic head edema.

Morbidity of the endoscopic procedure was 6.1% (11/134): nine bleeds, one retroperitoneal perforation and one acute cholecystitis. The complications were equally distributed between mild and severe disease and all were treated conservatively.

Mortality in the patients who underwent operative endo


scopy was 1.7% (6 out of 344). All the patients who died had severe pancreatitis and mortality was due to the complications of acute pancreatitis and not to the endoscopic procedure.

Eighty-three patients underwent ERCP and cholecystectomy (laparoscopic or open cholecystectomy) during the same hospitalization; ERCP and cholecystectomy were performed within 5.7 ± 5.3 d and 10.4 ± 5.8 from hospital admission respectively.

### DISCUSSION

**Practical and technical considerations**

Firstly, it should be pointed out that, of the 344 patients who underwent ERCP, only relatively few examinations were performed within 72 h from the onset of symptoms and this represents a clear deviation from the largely accepted guidelines (Table 3). Furthermore, comparing the data of the present survey with those previously published, we found that the number of ERCPs carried out was lower in the period from 2001 to 2003 (29.3%) than the number carried out from 1996 to 2000 (64.3%) and the number of interventional ERCPs carried out within 72 h, especially in patients with the severe form, was also equally low (Table 3). These data are similar to those reported in UK studies in which a check on the adherence of clinicians to the published guidelines was carried out. These data clearly represent a deviation from the largely accepted guidelines, a finding also demonstrated by the low morbidity (6.1%) rate of the procedure.

**Clinical considerations**

As suggested by Petrov et al, the trials considered for their meta-analysis in assessing the benefit of ERCP in acute biliary pancreatitis used different definitions for acute cholangitis and included different subgroups of patients with acute biliary pancreatitis. Folsch et al excluded all patients with a bilirubin greater than 5 mg per deciliter who might theoretically benefit from interventional endoscopy, Neoptolemos et al included all patients with acute pancreatitis and presented separate data on patients without acute cholangitis and Oria et al included only patients with acute biliary pancreatitis and clinical evidence of bili-pancreatic obstruction with acute cholangitis. The same problems of the above-mentioned randomized studies were observed in our survey; only a minority of patients underwent interventional endoscopy for cholangitis (6.6%) and 50% of subjects underwent ERCP for the presence of jaundice (a clear sign of cholestasis) whereas the most frequent indication for ERCP (90%) was suspicion of common bile duct stones. We believe that this situation reflects the fact that, at the time of the survey, the indications for ERCP in acute pancreatitis were probably misleading for several physicians; in fact, they have been revised in the recent AISP position statement.

**Endoscopic and surgical approaches in patients with gallstones**

As suggested by a number of guidelines, a combined approach (ERCP plus laparoscopic/open cholecystectomy) seems to be the most logical and it was proven suitable in mild pancreatitis. The delay of 4 d between endoscopy and surgery observed in our survey appears slightly too long and reflects some difficulties in planning early surgical procedures in Italy and in transferring patients from medical to surgical departments. Another important fact is that the majority of patients with mild acute pancreatitis do not have their gallbladder removed during the same hospitalization after the attack of acute pancreatitis. It should be pointed out that the endoscopic approach may be the only and definitive treatment in patients with a high anaesthesiological risk and in those with advanced age for preventing further attacks of acute pancreatitis.

**Suggestions for the future**

More effort needs to be made by national and interna-

| Table 3 Number of cases and respective frequency of patients who underwent endoscopic retrograde cholangiopancreatography in the two Italian surveys |
|-----------------------------------------------|
| Survey 1996-2000 | Present survey 2001-2003 |
| Overall population (N = 1005) | Mild AP (n = 753) | Severe AP (n = 252) |
| Overall population (N = 1173) | Mild AP (n = 1006) | Severe AP (n = 167) |
| Interventional ERCP | 646/1005 (64.3%) | 482/753 (64.0%) | 164/252 (65.1%) |
| Interventional ERCP within 72 h | 205/646 (45.4%) | 227/482 (47.1%) |
| n/N (%) | 7/1173 (39.3%) | 308/1006 (30.6%) |
| Interventional ERCP within 72 h | 66/163 (40.2%) | 89/344 (25.9%) |
| n/N (%) | 20/167 (12.1%) | 20/36 (55.6%) |
Endoscopic treatment of acute pancreatitis

The decision for the management of patients with predicted severe acute biliary pancreatitis is still a matter of debate, even if endoscopic treatment appears to be safe and effective and may be the definitive treatment in patients with acute pancreatitis with a high anesthesiological risk.

Research frontiers

To evaluate the data of a survey carried out in Italy regarding the endoscopic approach to acute pancreatitis in order to obtain a picture of what takes place after the release of an educational project on acute pancreatitis sponsored by the Italian Association for the Study of the Pancreas.

Innovations and breakthroughs

The results of the Italian nation-wide survey indicate a lack of compliance with the guidelines for the indications for interventional endoscopy. Further effort should be made by scientific societies and by the National Health Services to release updated guidelines and evaluate their correct application in clinical practice.

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