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Original article

Detection of painless pancreatitis by computed tomography in patients with post-endoscopic retrograde cholangiopancreatography hyperamylasemia

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ABSTRACT

Objectives: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis is diagnosed on the basis of pancreatic pain and hyperamylasemia. However, because the diagnosis of abdominal pain is not objective, there may be some cases of painless pancreatitis among patients with post-ERCP hyperamylasemia (PEH). We reviewed the computed tomography (CT) findings of PEH cases to determine the incidence of painless pancreatitis.
Methods: Between July, 2005 and December, 2011, CT was performed in 91 patients with hyperamylasemia 18 h after ERCP. We reviewed the CT findings and graded the severity of pancreatitis according to the Balthazar grading system. Grades C, D, and E were defined as pancreatitis.
Results: Thirty-four patients (37%) had pancreatitis according to the CT findings. There was a significant difference in the serum amylase levels between the positive- and negative-CT finding groups (1306 ± 833 vs. 786 ± 315 IU/L, respectively; $p = 0.0012$). Receiver operating characteristic curve analysis showed that the amylase cut-off value for discriminating between the 2 groups was 795 IU/L (6.36 times the upper normal limit).
Conclusions: Thirty-seven percent of PEH patients had painless pancreatitis. CT is useful to determine pancreatitis in patients taking analgesics, steroids, or anti-immunological drugs and those with diabetes mellitus and 18-h serum amylase levels of >6 times the normal upper limit.

1. Introduction

Acute pancreatitis is the most common and important complication after endoscopic retrograde cholangiopancreatography (ERCP). According to Cotton's criteria, patients are diagnosed with post-ERCP pancreatitis (PEP) when they have pancreatic pain lasting for at least 24 h with serum amylase levels of >3 times the upper normal limit, whereas patients without pancreatic pain are simply diagnosed with post-ERCP hyperamylasemia (PEH) [1]. However, the diagnosis of abdominal pain is not objective and is sometimes very difficult because it depends on the patient's complaint.

Hyperamylasemia after ERCP occurs in 7.7%–19.7% of patients [2–6], and its incidence is higher than that of pancreatitis (2.6%–13.1%) [1,6–10]. Several studies have suggested that the etiology of pancreatitis is different from that of hyperamylasemia, although the differences are not sufficiently clear [5]. It is also unclear whether additional therapy is required in patients with hyperamylasemia. However, several cases of painless pancreatitis have been reported [11–13]. In some of these cases, computed tomography (CT) findings showed severe pancreatitis (Balthazar grade E) [12]. Painless pancreatitis may be related to analgesic or steroid use, dementia, neurological disturbance, or immunosuppression, but this is uncertain [13].

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Considering these reports, there may be some patients with painless PEP. Some patients with PEH may also have acute pancreatitis; therefore, objective parameters should be established for the diagnosis of PEP. Painless pancreatitis may be missed in patients who are diagnosed according to Cotton's criteria. Therefore, we reviewed the CT findings and clinical courses of patients with PEH to determine whether they were suggestive of acute pancreatitis.

2. Methods

2.1. Study design

This study was conducted as a single-center retrospective analysis and was approved by the institutional review board. We obtained written informed consent for performing ERCP and CT with or without contrast enhancement.

2.2. Patient selection

We selected patients with PEH from the ERCP database who were treated in our institution between July, 2005 and December, 2011. The patients who underwent CT were identified by reviewing the clinical charts. CT was performed in PEH patients at the discretion of the doctors; however, between December, 2007 and December, 2011, we performed CT for consecutive PEH cases to decrease the influence of selection bias. The patients who had acute pancreatitis when ERCP was performed were excluded from this analysis.

2.3. Endpoints

The primary endpoint was the incidence of painless pancreatitis in patients with PEH. Other endpoints were the relationship between amylase level and incidence or severity of pancreatitis.

2.4. Definitions

Patients were diagnosed with PEP when they had new-onset or increased abdominal pain lasting for at least 18 h and serum amylase levels of >3 times the upper normal limit (125 IU/L), whereas patients without abdominal pain were diagnosed with PEH [1].

The CT findings were classified according to the Balthazar grading system [14] (Table 1). Balthazar CT grades A and B were defined as negative findings for pancreatitis, and grades C, D, and E were defined as positive findings for painless pancreatitis.

2.5. Data collection

Serum amylase, p-amylase, C-reactive protein (CRP), and blood count were routinely measured before and 18 h after ERCP. Abdominal pain was assessed 3 h and 18 h after the procedure and at any time a patient complained of pain. At our institution, it is a rule to follow-up all patients for at least 2 days after ERCP on admission. Some endoscopists are afraid that pancreatitis will develop after initiating food intake in patients with high serum amylase levels, and they hesitate to initiate oral food intake. In most of these cases, food intake was initiated when serum amylase levels were almost normal. We reviewed the fasting period and treatments, such as intensive rehydration therapy for pancreatitis, in patients with PEH. In patients diagnosed with PEH, the decision to perform CT was taken by the endoscopist.

Table 1
Balthazar grades.

Grade A	Normal pancreas
Grade B	Focal or diffuse enlargement of the pancreas
Grade C	Intrinsic pancreatic abnormalities associated with haziness and streaky densities representing inflammatory changes in the peripancreatic fat
Grade D	Single ill-defined fluid collection
Grade E	Two or more poorly defined fluid collections or presence of gas adjacent to the pancreas

2.6. Statistical analysis

The χ^2 test or Fisher's exact test was used to compare categorical variables, when appropriate. Student's *t*-test or Welch's *t*-test was used to compare continuous variables, which were reported as the mean ± standard deviation. The Wilcoxon rank sum test was used to compare the fasting periods. A two-tailed *p* value of <0.05 was considered significant. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off serum amylase level for CT findings of pancreatitis. JMP version 9 (SAS Institute Inc., Cary, NC, USA) was used to perform all data analyses.

3. Results

3.1. Patients

Between July, 2005 and December 2011, 3867 ERCP-related procedures were performed at our institution on admission. PEP occurred in 150 patients (3.9%), and PEH occurred in 244 patients (6.3%). We reviewed the CT findings in 91 patients to determine if they were suggestive of acute pancreatitis according to the Balthazar grades. The baseline characteristics of these patients are summarized in Table 2. The most common indication for ERCP was common bile duct stone (40.7%), followed by malignant biliary stenosis (30.8%).

3.2. Outcomes

There were 34 cases (37%) of painless pancreatitis in 91 patients with PEH according to the CT findings (Table 3). Almost all patients were classified as grade C, but 3 cases were classified as grade E. One of the 3 patients regularly took opioids and nonsteroidal anti-inflammatory drugs, and another patient took steroids and tacrolimus hydrate. These medications probably reduced the sensitivity to abdominal pain. The remaining patient did not regularly take analgesics but had long-standing diabetes mellitus for 20 years. The fasting periods for these 3 patients were 4, 9, and 11 days, respectively. They were treated with large amounts of rehydration and ulinastatin, similar to the patients with pancreatitis.

The baseline characteristics and ERCP procedures were similar between the positive- and negative-CT finding groups (Table 4). Most patients with hyperamylasemia received rehydration and

Table 2
Characteristics of the study population.

Male/female	58/33
Mean age, years (range)	68 (39–91)
Main indication for ERCP	
CBD stone	37
Malignant biliary stenosis	28
Benign biliary stenosis	6
PSC	4
Cholangitis	6
Cholecystitis	3
IPMN	3
Chronic pancreatitis	2
Liver abscess	1
Infected biloma	1

ERCP: endoscopic retrograde cholangiopancreatography; CBD: common bile duct; PSC: primary sclerosing cholangitis; IPMN: intraductal papillary mucinous neoplasm.