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Prediction of Post-ERCP Pancreatitis

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1. Introduction

Diagnostic accuracy in regard to biliary and pancreatic diseases has improved markedly since the introduction of computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP)(1,2), but detection of small bile duct cancers and small pancreatic cancers is difficult even by those modalities. Endoscopic retrograde cholangiopancreatography (ERCP) remains the most accurate and reliable procedure for cytodiagnosis and precise staging of biliary and pancreatic neoplasms, and it is indispensable to the endoscopic treatment of biliary and pancreatic diseases.

Pancreatitis remains the most common complication of ERCP and results in substantial morbidity and, occasionally, in death (3-5). The mechanisms responsible for the development of post-ERCP pancreatitis are not fully understood, but they are thought to be multifactorial. A number of specific risk factors have been proposed as predictors of post-ERCP pancreatitis (6-15), and they include patient-, endoscopist-, and procedure-related factors. We therefore think that clear identification of risk factors is facilitated by analyzing the data for diagnostic ERCP and therapeutic ERCP separately.

Early identification of patients who are likely to develop post-procedure pancreatitis is highly desirable in terms of planning long-term follow-up in the hospital and an early therapeutic approach. Hyperamylasemia is common after ERCP, and amylase values have been found to peak between 90 min and 4 h post-ERCP (16,17). Testoni et al. (18) concluded that the serum amylase level measured 4 h after endoscopic sphincterotomy was the most reliable predictor of post-ERCP pancreatitis, and Thomas et al.(19) showed that the 4-h post-procedure amylase level is clinically significant as a predictor of post-ERCP pancreatitis. We therefore hypothesized that the 4-h amylase level is the most accurate amylase value for predicting subsequent pancreatitis.

Several studies (20-24) have demonstrated that the serum lipase level is more sensitive indicator than the serum amylase level for diagnosing other forms of acute pancreatitis, but only a few studies (25-27) have compared measurements of various pancreatic enzymes as a means of predicting post-ERCP pancreatitis. Moreover, it is still unclear whether there are differences in the diagnostic accuracy of pancreatic enzyme levels for predicting post-ERCP pancreatitis according to the procedures, in other words, whether the ERCP is diagnostic or

therapeutic. In the present study we evaluated the 4-h post-ERCP serum amylase level and serum lipase level as predictors of pancreatitis, with special focus on comparison of the two as a means of predicting post-ERCP pancreatitis, in a retrospective single-center design in Japan.

2. Patients and methods

We conducted a retrospective study in a single center by reviewing the 1631 consecutive cases in which ERCP was performed between January 1999 and December 2004 and (male:female ratio= 974:657 (1.48/1) ; age range 8-97 years old, median 67 years old). Diagnostic ERCP had been performed in 910 cases (male:female ratio=518:392 (1.32/1); age range 8-90 years old, median 63 years old), and therapeutic ERCP in 721 cases (male: female ratio=456:265 (160/1); age range 19-97 years old, median 67 years old). All patients were enrolled in this study, and there were no exclusion criteria. Diagnostic ERCP included brushing cytology (biliary tract, pancreatic duct) and intraductal ultrasonography (IDUS). Therapeutic ERCP included endoscopic papillary balloon dilatation (EPBD), endoscopic sphicterotomy (EST), stone removal, and bile duct drainage.

All ERCP patients were intravenously infused over 4 hours with one of the following protease inhibitor solutions beginning 30 minutes before the ERCP examination: Gabexate mesilate 200 mg in 0.9% saline, 500 ml, Nafamostat mesilate 20 mg in 0.9 % saline, 500 ml; or Ulinastatin 50,000 U in 0.9 % saline, 500 ml. The choice of inhibitor was at the discretion of the chief physician responsible for the patient's care.

All patients remained in the hospital for at least 24 hours after the procedure to monitor them for clinical manifestations of pancreatitis. Serum amylase and lipase levels were measured before and 4 and 16-18 hours (the next morning) after ERCP. We evaluated 23 variables, including patient-related factors, an endoscopist-related factor, and procedure-related factors that could be analyzed in detail based on information in the patients' charts. We also evaluated and compared the 4-h post-ERCP serum amylase level and serum lipase level as predictors of pancreatitis based on receiver-operator characteristic (ROC) curves. To compare the ROC curves, we analyzed only the data from cases in which both amylase and lipase could be measured, in other words, we made a matched pair comparison. We analyzed the data of a total of 1267 patients, consisting of 65 pancreatitis patients and 1202 non-pancreatitis patients. A total of 688 patients, consisting of 39 pancreatitis patients and 649 non-pancreatitis patients had undergone diagnostic ERCP, and a total of 579 patients, consisting of 26 pancreatitis patients and 553 non-pancreatitis patients, had gone therapeutic ERCP.

Data related to the procedures were gathered in a prospective manner, but the global analysis was performed in a retrospective manner.

2.1 Endoscopists

The 1631 ERCP procedures were performed by 11 different endoscopists (median: 57 procedures per endoscopist, range: 8-423). Four of the endoscopists performed about 84% of the procedures, and each of the 4 had performed more than 200 ERCPs before the study. The other 7 endoscopists had performed fewer than 200 ERCPs each before the study.

2.2 Definition

High levels of emzymes was defined as an amylase level (normal range: 40-125 IU/l) and /or lipase level (normal range 13-49 IU/l) above the upper limit of the normal range. The criteria for the diagnosis of post-ERCP pancreatitis were: (1) abdominal pain that persisted for at least 24 hours; (2) a serum amylase level and/or lipase level measured 16-18 hours after the procedure (next morning) that was more than three times the upper limit of the normal range; (3) pancreatic swelling with or without fluid collection on an abdominal US and/or CT examination the next morning. Fulfillment of criterion 1 plus criterion 2 and/or 3 was required to make the diagnosis. Pancreatitis was graded as follows according to the scoring system proposed by the Ministry of Health, Labour and Welfare of Japan (JPN score) (28,29): mild (0 points); moderate (1 point); severe (2 points or more).

The injection pressure of contrast medium into the pancreatic duct was scored as follows based on the degree of pancreatic duct visualization, according to a modification of the criteria proposed by Tsujino et al. (30): 0, no pancreatic duct visualization; 1, visualization of the main pancreatic duct alone; 2, 1 and visualization of primary branches; 3, 2 and visualization of secondary branches; and 4, 3 and/or visualization of acini (acinarization).

2.3 Statistical analysis

In the first step, a univariate analysis was performed by the chi-square method for each of the potential risk factors. In the second step, factors with a p value <0.2 according to the chi-square analysis were included in a multivariate (logistic regression) analysis performed using Statview 5.0 software. A p value <0.05 was considered statistically significant. The odds ratios are reported with their 95% confidence limits.

ROC curve analyses for the serum amylase and lipase values were performed using Medcalc software. We assessed whether the difference in area under two ROC curves was significant based on the methods proposed by Hanley JA et al (31). In short, the difference in area under two ROC curves derived from the same set of patients is calculated as a critical ratio z by using the formula:

$$z= (A_1-A_2)/\sqrt{(SE_1^2+SE_2^2-2rSE_1SE_2)},$$

where A1 is the observed area and SE1 is estimated error of the ROC area associated with modality 1, A2 and SE2 are the corresponding values for modality 2, and r is a constant calculated from (A1+A2)/2 and (rn+ra)/2, where rn is the coefficient for the correlation between modality 1 and modality 2 in the control group (non-pancreatitis group in this study), and ra is the coefficient for the correlation between modality 1 and modality 2 in the diseased group (pancreatitis group in this study). This quantity z is then referred to tables of the normal distribution and values of z above a certain cutoff are taken as evidence of a difference between the 'true' ROC areas.

We selected optimal cutoff values for the serum amylase and lipase values as predictors of post-ERCP pancreatitis based on their sensitivity and specificity and especially their positive predictive value (PPV) and negative predictive value (NPV), by using a prior probability value for post-ERCP pancreatitis of 4.2% (incidence rate among the cases in this study as a whole).

3. Results

3.1 Incidence of post-ERCP pancreatitis

Pancreatitis developed after 67 (4.2%) of the 1631 ERCP procedures. According to the JPN scores the pancreatitis was mild after 60 (3.7 %) of the procedures, moderate after 5 (0.3%), and severe after 4 (0.2%). There were no deaths in our series. Pancreatitis developed after 40 (4.4%) of the 910 diagnostic ERCPs, and after 29 (4.0%) of the 721 therapeutic ERCPs. The difference between the incidence of post-ERCP pancreatitis after diagnostic ERCP and after therapeutic ERCP was not statistically significant.

The incidence of post-ERCP pancreatitis after diagnostic ERCP in the Gabexate mesilate group, Nafamostat mesilate group, and Ulinastatin group was 4.7% (31/666), 3.8% (7/184), and 3.3% (2/66), respectively, and there were no statistically significant differences in the incidence of post-ERCP pancreatitis between the three groups. The incidence of post-ERCP pancreatitis after therapeutic ERCP in the Gabexate mesilate group, Nafamostat mesilate group, and Ulinastatin group was 4.4% (19/428), 3.4% (7/209), and 3.6% (3/84), respectively, and there were no statistically significant differences in the incidence of post-ERCP pancreatitis between the three groups.

3.2 Risk factors for post-ERCP pancreatitis

3.2.1 Diagnostic ERCP

3.2.1.1 Univariate analysis

The univariate analysis revealed statistically significant associationss between an increased risk of post-ERCP pancreatitis and 4 of the13 patient-related factors and 4 of the 9 procedure-related factors (Tables 1 and 2). The patient-related factors that significantly increased the risk of pancreatitis were: age 65 years or over, presence of hyperamylasemia and/or hyperlipasemia before ERCP, past or present pancreatitis and IPMN. The significant procedure-related risk factors according to the univariate analysis were: injection of contrast medium into the pancreatic duct score >= 3, brushing cytology in the pancreatic duct, IDUS, and endoscopic nasobiliary drainage (ENBD).

3.2.1.2 Multivariate analysis

Five risk factors were significant according to the multivariate analysis. Two were patient-related factors, age (OR=1.043/1 yr increase in age) and presence of hyperamylasemia and/or hyperlipasemia before ERCP (OR=2.291), and the other three were procedure-related factors, high contrast medium injection pressure into the pancreatic duct (OR=2.406/ 1 point increase), brushing cytology in the pancreatic duct (OR=4.135), and IDUS (OR=4.373). The R-square value was 0.204.

3.2.2 Therapeutic ERCP

3.2.2.1 Univariate analysis

The univariate analysis revealed a statistically significant association between an increased risk of post-ERCP pancreatitis and only one endoscopist-related factor: inexperienced endoscopist (Tables 3 and 4).

Patient-related factors	Pancreatitis (n=40)	Non-pancreatitis (n=870)	p value
Significant			
Age (>=65years/<65years)	**26/14**	**378/492**	**<0.001**
Hyperamylasemia and/or hyperlipasemia (yes/no)	**18/22**	**184/686**	**<0.001**
Past or present pancreatitis (yes/no)	**9/31**	**76/773**	**0.004**
IPMN	**12/28**	**131/739**	**0.011**
Not significant			
Gender (male/female)	**17/23**	**501/369**	**0.062**
Past-post ERCP pancreatitis(yes/no)	**1/39**	**6/864**	**0.200**
Past or presenting cholangitis (yes/no)	**1/39**	**79/791**	**0.151**
Periamupullary diverticulum (yes/no)	**3/37**	**66/804**	**0.984**
Chronic pancreatitis (yes/no)	**5/35**	**97/773**	**0.791**
Pancreatic cancer (yes/no)	**2/38**	**108/762**	**0.160**
Pancreas divisum (yes/no)	**1/39**	**30/840**	**0.746**
Anomalous pancreatic-biliary junction (yes/no)	**2/38**	**25/845**	**0.438**
Bile duct stone (yes/no)	**1/39**	**40/830**	**0.532**

IPMN, intraductal papillary mucinous neoplasia
ERCP: Patient-related Factors (ref 34))

Table 1. Univariate Analysis of Risk Factors for Post-ERCP Pancreatitis after Diagnostic

Endoscopist-related factor and Procedure-related factors	Pancreatitis (n=40)	Non-pancreatitis (n=870)	p value
Significant			
Injection pressure of contrast medium into the pancreatic duct (score 3,4/0-2)	**29/11**	**348/522**	**<0.001**
Brushing cytology in the pancreatic duct (yes/no)	**11/29**	**69/801**	**<0.001**
IDUS (yes/no)	**8/32**	**55/815**	**<0.001**
ENBD (yes/no)	**1/39**	**3/867**	**0.040**
Not significant			
Endoscopist experience (<=200 ERCPs/>200 ERCPs)	**9/31**	**125/745**	**0.156**
EST (yes/no)	**0/40**	**1/869**	**0.830**
EPBD (yes/no)	**0/40**	**0/870**	**N.E.**
Bile duct stone exploration (yes/no)	**0/40**	**0/840**	**N.E.**
Brushing cytology in the bile duct (yes/no)	**1/39**	**44/826**	**0.466**
Biliary stenting (yes/no)	**0/40**	**0/870**	**N.E.**

ERCP: An Endocopist-related Factor and Procedure-related Factors (ref 34))
IDUS, intraductal ultrasonography; EST, endoscopic sphincterotomy; EPBD, endoscopic papillary balloon dilation; ENBD, endoscopic nasobiliary drainage

Table 2. Univariate Analysis of Risk Factors for Post-ERCP Pancreatitis after Diagnostic

Patient-related factors	Pancreatitis (n=29)	Non-pancreatitis (n=692)	p value
Not Significant			
Age (>=65years/<65years)	19/10	391/301	0.337
Gender (male/female)	21/8	435/257	0.300
Hyperamylasemia and/or hyperlipasemia (yes/no)	8/21	207/485	0.788
Past or present pancreatitis(yes/no)	1/28	49/643	0.450
Past-post ERCP pancreatitis(yes/no)	1/39	6/864	0.200
Past or presenting cholangitis (yes/no)	13/16	313/379	0.966
Periamupullary diverticulum (yes/no)	8/21	115/577	0.123
Chronic pancreatitis (yes/no)	1/28	18/674	0.780
Pancreatic cancer (yes/no)	3/26	112/580	0.400
Pancreas divisum (yes/no)	0/29	1/691	0.838
IPMN(yes/no)	0/29	2/690	0.772
Anomalous pancreatic-biliary junction (yes/no)	1/28	6/686	0.165
Bile duct stone (yes/no)	14/15	350/342	0.808

IPMN, intraductal papillary mucinous neoplasia

Table 3. Univariate Analysis of Risk Factors for Post-ERCP Pancreatitis after Therapeutic ERCP: Patient-related Factors (ref34))

Endoscopist-related factor and Procedure-related factors	Pancreatitis (n=29)	Non-pancreatitis (n=692)	p value
Significant			
Endoscopist experience (<=200 ERCPs/>200 ERCPs)	8/21	62/630	<0.001
Not significant			
Injection pressure of contrast medium into the pancreatic duct (score 3,4/0-2)	5/24	59/633	0.106
Brushing cytology in the pancreatic duct (yes/no)	0/29	10/682	0.514
IDUS (yes/no)	0/29	6/686	615
EST (yes/no)	5/24	98/594	0.642
EPBD (yes/no)	8/21	114/578	0.118
Bile duct stone exploration (yes/no)	7/22	156/536	0.841
Brushing cytology in the bile duct (yes/no)	1/28	20/672	0.861
Biliary stenting (yes/no)	4/25	120/572	0.620
ENBD (yes/no)	5/24	231/461	0.070

ERCP: An Endocopist-related Factor and Procedure-related Factors (ref34))
IDUS, intraductal ultrasonography; EST, endoscopic sphincterotomy; EPBD, endoscopic papillary balloon dilation; ENBD, endoscopic nasobiliary drainage

Table 4. Univariate Analysis of Risk Factors for Post-ERCP Pancreatitis after Therapeutic

3.2.2.2 Multivariate analysis

Two risk factors were significant according to the multivariate analysis. One was an endoscopist-related factor, inexperienced endoscopist (OR=4.407), and the other was a procedure-related factor, high contrast medium injection pressure into the pancreatic duct (OR=1.693/ 1 point increase). The R-square value was 0.073.

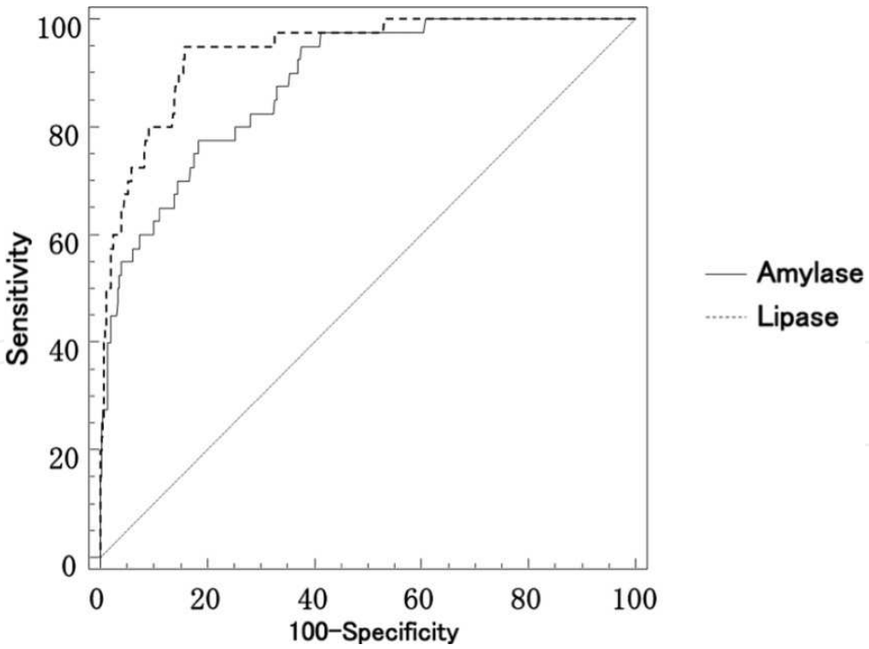
3.2.2.3 Multivariate analysis of the cases as a whole

Six risk factors were significant according to the multivariate analysis for whole cases. Two were patient-related factors, age (OR=1.038/1 yr increase in age) and presence of hyperamylasemia and/or hyperlipasemia before ERCP (OR=1.807). One was an endoscopist-related factor, inexperienced endoscopist (OR=2.645), and the other three were procedure-related factors, high contrast medium injection into the pancreatic duct (OR=1.608/1 point increase), brushing cytology in the pancreatic duct (OR=2.605), and IDUS (OR=2.602). R-square value was 0.114.

3.2.3 Prediction of pancreatitis following ERCP by the 4-h post-procedure serum amylase level and lipase level

3.2.3.1 Diagnostic ERCP

The receiver-operating characteristics (ROCs) of both the 4-h amylase level and lipase level after diagnostic ERCP showed good test performance, with an area under the curve of 0.88 (95% CI: 0.85-0.91) and 0.94 (95% CI: 0.92-0.96), respectively (Figure 1). The 4-h



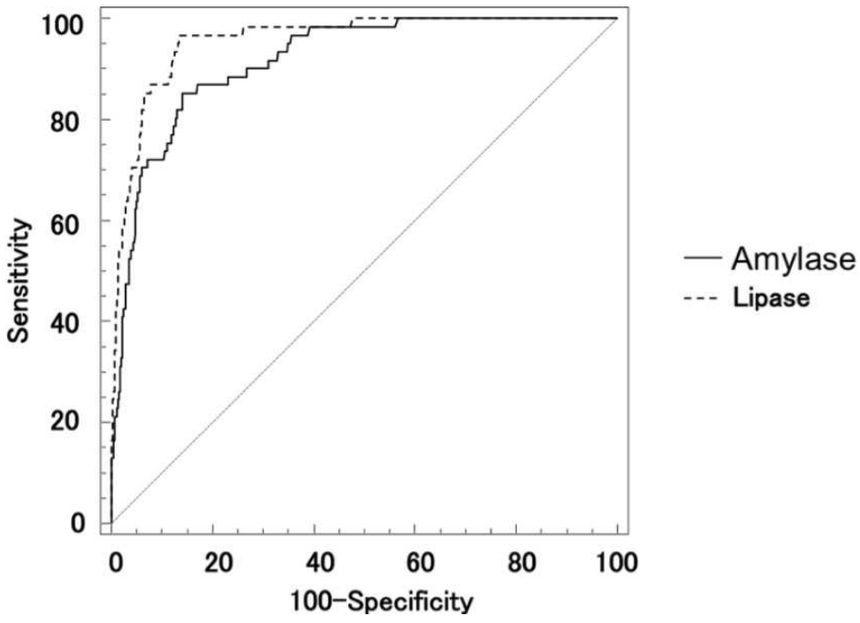
The area under the curve of the amylase levels was 0.88 (95% CI: 0.85-0.91).
The area under the curve of the lipase levels was 0.94 (95% CI: 0.92-0.96).

Fig. 1. ROC curve of the 4-h post-procedure serum amylase levels and lipase levels after diagnostic ERCP.

post-procedure serum lipase level was a more effective predictor of post–ERCP pancreatitis than the amylase level based on the areas under the ROC curves (p=0.025).

3.2.3.2 Therapeutic ERCP

The receiver-operating characteristics (ROCs) of both the 4-h amylase level and lipase level after therapeutic ERCP showed good test performance, with an area under the curve of 0.92 (95% CI: 0.90-0.93) and 0.96 (95% CI: 0.94-0.97), respectively (Figure 2). The 4-h post-procedure serum lipase level was a more effective predictor of post–ERCP pancreatitis than the amylase level, based on the area under the ROC curves (p=0.035).

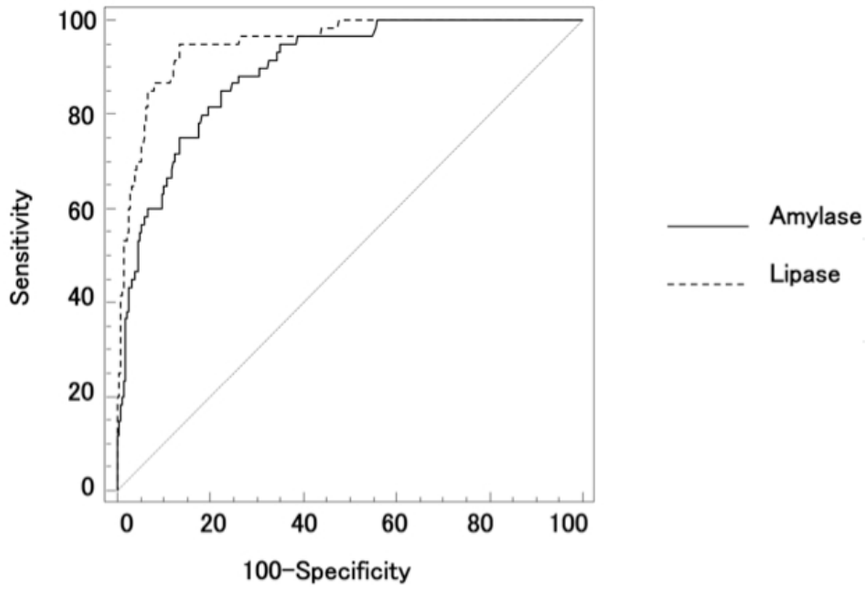


The area under the curve of the amylase levels was 0.92 (95% CI: 0.90-0.93).
The area under the curve of the lipase levels was 0.96 (95% CI: 0.94-0.97).

Fig. 2. ROC curve of the 4-h post-procedure serum amylase levels and lipase levels after therapeutic ERCP.

3.2.3.3 ERCP cases as a whole

The receiver-operating characteristics (ROCs) of both the 4-h amylase level and lipase level after ERCP for the cases as a whole showed good test performance, with an area under the curve of 0.91 (95% CI: 0.89-0.92) and 0.96 (95% CI: 0.94-0.97), respectively (Figures 3). The 4-h post-procedure serum lipase level was a more effective predictor of post–ERCP pancreatitis than the amylase level based on the areas under the ROC curves (p=0.007).



The area under the curve of the amylase levels was 0.91 (95% CI: 0.89-0.92).
The area under the curve of the lipase levels was 0.96 (95% CI: 0.94-0.97).

Fig. 3. ROC curve of the 4-h post-procedure serum amylase levels and lipase levels after ERCP in the cases as a whole.

3.2.3.4 Optimal cutoff values for amylase and lipase

The optimal cutoff values for amylase were five times (625 IU/l) the upper limit of the normal range in the diagnostic ERCP cases, therapeutic ERCP cases, and ERCP cases as a whole based on their sensitivity and specificity and especially on their PPV and NPV (Table 5).

	Amylase level	Sensitivity (%)	Specificity(%)	PPV (%)	NPV (%)	Likelihood ratio
Diagnostic						
	> 3 times	82.5	70.3	10.8	98.9	2.78
	> 4 times	77.5	79.9	14.5	98.8	3.86
	> 5 times	70.0	85.1	17.1	98.5	4.37
Therapeutic						
	> 3 times	90.2	72.4	14.5	99.4	3.26
	> 4 times	86.9	79.7	17.8	99.3	4.29
	> 5 times	85.2	86.1	21.2	99.3	6.13
All cases						
	> 3 times	89.8	72.9	12.7	99.4	3.32
	> 4 times	84.7	80.4	16.0	99.2	4.36
	> 5 times	78.0	85.8	19.5	98.9	5.51

Post-ERCP pancreatitis (ref34)). PPV, positive predictive value; NPV, negative predictive value.

Table 5. Diagnostic Accuracy of Various Amylase Cutoff Levels for Predicting

The optimal cutoff values for lipase were ten times (490 IU/l) the upper limit of the normal range in diagnostic ERCP cases, therapeutic ERCP cases, and ERCP cases as a whole based on their sensitivity and specificity and especially on their PPV and NPV (Table 6).

	Lipase level	Sensitivity (%)	Specificity(%)	PPV (%)	NPV (%)	Likelihood ratio
Diagnostic						
	> 6 times	**95.0**	**73.6**	**13.6**	**99.7**	**3.60**
	> 8 times	**95.0**	**82.0**	**18.8**	**99.7**	**5.21**
	> 9 times	**95.0**	**83.7**	**20.1**	**99.7**	**5.84**
	> 10 times	**92.5**	**84.5**	**21.2**	**99.6**	**5.97**
Therapeutic						
	> 6 times	**96.7**	**81.4**	**18.5**	**99.8**	**5.16**
	> 8 times	**96.7**	**85.1**	**22.9**	**99.8**	**6.48**
	> 9 times	**96.7**	**86.1**	**24.2**	**99.8**	**6.94**
	> 10 times	**95.1**	**86.8**	**26.8**	**99.8**	**7.23**
All cases						
	> 6 times	**96.6**	**80.8**	**18.1**	**99.8**	**5.05**
	> 8 times	**96.6**	**84.8**	**21.8**	**99.8**	**6.34**
	> 9 times	**96.6**	**85.9**	**23.1**	**98.8**	**6.85**
	> 10 times	**94.9**	**86.4**	**23.8**	**99.7**	**7.04**

Table 6. Diagnostic Accuracy of Various Lipase Cut-off Levels for Predicting Post-ERCP pancreatitis (ref34)). PPV, positive predictive value; NPV, negative predictive value..

4. Discussion

Pancreatitis remains the most common complication of ERCP, occurring after 1% to 30% of procedures (4-15), and its reported incidence has varied with the thoroughness of follow-up, the definition used, factors related to patient susceptibility, case mix, types of maneuvers performed, and the endoscopist. Rates of pancreatitis of 2% to 9% have been typical in unselected large prospective series (6-14). The subjects of the present study were consecutive patients who underwent diagnostic or therapeutic ERCP, and the incidence rate of pancreatitis was 4.2% in the subjects as a whole, 4.4 % in the diagnostic ERCP group, 4.0 %. In therapeutic ERCP group. These figures are comparable to those reported in recent prospective studies in which the definition and study population were similar to those in our study.

A number of specific risk factors, acting independently or in concert, have been proposed as predictors of post-ERCP pancreatitis (6-14). The present study assessed 23 risk factors that included patient-related, procedure-related, and endoscopist-related variables. The results of the multivariate analysis showed that older age, hyperamylasemia and/or hyperlipasemia before ERCP, endoscopist experience with fewer than 200 ERCPs, high contrast medium injection pressure into the pancreatic duct, brushing cytology in the pancreatic duct, and IDUS each increased risk independently. The results of this study also demonstrated that the risk of post-ERCP pancreatitis is as much related to patient characteristics as to endoscopic technique and/or maneuvers, as previously reported (6-10,14). However, the limitation of the present study is that it was a retrospective study. In spite of the fact that data were obtained from consecutive ERCP cases, minimal bias must be taken into account.

Previous studies have suggested that early hyperamylasemia is useful as a predictor of post-ERCP pancreatitis (18,19,32,33). Thomas et al. (19) found that a 4-h amylase level threefold higher than normal was a useful predictor of pancreatitis and had a sensitivity and specificity of 70% and 95.3%, respectively. Testoni et al. (18) reported that a serum amylase level fivefold higher than normal 4 h after the procedure is a reliable predictor of post-procedure pancreatitis, with a sensitivity of 68.4%. In the present study the ROC of both the 4-h amylase level and the 4-h lipase level after diagnostic ERCP showed good test performance, with an area under the curve of 0.88 and 0.94, respectively, and the ROC of both the 4-h amylase level and the 4-h lipase level after therapeutic ERCP also showed good test performance, with an area under the curve of 0.92 and 0.96, respectively. In addition, the ROC of both the 4-h amylase and the 4-h lipase level after ERCP in the cases as a whole showed good test performance, with an area under the curve of 0.91 and 0.96, respectively. The optimal cutoff values for the amylase level after diagnostic ERCP, therapeutic ERCP, and ERCP as a whole were 5 times (625 IU/l) the upper limit of the normal range, and the sensitivity and specificity of the cutoff value for the as a whole cases was 78.0% and 85.8%, respectively. The optimal cutoff values for the lipase level after diagnostic ERCP, therapeutic ERCP, and ERCP as a whole cases were 10 times (490 IU/l) the upper limit of the normal range, and their sensitivity and specificity in the cases as a whole were 94.9% and 86.4%. The results of this study confirmed that the 4-h post-procedure serum amylase and lipase level are good predictors of pancreatitis both after diagnostic ERCP and after therapeutic ERCP.

Comparisons of measurements of various pancreatic enzymes as a means of detecting of acute pancreatitis other than post-ERCP pancreatitis have shown that the blood lipase level is almost as sensitive as the total blood amylase level and has better specificity (20). Other studies (21-23) have demonstrated that the blood lipase level is more sensitive than the blood amylase level, and still another study concluded that the blood lipase level is an important diagnostic indicator for acute pancreatitis and that measuring it should be given top priority (24). By contrast, few studies have compared measurements of various pancreatic enzymes as a means of diagnosing post-procedure pancreatitis (25-27). Panteghini et al. (25) found that the serum lipase level increased faster than the levels of the other enzymes measured and that the average peak in lipase level was the highest in post-procedure pancreatitis. Doppl et al. (26) concluded that serum lipase measurement is the most sensitive diagnostic test for post-ERCP pancreatitis. The results of the present large retrospective study demonstrated that serum lipase was a more effective marker than amylase for predicting post-ERCP pancreatitis both after diagnostic ERCP and after therapeutic ERCP, based on the area under the ROC curves. A further prospective study should be performed to confirm the superiority of serum lipase over amylase as a predictor of post-ERCP pancreatitis.

In conclusion, the 4-h post-ERCP serum amylase level and the 4-h post-ERCP lipase level, in particular, were found to be a useful means of predicting pancreatitis both after diagnostic ERCP and after therapeutic ERCP in a large retrospective study in a single center. A prospective study should be undertaken to confirm the usefulness of the 4-h post-ERCP amylase and lipase levels as predictors of post-ERCP pancreatitis.

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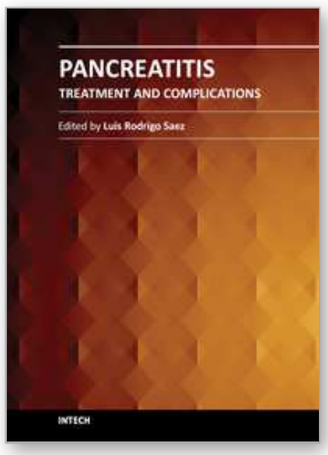
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Pancreatitis may be acute or chronic. Although they can be caused by similar aetiologies, they tend to follow distinct natural histories. Around 80% of acute pancreatitis (AP) diagnoses occur as secondary to gallstone disease and alcohol misuse. This disease is commonly associated with the sudden onset of upper abdominal that is usually severe enough to warrant the patient seeking urgent medical attention. Overall, 10 to 25% of AP episodes are classified as severe, leading to an associated mortality rate of 7 to 30%. Treatment is conservative and consists of general medical support performed by experienced teams, sometimes in ICUs. Although most cases of acute pancreatitis are uncomplicated and resolve spontaneously, the presence of complications has significant prognostic importance. Necrosis, hemorrhage, and infection convey rates of up to 25%, 50%, and 80% mortality, respectively. Other complications such as pseudocyst formation, pseudoaneurysm formation, or venous thrombosis increase morbidity and mortality to a lesser degree. The presence of pancreatic infection must be avoided.

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