Clinical Analysis of the Efficacy in Lipase/ Amylase Ratio for Acute Pancreatitis

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Abstract

The mortality rate is high in complicated pancreatitis. The serum lipase/amylase (L/A) ratio had been proposed to distinguish the etiology of pancreatitis, the efficacy to predict the severity of acute pancreatitis is assessed in this study. From July 1, 2001 to June 30, 2002, 247 patients with acute pancreatitis were enrolled. We included 141 (57.1%) men and 106(42.9%) women with a mean age of 53.6 years, ranging from 21 to 90 years. They were divided into 3 subgroups according to their attributed etiology such as alcohol (n=54), biliary (n=111), miscellaneous causes (n=82) and their serum L/A ratio level were compared. Besides, the relationship between the severities of pancreatitis by computed tomography (CT) findings and L/A ratio levels were also analyzed. Results showed that 47 patients were alcoholic acute panceatitis (21.9 %, 52 male and 2 female), 111 patients with biliary acute pancreatitis (44.9%), and 82 patients with miscellaneous acute pancreatitis (33.2%). Significant factors were: mean age 40 ± 9.4 years in alcoholic group versus 59.2 ± 14.7 years in biliary group; male predominance in alcoholic group and female dominated the biliary group; the elevation of serum amylase level in biliary group (1344.2±1453.7 IU/L) versus in alcoholic group (346.9 \pm 374.9 IU/L), and serum lipase level in biliary group (13072.0±18807.9 IU/L) versus in alcohol group (3119.7 \pm 4923.7 IU/L).

Instead, the serum L/A ratio showed no significant changes among each group. If L/A ratio > 2, it had 89.5% negative predictive rate of alcoholic pancreatitis. In this study, the alcoholic acute pancreatitis is more severe than biliary ones. There was also no difference in serum enzyme levels (amylase, lipase, and L/A ratio) observed among patients without apparent imaging signs of acute pancreatitis, those with signs of moderate and severe pancreatitis. Therefore, we conclude that gender difference plays an important role in the etiology of acute pancreatitis. The serum amylase and lipase concentrations are not able to establish either etiology or to predict the severity of acute pancreatitis as assessed by imaging techniques. The L/A ratio is not a good predictive factor in distinguishing acute episode of alcoholic and non-alcoholic acute pancreatitis but the L/A ratio > 2 has 89.5 % of negative predictive rate for alcoholic panceatitis. (J Intern Med Taiwan 2005; 16: 113-120)

Key Words : Acute pancreatitis, Amylase, Lipase, Lipase/amylase ratio

Introduction

An elevated serum pancreatic enzyme supports clinical diagnosis of acute pancreatitis. Numerous reports, however, describe the lack of usefulness of serum enzyme levels to determine the prognosis in acute pancreatitis 1-4. Although Cherry and Crandl 5 first described an association between pancreatic injury and elevated serum lipase levels in 1932, the routine study of serum lipase levels has yet to gain widespread popularity. In the Western countries, alcohol is the most common cause of acute pancreatitis ⁶⁻¹⁰ but a diagnostic workup must be undertaken to identify treatable causes 11. It was reported that patients with acute alcoholic pancreatitis had serum concentrations of amylase lower than those with nonalcoholic pancreatitis, but the serum lipase concentrations were similar in the both forms of the disease 12. The serum lipase/amylase (L/A) ratio was significantly higher in alcoholic acute pancreatitis than in the nonalcoholic form of the disease. On the basis of these findings Gumaste et al 13 proposed that this index (L/A ratio >2) could differentiate acute episodes of alcoholic from those nonalcoholic acute pancreatitis. However, the most common cause of acute pancreatitis is biliary origin in Taiwan 14. Therefore, we design this retrospective study with the purpose to assess the efficacy of the L/A ratio and computed tomography severity index 15 in the evaluation of the prognosis of different etiologies of acute pancreatitis in Southern Taiwan.

Materials and methods

Two hundred forty-seven patients (141 male, 106 female) with acute pancreatitis were enrolled in the study from July 1, 2001 to June 30, 2002. The diagnosis of acute pancreatitis is based on the evidence of two or more combination of the following presentations: at least three folds increase in serum amylase and/or lipase levels, in addition to history of upper abdominal pain and further confirmed by ultra-

sonography (CT) and/or contrast enhanced computed tomography performed during hospital stay. All patients with questionable diagnosis of other possible abdominal conditions and incomplete data collections were excluded in this study. All patients with clinical presentations suggestive of chronic pancreatitis such as pancreatic calcifications, pancreatic duct dilatation, and malabsorption syndrome were also excluded.

The etiology of the pancreatitis was biliary origin in 111 patients, alcoholic abuse in 54 patients (mean daily pure alcohol intake > 80 g), due to other causes in 82 patients (associated with diabetes mellitus: 23, trauma: 14, hyperlipidemia: 13, end stage renal disease: 19, postoperation: 13). There were 130 patients received abdominal CT examination. According to the Balthazar criteria 15, we classified patients with acute pancreatitis into three groups: Grade Mild (n=59): normal, local or diffuse enlargement of the pancreas; Grade Moderate (n=18): pancreatic gland abnormalities associated with peripancreatic inflammation; Grade Severe (n=53): fluid collection in one or more location and/ or the presence of gas in or adjacent to the pancreas. The serum amylase and lipase concentration were checked simultaneously after admission and thus calculating the L/A ratio. The normal ranges of the enzymes in our hospital are 0-190 IU/L for lipase and 27-137 IU/L for amylase. The relationship of L/A ratio with CT findings for indirectly evaluating the severity of pancreatitis in 130 patients was also analyzed.

Statistical analysis was performed using the ANOVA tests, Nonparametric test and κ^2 test when comparing these 3 groups of patients.

Results

Our study showed that 54 patients were related to alcohol (21.8%, male to female ratio was 52:2, mean age: 40.6 ± 9.4 years), 111 patients were biliary origin (44.9%, male to female ratio was 48:63,

Table 1. Serum Lipase-Amylase ratio level in different etiologic subgroup

	Alcohol (n=54)	Biliary (n=111)	Miscellaneous (n=82)	P value
Age	40±9.4*	59.2±14.7	54.6±6.3	< 0.05
M/F	52/2 ⁺	48/63	41/41	< 0.05
Amylase	346.9±374.9 [*]	1344.2±1453.7	571.6±666.8	< 0.05
Lipase	3119.7±49223.7 [¢]	13072.0±18807.9	5279.3±9395.7	< 0.05
Lipase/Amylase	7.99 ± 6.83	8.56 ± 6.63	7.05 ± 5.96	0.29

^{(*}Alcoholic pancreatitis vs biliary pancreatitis, Alcoholic pancreatitis vs Miscellaneous pancreatitis in age, P<0.05)

Table 2. Relationship between CT findings and lipase-amylase levels

	Normal to mild (n=59)	Moderate (n=18)	Severe (n=53)	P value
Alcohol	3	2	22 ⁺	< 0.001
Biliary	38 [‡]	10	9	< 0.001
Miscellaneous	18	6	22	NS
Age	60.4±15.3*	55.8 ± 14.8	48.0 ± 16.6	< 0.001
Male/Female	33/26	10/8	34/19	NS
Amylase	1034.5 ± 1174.9	1222.0 ± 1223.5	828.6 ± 1059.4	NS
Lipase	9264.0±13495.0	9712.4±9196.3	7922.8±16788.1	NS
Lipase/Amylase	7.50 ± 5.19	8.84 ± 5.65	7.43±5.93	NS

^{(*} Mild pancreatitis vs Severe pancreatitis , P<0.05)

Table 3.Sensitivity and specificity of the lipase/amylase ratio in 247 patient with acute alcohol-induced (n=54) and non-alcohol-induced (n=193) pancreatitis

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lipase/amylase ratio	> 2.0	> 4.2	> 5.0
Sensitivity (%)	92.6	64.8	57.4
Specificity (%)	17.6	34.2	38.3
Positive predictive value	25.8	21.6	20.7
Negative predictive value	89.5	77.6	76.3
Accuracy predictive value	34.0	40.9	42.5

mean age:59.2 \pm 14.7 years) and 82 patients were related to miscellaneous cause (33.2%, male to female ratio was 41:41 ,mean age:54.6 \pm 16.3 years). The median age was significantly youngest in alcoholic pancreatitis than in those with biliary and miscellaneous pancreatitis (P<0.05). The mean serum amylase level was significantly lower in alcoholic group (346.9 \pm 374.9 IU/L in alcoholic group versus 1344.2 \pm 1453.7 IU/L in biliary group versus 571.6 \pm 666.8 IU/L in miscellaneous group, P<0.05).

Table 4.Predict sensitivity and specificity of acute pancreatitis by lipase/amylase ratio in 130 patient with non-severe pancreatitis (n=77) and severe

pancreatitis(n=53)			
Lipase/Amylase ratio	> 2.0	> 4.2	> 5.0
Non-severe	61	51	48
Severe	22	14	13
Sensitivity (%)	26.5	21.5	21.3
Specificity (%)	34.0	40.0	42.0
Positive predictive value (%)	41.5	26.5	24.5
Negative predictive value (%)	20.8	33.8	37.7
Accuracy predictive value (%)	29.2	30.7	32.3

The mean serum lipase level was also significantly lower in alcoholic group (3119.7 ± 4923.7 IU/L in alcoholic group versus 13072.0 ± 18807.9 IU/L in biliary group versus 5279.3 ± 9395.7 IU/L in miscellaneous group, P<0.05). However, the L/A ratio was not significantly different among them. Besides, one hundred and thirty patients (52.6%) with pancreatitis received abdominal CT examination were

^{(†} Icoholic pancreatitis vs biliary pancreatitis, Alcoholic pancreatitis vs Miscellaneous pancreatitis in sex, P<0.05)

^{(&}quot;Icoholic pancreatitis vs biliary pancreatitis, Alcoholic pancreatitis vs Miscellaneous pancreatitis in amylase, P<0.05)

^{(*}Icoholic pancreatitis vs biliary pancreatitis, Alcoholic pancreatitis vs Miscellaneous pancreatitis in lipase, P<0.05)

^{(*} Alcoholic pancreatitis vs biliary pancreatitis in Mild grade, P<0.001)

^{(&}lt;sup>†</sup> Alcoholic pancreatitis vs biliary pancreatitis vs Miscellaneous pancreatitis in Severe grade, P<0.001)

summarized in Table 2, by comparing their mean values of serum lipase and amylase concentrations, age, sex, L/A ratio in accordance to their severity. Patients with mild pancreatitis were significant older than those with moderate and severe pancreatitis. Alcoholic pancreatitis had more severe CT findings than in those with biliary and miscellaneous pancreatitis. There is no significant difference in amylase, lipase and L/A ratio among them.

The L/A ratio > 2.0 was present in 50 of the 54 (92.6%) patients with alcoholic pancreatitis, in 159 of the 193 (82.3%) patients with non-alcoholics pancreatitis, and the sensitivity and specificity in determining the alcoholic acute pancreatitis were 92.6%, and 17.6%, respectively; positive and negative predictive values 25.8% and 89.5% (Table 3). Calculation of separating ratio levels above 4.2 for alcoholics and non-alcoholics, the sensitivity and specificity in determining the alcoholic acute pancreatitis were 64.8%, and 34.2%, respectively; positive and negative predictive values 21.6% and 77.6%. Using the L/A ratio >5.0 for alcoholics and non-alcoholics, the sensitivity and specificity were 57.4%, and 38.3%, respectively; positive and negative predictive values 20.7% and 76.3%.

The sensitivity and specificity to predict pancreatitis between the non-severe (mild and moderate) and severe group were also compared (Table 4). At the L/A ratio > 2.0 the sensitivity and specificity in determining the acute pancreatitis in the severe group were 26.5%, and 34.0%, respectively; positive and negative predictive values 41.5% and 20.8%. Using the L/A ratio > 4.2, the sensitivity and specificity were 21.5%, and 40.0%, respectively; the positive and negative predictive values 26.5% and 33.8%. Using the L/A ratio > 5.0, the sensitivity and specificity were 21.3%, and 42.0%, respectively; the positive and negative predictive values 24.5% and 37.7%.

Discussion

In the western literature, alcohol is the most

common cause of acute pancreatitis 6-10. However, biliary pancreatitis has been predominant in England, Hong Kong, Japan, and Taiwan 14,17-19. This was similar to our results with 44.9 % associated with biliary diseases. Wu et al reported that most of these cases with acute pancreatitis were between the age of 21 to 40 years old, which accounted 57.7% of the total cases and 64.1% of female cases was in age groups of 21 to 30 years old 20, which was much younger than reported in other Asian countries 12,21. However, there was no documented report comparing the different etiologic groups. In our study, the mean age was 53.6 year-old, from 21 to 90 years old. This was significantly youngest in alcoholic pancreatitis than in those with biliary acute pancreatits and miscellaneous acute pancreatitis (P<0.05). The biliary pancreatitis predominated in women in Taiwan could be related to the more prevalence of biliary calculi in Taiwanese women 18. In contrast, alcoholic acute pancreatitis predominated in Taiwanese male gender.

Previous studies showed that the increase in serum concentration of amylase in patients with alcoholic acute pancreatitis was significantly lower than of patients with biliary pancreatitis ^{12,13,21}, but that serum lipase concentrations were not significantly difference ^{12,21}. Our study showed the same result that serum amylase elevations were least in patients with alcoholic acute pancreatitis than those with biliray and other cause of pancreatitis. However, our results showed that the lipase elevations were also significantly lower in the alcoholic acute pancreatitis than the other two groups of patients.

Our results indicate that the L/A ratio is not useful to distinguish alcoholic from nonalcoholic acute pancreatitis. As in the previous original study ¹³, our patients with alcoholic acute pancreatits were male patients, whereas most of the patients with biliary pancreatitis were female. For these reasons, others ^{12,22} have hypothesized that the L/A ratio in the Gumaste study ¹³ differentiated between men and women but not between alcoholic patients and nonalcoholic pa-

tients. The study of Laurent-Puig et al. and Lankish et al ^{23,24}. also could not confirm the usefulness of the L/A ratio for differentiating between patients with acute pancreatitis of different etiologies and estimating the severity of the disease. Our result was not similar to Gamaste reports 13, but the same with Laurent-Puig and Lankish reports ^{23,24}. In fact, Gumaste et al 13 suggested that an L/A ratio value >2 had a sensitivity and specificity for the diagnosing the acute alcoholic pancreatitis of 91.0 % and 78.0 %, respectively. We found the sensitivity was 92.6 % but the specificity was low (17.6%). The negative predictive rate is 89.5 % in L/A ratio > 2 mean that if L/A ratio less than 2, the alcoholic pancreatitis is estimated about 10%. Tenner et al 21 reported that the L/A ratio > 5 is characteristic exclusively of alcoholic patients and show a low sensitivity (31%). Kazmierczak et al ²⁵ found that the L/A ratio > 4.2 had a sensitivity of 96 % but a low specificity (57 %), whereas our result showed a sensitivity of 64.8% and specificity of 34.2% (Table 3). We had different results by using the L/A ratio > 5, we found that the specificity was 38.3% and the sensitivity was 57.4%. Based on theses reports (including our results), there was still no agreement about the value of the L/A ratio in distinguishing alcoholic from nonalcoholic acute pancreatitis in the studies that report the clinical usefulness of the index in the clinical practice 21. The reason for these variations could be that all the studies 13,21,25 indicating the L/A ratio was useful had a preponderance of patients with acute alcoholic pancreatitis. In our study patients with nonalcoholic pancreatitis outnumbered those with alcoholic pancreatitis. The difference in patient population could partly be responsible for the different result.

Only a few studies reported the relationship between serum pancreatic enzyme levels and the severity of acute pancreatitis as assessed by imaging procedure ²⁶⁻²⁸. Hjelmqvist et al found serum amylase levels was not statistically different between patients with severe acute and those with mild, moderate pan-

creatitis as defined by CT²⁶. The presence and severity of pancreatic inflammation is often difficult to assess clinically. The Aksel et al studied acute pancreatitis patients with computed tomography and found in the group as a whole the serum amylase level was inversely related to the CT-grade severity of the acute pancreatitis due to the greater number of patients with" biliary hyperamylasemia " in the less severe CT grade²⁸; The patients with this condition had a significantly higher initial serum amylase level compared with alcoholic pancreatitis or pancreatitis from the other cause. The mean serum amylase level in each etiology group showed no correlation with the extent of pancreatitis involvement, visualized by CT. The previous study had established that there is a clear relationship between CT findings of the pancreas and the clinical course in patients with acute pancreatitis 28,29. Mild pancreatitis (CT findings: normal to local enlargement of the pancreas) and moderate pancreatitis (pancreas inflammation associated with peripancreatic inflammation) is a self-limited disease, with transient edema of the gland. The serum amylase is highest in these patients. With the more inflammatory reactions and the tissue destruction (CT findings: inflammatory extension into one or more peripancreatic spaces) the clinical course is more severe and conversely the amylase level is lower. The result of our study, most of patients in biliary pancreatitis with CT evidence mild pancreatitis had a higher amylase and lipase level than with CT evidence severe of pancreatitis. The patients in alcoholic pancreatitis with CT evidenced severe pancreatitis had serum amylase and lipase is lower than those with mild and moderate pancreatitis. The amylase and lipase level differences between biliary and alcoholic pancreatitis was reported by Spechler³⁰. A typical attack of acute pancreatitis in an alcoholic might present with a relatively lower amylase value 30,31 than a nonalcoholic patient who present with acute gallstone pancreatitis. They found that patients with acute pancreatitis frequently had normal serum amylase levels. Furthermore, in patients with alcoholic acute pancreatitis, indicating a parenchyma that no longer able to produce sufficient amounts of enzymes. It is clear to this stage that there is still no biochemical test that can be considered to be a gold standard for the diagnosis or assessment of severity of acute pancreatitis. However, our results may imply that the amylase and lipase remain important tests in the diagnosis but not able to establish either etiology or to predict the severity of acute pancreatitis as assessed by imaging techniques in this report. We concluded that the L/A ratio is not a good predictor factor and is useless in distinguishing acute episode of alcoholic from biliary and miscellaneous acute pancreatitis. Combinations of the clinical presentations of abdominal pain, serum amylase and/or lipase levels, in addition to ultrasonography and/or contrast enhanced computed tomography are still the standard in the diagnosis of acute pancreatitis.

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台灣地區急性胰臟炎病患之Lipase/Amylase之 比值之臨床意義分析

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摘 要

急性胰臟炎的臨床表現主要是以腹痛來表現,但是嚴重而有併發症者其死亡率相當 高。本研究利用脂肪酶,澱粉酶和脂肪酶/澱粉酶之比值來預測在台灣地區急性胰臟炎因 不同致病因而造成是否也會因致病原因之Amylase/Lipase 比值不同而有所不同臨床意義。從 2001年7月到2002年6月期間,我們總共收集247例急性胰臟炎包括酒精性,膽石性和其 他原因如糖尿病,外傷性,高血酯症,末期腎臟病,並針對此三組之致病原因和澱粉酶, 脂肪酶,脂肪酶/澱粉酶之比值及腹部電腦斷層嚴重程度分類來作比較。急性胰臟炎診斷 是根據臨床上有典型急性胰臟炎症狀,住院之澱粉酶/脂肪酶值和腹部電腦斷層或腹部超 音波之所見爲依據。本研究結果發現在247例急性胰臟炎中,在酒精性組之年齡較其他組 爲低:性別方面則酒精性組之男性比率較高;另外膽石性急性胰臟炎之血清澱粉酵素酶值 及血清脂肪酵素酶較其他兩組爲高且有顯著差異(P<0.005)除此之外,其他臨床表現,血清 脂肪酶 / 血清澱粉酶值比值並無有意義的差別,而且不能用來評估急性胰臟炎之嚴重度。 但是若脂肪酶/澱粉酶比值大於2時,則對酒精性胰臟炎有89.5%之陰性預測值。台灣地區 急性胰臟炎以酒精性胰臟炎年齡層較膽石性胰臟炎及其他原因胰臟炎者年輕。在性別上酒 精性胰臟炎以男性較多,而女性以膽石性胰臟炎居多。脂肪酶,澱粉酶值以膽石性胰臟炎 較高且有顯著差異,但在澱粉酶及脂肪酶比值中三組並無顯著差異,對於胰臟炎之嚴重度 也無預測之實際價值。