Author's response to reviews

Title: Comparison of clinical course and outcome of acute pancreatitis according to the two main etiologies: alcohol and gallstone

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Author's response to reviews: see over
Dear reviewers

Thank you very much for your kind comments.

We tried to revise the manuscript as much as possible according to the suggestions made by the reviewers, and enclosed revision detail and revised manuscript.

We hope all these revisions will be satisfactory and the manuscript has been improved.

Answers to Reviewer 1

Major Compulsory Revisions
To compare the clinical course, outcomes, and mortality between alcoholic and gallstone AP, it is important to determine the differences in the severity of AP on admission between these two conditions. The authors reported that, there were no significant differences in Ranson, BISAP, and APACHE-II scores within 48 hours after admission, whereas the prevalence of severe AP and the mortality were significantly higher in the alcohol group than in the biliary group. I am sure that these results indicated that there was no difference in the severity of AP on admission between alcoholic and gallstone AP, but the patients with alcoholic AP were more likely to become severe during the clinical course compared with gallstone AP. Authors should discuss more about this point.

We agree with your opinion and added this point in the “Discussion”.

Minor Essential Revisions
None.

Discretionary Revisions
In patients with gallstone pancreatitis, the severity, clinical course and prognosis could be associated with acute cholangitis and cholestasis. Recommend authors discuss this issue.
As your comments, the severity, clinical course and prognosis of biliary AP could be associated with concomitant acute cholangitis and cholestasis. In patients with acute cholangitis and ongoing biliary obstruction, urgent ERCP to remove bile duct stones may lessen the severity of biliary AP [26-29].

We described this with references in the “Discussion”

**Answers to Reviewer 2**

The authors aimed to investigate the difference between the clinical course of alcoholic and gallstone acute pancreatitis in 126 patients of the originally 153 retrospectively selected. The between the two groups were the incidence of pseudocysts that was higher in alcohol group that in the biliary group, CTSI higher in the alcohol group tan in the biliary group, the organ failure persisting beyond 48 hours higher in the alcohol group than in the biliary group and mortality also higher in the alcohol the in the biliary group.

**Major comments**

1. My main concern is the retrospective nature of the study that suffers of a bias of selection.

   As your comments, this is the main limitation of our study.
   To minimize selection bias, patients in this study were enrolled prospectively over the study period, and the data of these consecutive patients were analyzed retrospectively.
   We added this as a limitation of this study in the “Discussion”

2. The authors used the modified Atlanta criteria; however, in their series there are no walled-off necrosis and this should be explained.

   We closely reviewed CT findings again in all patients and found 1 patient in alcohol group developed walled-off necrosis after 4 weeks from the onset of acute necrotizing pancreatitis during the follow up period.
   We described this in the “Result” and “Table 2”.

3. In addition, according to the modified Atlanta criteria, the incidence of pseudocyst is lower than that of walled-off necrosis and the definition of pseudocyst is stricter than that of
original Atlanta classification system. Please comment.

Lower incidence of walled-off necrosis in this study may be explained in part by lower incidence of pancreatic and/or peripancreatic necrosis at the time of admission. The reason of lower occurrence of pancreatic necrosis in this study was unclear, but multiple factors such as BMI, genetic and environmental factors might be associated. We commented this in the “Discussion”.

4. The high number of pseudocysts in alcoholic pancreatitis may be related to a chronic pancreatitis: how many attack of pancreatitis there were in the alcoholic group; in other words, there was a difference in recurrence of pancreatitis in the two groups of patients studied. In the follow-up how of alcoholic patients developed chronic pancreatitis.

Patients with acute pancreatitis on pre-existing chronic pancreatitis and previous history of acute pancreatitis were excluded from this study. So, all patients with alcoholic pancreatitis was considered as acute pancreatitis at admission. However, the possibility of underlying chronic pancreatitis may be high as your comment because underlying pancreatic ductal stricture and dilation due to longstanding pancreatic damage by alcohol are presumably present in patients with alcoholic acute pancreatitis. We described this in the “Methods” and “Discussion” of the original manuscript. It was difficult to evaluate how many patients developed chronic pancreatitis during follow up because our study was retrospective design and did not perform long-term follow up in all patients.

5. Pseudocyst is a late complication of acute pancreatitis: the authors should report the time between the diagnosis of acute pancreatitis and the diagnosis of pseudocyst.

We diagnosed pancreatic pseudocyst according to the definition as an encapsulated fluid collection occurs more than 4 weeks after the onset of interstitial oedematous pancreatitis. We described the definition of pseudocyst and walled-off necrosis in the “Methods”.

6. The authors stated "We analyzed amylase, lipase, and lipase/amylase ratio when two patients with renal failure in the biliary group were excluded." The sentence has no sense and
should be reworded.

We reworded the sentence as follows.
“We compared serum pancreatic enzymes between two groups except two patients with renal failure in the biliary group.”

7. Why the authors evaluate the lipase/amylase ratio? There is evidence that this parameter is not useful to distinguish between alcoholic and non-alcoholic pancreatitis.

As your comments, later studies showed that a serum lipase-to-amylase ratio is not useful in differentiating alcoholic from non-alcoholic acute pancreatitis. 
So, we deleted the description about this.

8. References should be updated and more paper should be cited according to accuracy of lipase/amylase ratio.

We deleted references about lipase-to-amylase ratio.