

Dear Prof. Wang,

Thank you for your e-mail of 12-07-2018. Here are my responses to the reviewers' comments.

Reviewer 1 (02541859)

Comment 1: In the introduction, 9th sentence: instead of minimally invasive surgery, it should be ERCP.

Response: Yes, it has been revised in the paper.

Comment 2: Tokyo criteria of acute cholangitis should be mentioned either in introduction or discussion.

Response: Yes, these have been added into the discussion of the paper.

Comment 3: I do not see any mention of WBC count.

Response: Yes, these have been added into the Table 1 of the paper.

Comment 4: Was there any follow up of CA19-9 level after treatment of acute cholangitis.

Response: There were some patients who had significantly elevated serum CA19-9 level before operation, but it was obviously decreased after operation. Unfortunately, because most of the patients did not recheck serum CA19-9 level at the same time after operation, or a part of them lacked postoperative serum CA19-9 data. In view of incomplete data, the postoperative serum CA19-9 level was not listed in the article. We are well aware that this is an inadequacy of the study (A defect of the retrospective study). Therefore, in future, we will design a prospective randomized controlled trial to further demonstrate the reliability of the results and conclusions of this study by reexamination of postoperative serum CA19-9 level at the same time to supplement the complete data.

Reviewer 2 (03479389)

Comment 1: When is the timing of measurement of blood CA19-9 since the onset of acute cholangitis?

Response: The blood samples for serum tumor markers, liver function and blood

routine were collected between the two groups in the next morning after admission. The blood samples of all patients were collected within 24 hours of the onset of acute cholangitis, and even some patients were completed before the onset of acute cholangitis.

Comment 2: In this study, please describe the severity of acute cholangitis in the Tokyo Guidelines (TG18).

Response: Yes, these have been added into the paper.

Comment 3: Is there a relation between blood CA19-9 levels and severity of cholangitis?

Response: By reason of active in the treatment of our hospital for patients with acute cholangitis, almost all of the hospitalized patients have been intervened in the early of the onset of acute cholangitis. Therefore, in hospitalized patients, there are few patients represented the severe acute cholangitis. For most patients with severe acute cholangitis, the onset time have been more than 24 hours before admission. In order to avoid the effect on objective results of irregular treatment before hospitalization, so the above cases were excluded. According to diagnostic criteria and severity assessment of acute cholangitis: Tokyo Guidelines, the patients of observation group were mild (grade I) or moderate (grade II), without severe cholangitis (grade III). Therefore, the correlation between CA199 and the severity of acute cholangitis was not studied in this study. Therefore, there was no correlation analysis was completed between blood CA19-9 and the severity of acute cholangitis.

Comment 4: As a clinical factor for cholangitis, please conduct multivariate analysis including CA19-9 and other inflammatory markers such as CRP.

Response: Because the blood samples for serum tumor markers, liver function and blood routine were collected between the two groups in the next morning after admission. At this moment some patients did not show the acute cholangitis, so the serum CRP, PCT and other inflammatory markers were not tested routinely. Therefore, this study focused on investigating the relationship between abnormal serum CA19-9 level and acute biliary tract, and the data of the above inflammatory markers were not listed in the article. Of course, this is an inadequacy of the study (A defect of the

retrospective study). Therefore, in future, we will design a prospective randomized controlled trial to further demonstrate the reliability of the results and conclusions of this study by correlation analysis of multiple factors.

Reviewer 3 (01557045)

Comment 1: Accepted with minor modification State how many of the patients had hepatolithiasis. The cases analyzed had gallstones cholecystitis or gallbladder stones.

Response: According to the exclusion criteria, the patients of hepatolithiasis were excluded, and the patients of gallstones cholecystitis were also excluded. The proportion of patients accompanied with gallbladder stones were about 85%.

Comment 2: Did any patients in follow up had cholangiocarcinoma and/or other epithelial neoplasm?

Response: Up to date, there were no patients had cholangiocarcinoma and/or other epithelial neoplasm.

Reviewer 4 (02821831)

Comment: The study presents a clinical relevance; The authors reported that Abnormally elevated serum CA19-9 level has an important value in the diagnosis of acute cholangitis secondary to choledocholithiasis. This constitutes a inflammatory marker for acute cholangitis. The test seems rapid is worthy is worthy to be applied in clinical settings. The authors must discuss in Section Discussion (one or two sentences) the real benefit in complications stage. I suggest a minor revision.

Response: Yes, these have been added into the discussion of the paper.