

ANSWERING REVIEWERS



August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: Mucocele of the appendix: An unusual cause of lower abdominal pain in a patient with ulcerative. A case report and review of the literature

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1.

1. Why did the patients from group A undergo MRCP. Did some patients have acute or chronic biliary events at or around the time of MRCP examination? What is the time interval from biliary events to MRCP experience and whether these patients accepted according treatment? Since the cholangitis was also included in the biliary events, were patients with CBD stones also included?

The patients from group A underwent MRCP for detecting CBD stones to prepare a cholecystectomy usually. The patients with cholecystitis and cholangitis were underwent MRCP within 3 days from biliary event, But the interval between biliary event and MRCP is ambiguous in biliary colic patients. The 16 patients with cholangitis had CBD stones surely, 12patients with acute cholecystitis had CBD stones, and the remains did not have CBD stone. CBD stones might be influence the CBD diameter and angle between CBD and cystic duct, but we estimated that CBD stone did not affect our results. So we included the patients with CBD stone (28 patients)

2. Was the diameter of cystic duct measured the outer or inner diameter. If it were the inner diameter and the patients were not experiencing acute biliary events, the results were really too large although the authors had some explanation about it.

Yes, we definitely agree with your opinion. Cystic duct was too large than previous reports. So we tried to find out the reason. It may be occurred from the character of MRI, motion artifact, as previous mentioned at the paper. We estimated that new protocol of MRI would be needed to check the proper cystic duct diameter. But this study was retrospective study. thus we could not validate this factor.

3. A sentence in the first paragraph of the 'Discussion' section: "Other published risk factors for the progression to symptomatic gallstone disease include calculi > 2 cm in diameter, calculi < 3 mm in diameter, a patent cystic duct, a non-functioning gallbladder, and perioperative

detection of incidental stones". What does the '2 cm' mean?

Some articles alleged that the calculi size can cause cholecystitis. But there are some controversies. One article was mentioned that the gallstone disease occurred when the diameter of gallstone is larger than 2 cm, but another was reported that the small gallstone, smaller than 3 mm, is the risk factor of gallstone related disease. We described those points all in this article. And we are afraid to be a confusion to understand as you did. Thus, we adjust this part. Thank you for your kind review.

4. 4. Since the authors concluded smaller cystic duct diameters were associated with the occurrence of gallstone-related biliary events, why did not use the narrowest diameter instead of the widest diameter as an index?

Right, the narrowing cystic diameter measuring may be suitable than widest diameter in our thought too. But cystic duct exercise peristalsis continuously, we thought that the largest diameter could represent the mean diameter of cystic duct. In addition, sometimes, measuring the narrowest diameter was impossible in MRCP finding, because the cystic duct was usually tortuous and cutting off showing frequently. Thus we thought that the narrowest diameter is not suitable to use the risk factors.

5. 5. What is the advantage to predict the biliary events by using MRCP compared to ultrasonography? The ultrasonography is more acceptable than MRCP for the patients who do not have the experience of gallbladder stones.

To be honest, we were supposed to study this project with ultrasonography. But the ultrasonography has a limitation in measuring the cystic duct diameter and also the angle between cystic duct and gallbladder. In the aspect of measuring the angle and diameter, MRCP is more potent than the ultrasound. But we definitely agree with your opinion clinically. We estimate that another study using ultrasound to find out the risk factor of biliary event would be possible.

Reviewer 2

1. The results paragraph relative to cystic duct diameter is confusing as the hypothesis based on mean diameters of groups A and B was that small diameter would cause biliary events, while classification of patients below or above 7 mm suggests that biliary events are more frequent in patients with larger cystic duct diameter. Apparent discrepancies with other studies are well discussed in the discussion section.

We rewrote in the revised manuscript.

2. Figure 3 is not relevant.

We removed the figure from this article.

3. The angle between the gallbladder and the cystic duct was measured by the intersection of 2 virtual lines that are defined by the pathologist. Did the authors considered a potential operator dependent deviation?

Much to our regret, we could not measure the angle by histological examination.

Because this study is retrospective study, we could not get the information by histological examination. and there would be the bias when measuring the angle, but the angle was measured by one radiologist to reduce the bias.

4. 4. The authors and affiliations are not indicated in the manuscript.

We described it in detail and rewrote in the revised manuscript.

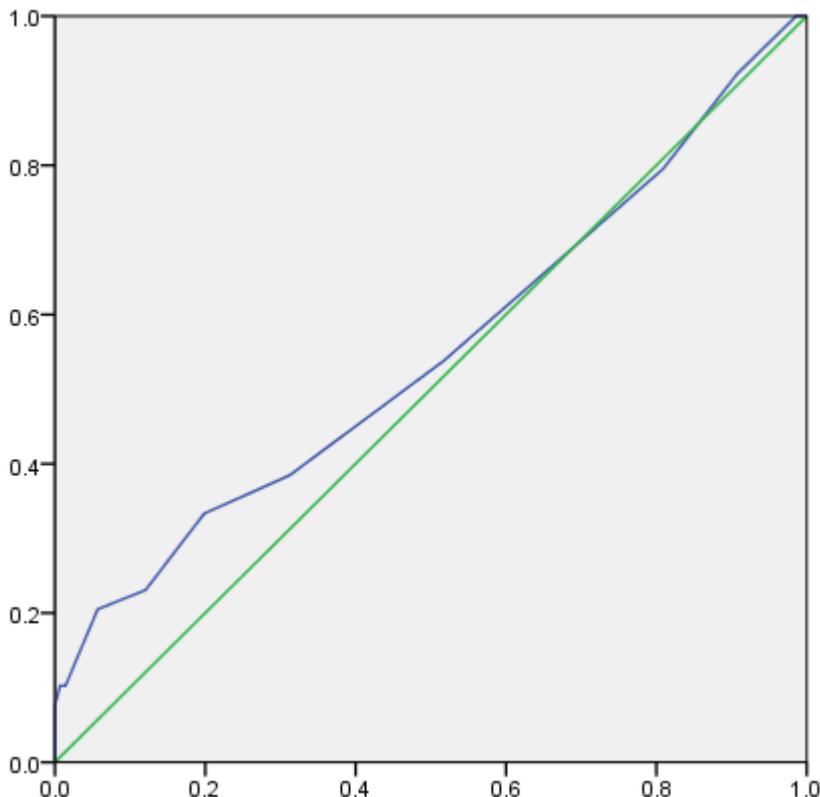
Reviewer 3

1. Have you data on the timing of MR imaging in relation to biliary event? It can be postulated that anatomical position changes if we are far from the biliary event.

Yes, we absolutely agree with your opinion. The patients with cholecystitis or cholangitis had underwent MRCP within 3 days from biliary event. but the patients with biliary colic, we could not measure the interval between MRCP and biliary colic. Because the occurrence date of biliary colic was ambiguous.

2. I don't understand very well the cut off at 7 mm (I think this is the result of ROC analysis) for cystic duct whereas the mean cystic duct diameter was 5.9 mm in group A and 6.9 in group B. Can you provide median and range in the two groups for this data and number of patients <7 mm and > 7 mm in the groups A and B? It is also possible to provide the figure of the ROC for this variable Minor:

Since we measured the cystic diameter in units of millimeter, it was hard to measure smaller units in MRCP, the median diameters of cystic duct in two groups were not different. (Group A: 6 mm range 2-12, Group B: 6mm, range 3-18) however, the mean cystic duct diameter showed a significant difference. Thus, we used the 6mm as the cut-off value, in addition, ROC analysis showed the high sensitivity and specificity in the section of 6-7. But there was a stupid mistake during the writing process, we confused < 6 , ≥ 6 and ≤ 7 , > 7 because we used units of millimeter. I am really sorry for confusing to you. Actually the cut off value was 6. In biliary event group, the number of patients < 6 mm was 59 patients and patients ≥ 6 was 72. On the other hands, the number of patients < 6 mm was 18 and patients ≥ 6 was 21 in non-biliary event group. ROC curve was as follows. We rewrote in the revised manuscript.



3. Page 2: 180 patients and not 190 Page 8: The hypothesis will be better placed in the Methods or Discussion and not in the Result section.

We described it in detail and rewrote in the revised manuscript.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,
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