

## Reply to reviewer

#Reviewer 70776

Thank you very much for reviewing our manuscript.

#Reviewer 3213658

Thank you very much for reviewing our manuscript and providing helpful criticisms. I would like to offer the following answers in response to your suggestions.

1. Following your suggestion, we have changed the word “aggressively” to “extensively” in the conclusion of the abstract.

2. You recommended that we address the coexistence of stone. Therefore, we described that in the discussion as follows (Discussion section 5 paragraph line 7 ):

On the other, there is some debate as to the coexistence of stones with gallbladder cancer. In our cases, the patients with XGC were associated with a higher incidence of gallstones than the patients with GB carcinoma ( $p=0.015$ ). However, due to the limited number of cases, we couldn't conclude whether the existence of a gallstone is helpful in the differential diagnosis between the XGC and the GB carcinoma.

3. You raised the question about the bias of the CT findings. The images were assessed by two radiologists to reduce bias. Therefore, we added the following sentences in the Method section (page 5, line 15).

Two radiologists evaluated these images independently and by consensus for the diagnosis.

4. You noted the lack of a general introduction of the two groups. Therefore, we described in more detail the diagnosis and treatment in the Method section as follows (Method section, line 7):

Preoperative evaluation was carried out with ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), and FDG-PET. In addition, some patients underwent endoscope retrograde cholangiopancreatography (ERCP) and/or percutaneous transhepatic biliary drainage (PTCD) for diagnosis and/or biliary decompression. Based on these image findings, surgical treatment was performed following the guidelines for the management of biliary tract and ampullary

carcinomas (J Hepatobiliary Pancreat Surg 2008;15(1):41–54).

5. You advised that radical resection is mistaken for XGC. We have changed the conclusion as follows:

Although XGC is often difficult to differentiate from GB carcinoma, it is possible to obtain an accurate diagnosis from intraoperative careful gross observation, and several frozen intraoperative frozen sections could prevent extended resections.

6. Following your suggestion, we deleted the following reference.

12 Reyes CV, Jablow VR, Reid R. Xanthogranulomatous cholecystitis: report of seven cases. The American Surgeon 1981;47(7):322–325.

# Reviewer 70545

Thank you very much for reviewing our manuscript. You have raised the possibility of reducing the extent of the operation based on the result of the frozen biopsy. We thought that detailed observation during the operation and intraoperative frozen sections could prevent the extension of the operation. Therefore, we have changed the conclusion based on your advice as follows:

Although XGC is often difficult to differentiate from GB carcinoma, it is possible to obtain an accurate diagnosis from intraoperative careful gross observation, and intraoperative several frozen sections could prevent extended resections.

# Reviewer 3261350

Thank you very much for reviewing our manuscript and providing helpful criticisms. I would like to offer the following answers in response to your suggestions.

1. You advised that we should provide both the pre- and post- operative diagnosis. We suspected GB carcinoma in all cases including XGC in this series. Therefore, we added the following sentence to make up for Table 1 in the results (Result section paragraph 1, line 1).

Based on the preoperative image findings, we suspected GB carcinoma in all cases

including XGC in this series. Additionally, we found by pathological examination that the group of patients with XGC contracted inflammatory disease after the operation.

2. You raised questions about the intraoperative frozen sections and the reliable factors to instruct the extensiveness of surgical resection. Unfortunately, we didn't perform intraoperative frozen sections except in case 2 to prevent major liver resection. In our experience, it was difficult to differentiate between XGC and GB carcinoma based on clinical manifestations and preoperative imaging. However, based on the careful gross observation and intraoperative frozen sections from case 2, it is possible to prevent an extended operation. Therefore, we have changed the conclusion as follows:

Although XGC is often difficult to differentiate from GB carcinoma, it is possible to obtain an accurate diagnosis from intraoperative careful gross observation, and intraoperative several frozen sections could prevent extended resections.

# Reviewer 919251

1. Thank you very much for reviewing our manuscript and providing helpful criticisms. Following your suggestion, we have changed the conclusion as follows:

Although XGC is often difficult to differentiate from GB carcinoma, it is possible to obtain an accurate diagnosis from intraoperative careful gross observation, and intraoperative several frozen sections could prevent extended resections.

2. We added the following sentence on Discussion section paragraph 6, line 14:  
Therefore, in addition to several frozen section examinations, careful gross observation during operation is needed even if the pre-operative diagnosis is XGC.

3. Following your suggestion, we deleted the following sentence on Discussion section paragraph 7, line 9:  
Therefore, radical liver resection still needs to be done when XGC exhibits similar imaging and intraoperative findings to advanced gallbladder cancer.

4. We added the following sentence on page 16, line 6:  
We need careful gross observation during operation and several frozen section examinations to treat the XGC which extensively to the surrounding organs.