

ANSWERING REVIEWERS



December 3, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6088-review.doc).

Title: Classifying extrahepatic bile duct metachronous carcinoma by de novo neoplasia site

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Name of Journal: *World Journal of Gastroenterology*

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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

(1) We corrected the conclusion as following in the part of conclusion as following (p2).

Metachronous EHBD cancer should be distinguished from an unresectable recurrent tumor carefully by various imaging methods through the regular follow up. Classifying metachronous EHBD cancer may be helpful in identifying rare metachronous tumors.

(2) We included the definition of multiple primary cancer by Warren and Gates and metachronous cancer by Moertel in the part of introduction as following (p4)

Warren and Gates [5] established a set of criteria for multiple primary malignant neoplasms: Each tumor must have definite features of malignancy; each tumor should be distinct and separate excluding the probability of one tumor being a metastasis of the other tumor. Moertel proposed a definition for synchronous cancers as those occurring within 6 months of the first primary cancer and for metachronous cancers as those occurring more than 6 months later .

(3) Regarding the matter of the incidence of metachronous bile duct cancer, it is not reported in the literature how rare it is. However, we listed almost all cases of metachronous bile duct cancer which underwent second surgery in Table 1.

(4) Regarding the oncologic therapy, we added the description in the part of discussion as following (p7).

Furthermore, it is difficult to clarify the role and optimal regimen of adjuvant treatment in the setting of locally recurrent bile duct cancer.

(5) Regarding the risk factors of metachronous EHBD cancer, we added the description as following because the risk factors of the metachronous EHBD cancer are not known

Similarly, when metachronous EHBD cancer is diagnosed after the first surgery, additional resections are required to achieve an R0 resection, although the incidence, risk factors, and clinical behavior of metachronous EHBD cancer are not well known.

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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