

ANSWERING REVIEWERS

January 23, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 8403-review.doc).

Title: Combined detection tumor markers for diagnosis and prognosis of gallbladder cancer

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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

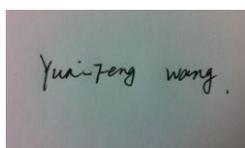
2 Revision has been made according to the suggestions of the reviewer

- (1) Late detection of gallbladder cancer is a problem of clinical relevance by all means. A tool enabling early detection or to confirm a suspected cancer would be an important step. Furthermore, patients would benefit regarding life expectancy from an early detection. General remark: The manuscript lacks page and line numbering. This aggravates mentioning the proper position of the reviewer's remarks. Therefore, the pages were numbered consecutively – beginning with the title page. Line numbers were counted beginning with the first written line including headline, blanks were not counted. Introduction: The introduction does not show any references, this is at least unusual. Statements like "... there is no ideal single tumor marker for GBC" should be covered by a literature citation (page 4, line 6).
- (2) Other statements like: "..., the 5-year survival is poor" are held very common and do not cover the quality requirements of WJG. There is literature with detailed figures available to support these statements (page 4, line 3). Hypothesis at the end of the introduction is worded clear and comprehensible. Materials and Methods Reference groups should be shown in more detail, socio demographic data is not provided as well. Furthermore, the statement "benign gallbladder disease" is very general. A more specific listing of the disease(s) should be provided (page 4, line 17). Presenting age and body weight with a range from... to... and following mean \pm SD is quite unusual (page 4, line 21 and 22). Either the values are normally distributed which would cover a presentation of the data with mean \pm SD or there is no normal distribution which would require median and range to present the data. Independent of this the application of BMI instead of body weight would be the more comprehensive value. It appears as if there is formatting problem in the downloadable Word document (page 4, line 24 and 25): finding 7 cases of phase II, 10 cases of phase IIIA, 33 cases of phase IIIB, 6 cases of phase IVA, and 22 cases of phase IVB. The numbers of the stadium is not displayed correctly. The same can be found at the storage temperature of the samples: and preserved at -80°C for use (page 5, line 12) and throughout the text certain punctuation marks appear wrong. This should be solved during final editing. The majority of gallbladder carcinomas are adenocarcinomas. From this point of view it should be considered to use only these 73 cases and exclude the further 5 cases. This would increase the comparability and validity (page 4, line 27 and 28).
- (3) Looking at the measured tumor marker values each of these 5 rarities triggers in at least one marker

extremely high values. Given the small sample size a statistical bias cannot be avoided. Classifying the gall bladder into bottom, neck, pipe section is very convenient but should be confirmed by literature citations where this classification is shown. Alternatively a chart presenting the data would be quite informative. Was the classification done clinically or by a pathologist based on tissue samples? Roche immunoluminescence is lab slang (page 5, line 20). The proper description would be: Electroimmunoluminescence immunoassay (ELIA), Cobas?, Roche Diagnostics, Germany Results: In the tables of the results section the order of the tumor markers is often switched. This is no mistake in general but makes it difficult for the reader to follow. Data regarding the value of the tumor marker level and the number of positive cases may be comprehended from table 2 and 3, whereby the first two line of table 3 are redundant to the text. Statements regarding the independency of the tumor marker level of sex and age (page 6, line 8) cannot be confirmed by the data provided in either table; at least the remark “data not shown” should be provided as explanation. Furthermore, the term “Combination Pc” is not explained. Which markers were combined? The statements regarding the dependency of the.....

3 References and typesetting were corrected

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

A rectangular box containing a handwritten signature in black ink on a light-colored background. The signature reads "YunFeng Wang" in a cursive script.

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