

March 18, 2016

Dear Editor,

Thank you for helping us revising our manuscript, and please find enclosed the entitled manuscript in Word format (file name: 24697-Revised manuscript.doc).

Title: Chinese expert consensus on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal malignancies

Author: Yan Li, Yun-Feng Zhou, Han Liang, Hua-Qing Wang, Ji-Hui Hao, Zheng-Gang Zhu, De-Seng Wan, Lun-Xiu Qin, Shu-Zhong Cui, Jia-Fu Ji, Hui-Mian Xu, Shao-Zhong Wei, Hong-Bin Xu, Tao Suo, Shu-Jun Yang, Cong-Hua Xie, Xiao-Jun Yang, Guo-Liang Yang

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 24697

The manuscript has been improved according to the reviewer suggestions:

1. The format has been updated.
2. References and typesetting have been corrected.
3. The following revisions have been made based on the reviewer`s suggestions:

Comment: I think that authors cite too many of their own publications and too many regional papers. In my opinion they should cite more current

worldwide known and fast mainly cited publications which constitute the literature con for each HIPEC scientist. I haven't found any paper published by Paul H. Sugarbaker, Beate Rau, or other important for this topic authors and scientists. Unfortunately, it's very important for the final value of this work! For example: the authors write in the abstract section "...intraperitoneal chemotherapy (HIPEC) has been developed by the pioneering oncologists, with proved efficacy and safety in selected patients....." I haven't found any information about this pioneering oncologists directly in the text.

Response: Thank you for your kind suggestion. In the past three decades, great progress has been reached by the efforts of the pioneering oncologists, and to emphasize this view, we have cited the milestone papers by Spratt JS, Elias D, Fujimoto S, Verwaal VJ, Spiliotis J, Lambert LA, *et al.*

The revised paper reads: "Accordingly, an integrated treatment strategy of cytoreductive surgery (CRS) +hyperthermic intraperitoneal chemotherapy (HIPEC) has been developed by the pioneering oncologists, with proved efficacy and safety in selected PC patients from PMP [4, 5], gastric cancer [6, 7], colorectal cancer [8], and ovarian cancer [9]. Gradually, CRS+HIPEC has been established and promoted in many cancer centers in Europe, America and Asia-Pacific regions [7, 10, 11] ".

Besides, we also cited papers of other famous oncologists in the revised manuscript, such as Moran B, Sugarbaker PH, Glehen O, Jacquet P, Yonemura, Hall JJ, Cascales-Campos, Deraco M, *et al.*

Comment: The title include such statement "...Expert consensus..." I do not find any specific or more detailed data for example in introduction explaining why authors consider themselves as experts in this field. Any of epidemiological, statistic and more detailed data should be listed.

Response: Thank you for your comment. All the authors listed here are active and experienced clinical oncologists in China with good academic record and reputation. For example, Prof. Yan Li, the only one Chinese

member of the Peritoneal Surface Oncology Group International, PSOGI), has engaged himself in PC treatment for more than 13 years, and already treated nearly 500 such patients. In 2014, he organized this Chinese Expert Consensus Meeting under the framework of China Anti-Cancer Association. We have modified the title of this manuscript, which reads: "Chinese expert consensus on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal malignancies".

Comment: If authors write an expert consensus, the potential reader should know: how many CRS+HIPEC procedures are performed in those expert centers, generally how important in discussion about HIPEC method their voice is "powerful", have they (or personally) do also something (or have a special influence on the development of this method?

Response: Up to now, we have already performed nearly 500 CRS+HIPEC procedures. Our work confirmed that this comprehensive strategy can improve survival of PC patients with acceptable safety. Over the past 13 years, we have also conducted a series of clinical studies and produced several influential results, including: 1. we established a diagnose system consisted of image examination and serum examination; 2. we conducted a series studies on CRS+HIPEC to treat PC of gastric cancer, colorectal cancer, ovarian cancer, including the first phase III randomized trial on CRS+HIPEC to treat PC of gastric which has been cited 217 times; 3. We introduced this comprehensive strategy in China, significantly enhanced the awareness of the peritoneal cancer among the oncology community in China.

Comment: The important information about demographic, epidemiological, and statistic data should be listed in such paper. The reader should know How many regionally (China, than in Asia and the worldwide) such procedures are performed yearly etc.

Response: It is very difficult to know exactly how many such procedures

have been performed in China, Asia or around the world because there is not an official institution to gather the data. Major data published are listed in Table 2, Table 3, and Table 4 of the manuscript. In the **LINICAL EPIDEMIOLOGY OF PC** section, we have provided the current statistics on PC epidemiological and demographic information.

Comment: Why authors do not listed any of chapter in which they explain open and close HIPEC method?

Response: Thank you for your comment. Both open and close HIPEC are used in clinical treatment, and each has its advantages and disadvantages, but we recommend the open HIPEC method. For close technique, the temperature may be more stable. But as we know, it is very important to achieve complete CRS. Therefore, proper abdominal exposure is necessary as we emphasized in the manuscript. In order to better eradicate the tumor cells, we also recommend to gently stir the abdominal cavity to make chemical agents penetrate as much tumor as possible, and to make heated chemotherapy solution circulate in the abdominal cavity. However, these objectives could not be adequately achieved by closed HIPEC method. Open technique is a better choice in this aspect.

Comment: In the section PREOPERATIVE EXAMINATIONS such sentence: "Medical image examinations" should be changed.

Response: Thanks for your suggestion. We have changed the sentence "Medical image examinations" into "Imaging examinations" in the manuscript.

Comment: It will be very interesting if authors in such large material which they consider as consensus write also an even though a short section about future of CRS+HIPEC. There are several in vivo and other novel projects and a large number of publications in which authors suggest many of

interesting development ways. If this work will be published as a large review and consensus in my opinion such final section should be also included.

Response: Thank you for your kind suggestion. In the conclusion section of the manuscript, we emphasized the recommendation of the clinical use and the prospect of CRS+HIPEC by the PSOGI, which may be the most professional group in PC field. We think these could be enough to show the future of this integrated treatment strategy.

The manuscript named “Chinese Expert Consensus.....” instead of others reviews usually used, because we think there are differences between a consensus and a review. In our opinion, the more comprehensive of the details, the better may be the review. But for a consensus, all contents are better to be associated with its clinical use. Therefore, we think it will be more appropriate to list any pre-clinical and in vitro data in a separate literature, not in this manuscript.

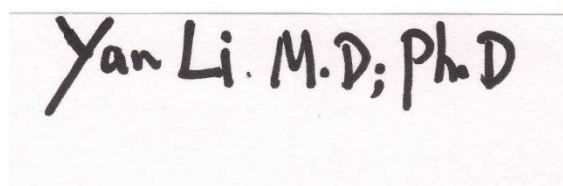
All the above revisions have been clearly marked using the tracking model in the revised manuscript.

We wish these point-to-point response could be adequate to the reviewers, and the revised manuscript could be up to your standard.

Thank you again for your kind, and special thanks reviewers for their comments.

With kind regards,

Yours Sincerely,

A handwritten signature in black ink on a light-colored background. The signature reads "Yan Li. M.D.; Ph.D" in a cursive, slightly slanted script.

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