Author's response to reviews

Title: Adjuvant Therapy in the Treatment of Gallbladder Cancer: A Meta-Analysis

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Dear editor:

We would like to submit the enclosed manuscript entitled "Adjuvant Therapy in the Treatment of Gallbladder Cancer: A Meta-Analysis", which we wish to be considered for publication in your magazine.

Gallbladder cancer (GBC) is an uncommon cancer but represents the most aggressive type among the biliary tree cancers (BTCs). Complete surgical resection offers the only chance for cure so far. In the United States, GBC accounts for approximately 9,760 new cases and 3,370 new deaths per year. Only 10% of patients of GBC present with early-stage disease are considered surgical candidates.

Regarding adjuvant therapy (AT) for GBC, only one phase III multicenter prospective randomized controlled trial (RCT) indicated that patients with gallbladder carcinoma who undergo R1 but not R0 resections may derive some benefit from systemic chemotherapy. However, other trials that had examined the values of AT, including chemotherapy (CT), radiotherapy (RT), and chemoradiotherapy (CRT), were limited by their small numbers of patients or their retrospective and non-randomized study design.

But the benefit of adjuvant therapy for gallbladder cancer (GBC) is unclear as evidenced by conflicting results from various nonrandomized studies while only one phase III multicenter prospective randomized controlled trial (RCT) up to now. There is still no meta-analysis of adjuvant treatments based on the study of retrospective and non-randomized studies except of RCT.

The aim of this study was to conduct a meta-analysis to identify whether AT, i.e. RT, CT, or CRT, could improve OS compared with surgery alone for the entire group or subgroups (node status, margins status, American Joint Committee on Cancer [AJCC] staging, and countries vary) of GBC on the basis of those retrospective and non-randomized data.

We used data from PubMed and Embase published between October 1967 and October 2014. Studies that evaluated AT compared with curative-intent surgery alone for resected GBC were included. Subgroup analyses of benefit based on node status, margins status, and American Joint Committee on Cancer (AJCC) staging were prespecified. Data were weighted and pooled using random-effect modeling. At last, ten retrospective studies involving 3,191 patients were analyzed. There was a nonsignificant improvement in OS with AT compared with surgery alone (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.56–1.03). A significant improvement was observed in OS with chemotherapy (CT) compared with surgery alone (HR, 0.42; 95% CI, 0.22–0.80) by sensitivity analysis. The greatest benefit for AT was also observed in those with R1 disease (HR, 0.33; 95% CI, 0.19–0.59), LN-positive disease (HR, 0.71; 95% CI, 0.63–0.81), and AJCC staging meeting or exceeding tumor Stage II (HR, 0.45; 95% CI, 0.26–0.79), but not in those with LN-negative or R0 disease.

Our results strongly support the use of CT as an AT in GBC. Moreover, patients with node positivity, margin positivity, or non–stage I disease are more likely to benefit from AT. We believe that the results of our meta-analysis will contribute to the use of CT as an AT in patients with GBC, especially those with the high risk factors described above.

We declare that we have no financial and personal relationships with other people or
organizations that can inappropriately influence our work; there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled.

What’s more, we have revised my manuscript to include line and page numbers according to the editor’s request and thanks very much.

With thanks for your consideration, I am Bin Wang. My E-mail: qcwangb@163.com.

Sincerely yours,

Bin Wang