Author’s response to reviews

Title: Necessity of prophylactic splenic hilum lymph node clearance for middle and upper third gastric cancer: a network meta-analysis

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Malcolm Hart Squires (Reviewer 1):

Comment 1: The authors present a meta-analysis to examine the association of prophylactic station #10 lymph node clearance at the time of gastrectomy for patients with upper and middle third gastric adenocarcinoma with the primary endpoints of perioperative complications and overall survival. This question and this analysis are relevant and of interest to the readership. The methods of this network meta-analysis are well-described and appropriate for extracting the data necessary to attempt to answer the primary aims.

Ten studies encompassing over 2500 patients were included in the meta-analysis. Gastrectomy alone (G-A) was associated with a significantly lower rate of perioperative complications and comparable 5-year OS versus gastrectomy plus splenectomy (G+S). Spleen-preserving splenic hilar lymph node dissection (G+SPSHD) at the time of gastrectomy was similarly associated with significantly perioperative complications and comparable 5-year OS versus gastrectomy plus splenectomy (G+S). On indirect comparison analyses, no significant difference in
perioperative complications or 5-year OS was demonstrated between gastrectomy-alone (G-A) compared to prophylactic SPSHD.

One significant limitation that the authors need to acknowledge and explain is the failure to account for potential differences in adverse clinicopathologic features among the 3 cohorts within this study (G-A, G+S, G+SPSHD) that certainly could confound the survival analysis and limit the conclusions that can be drawn from such a meta-analysis. The authors themselves note in the Discussion section on page 14 that splenic hilar lymph node involvement is correlated with larger tumor size, T stage, number of positive LNs, poor differentiation, and tumor localization. The overall conclusions of the manuscript need to appropriately parsed.

Answer: Thank you very much for your suggestions. There were potential differences in adverse clinicopathologic features among the 3 cohorts, mainly because retrospective studies cannot be completely randomized design. However, these studies made up for their biases by multivariate analysis. Furthermore, a summary of the risk of bias for each included study was shown in table 1, and all ten articles were scored≥7, which ensured the high quality of the included articles. Therefore, we think that the overall conclusions of the manuscript was reliable.

Comment 2: Routine splenectomy at the time of gastrectomy has previously been shown to be associated with increased morbidity without any significant improvement in recurrence rates or OS or DSS in a randomized, controlled fashion. Based on the results of the current meta-analysis, routine prophylactic SPSHD is not associated with any noted improvement in OS compared to gastrectomy alone.

Another limitation is that all of the studies included in the meta-analysis are from Asian populations (including 1 study from Turkey); given the inherent differences in disease biology between gastric cancer patients in the West vs East, particularly with regard to the utility of extended lymphadenectomies, whether these results are generalizable to Western populations of gastric cancer remains to be seen.

Answer: Thank you very much for your suggestions. It is the limitation of our present study that all of the studies included in the meta-analysis are from Asian populations. In the present study, studies with the following situations were excluded: (1) Studies with other kinds of gastric tumors, such as lymphoma, other organ tumors or multiple gastric tumors; (2) Studies with splenectomy induced by iatrogenic injury; (3) Studies with splenectomy also underwent distal pancreatectomy; (4) Studies with splenectomy or spleen-preserving splenic hilar dissection induced by enlarged nodes at splenic hilar were excluded; (5) Studies with distal gastric cancer (barely metastasize to splenic hilar lymph node). (6) Studies did not distinguish the G+S and G+SPSHD. Therefore, some studies with regard to prophylactic station 10 lymph node clearance have been excluded, including some studies in the West. Five studies were excluded because some patients received resection of distal pancreas[1-5]. Four studies were excluded because some distal gastric cancer patients were included [6-9]. Therefore, unfortunately, no study from Western populations was included in this meta-analysis.
Comment 3: The language of the manuscript needs to be cleaned up for ease of reading.

Answer: Thank you very much for your suggestions. We want to use the affiliates Nature Research Editing Service for professional help in revising this manuscript.

Jose Pimiento (Reviewer 2):

The authors evaluate the question of level 10 or splenic hilum dissection and the impact on outcomes for proximal gastric cancer.

Comment 1: the manuscript is easy to follow, and the methodology seems clear. The title however is not. Maybe defining as level 10 or splenic hilum, as the No10 can be confused with meaning 10 LN resected.

Answer: Thank you very much for your suggestions. We have carefully checked the manuscript and adjusted the title of the manuscript. The revisions have been highlighted in red color.

Comment 2: The discussion section is circular and I do not think the meta-analysis allows the authors for commenting much more than something is recommended or not. SO my recommendation is to cut more than half of the discussion and limit it to what the meta-analysis can support.

Answer: Thank you very much for your suggestions. We have considered your recommendation carefully and condensed the discussion. Some studies with regard to prophylactic station 10 lymph node clearance has been excluded by our meta-analysis. We want to discuss the data and key points of these articles in the discussion, so readers could gain more comprehensive information with regard to prophylactic station 10 lymph node clearance in our study.

Comment 3: The statistical technique used are beyond my statistical understanding so this paper should be evaluated by a statistician.

Answer: Thank you very much for your suggestions. Before we designed the study, we have consulted the statistician, and all of the statistical analysis were done under the guidance of the statistician.

Comment 4: The labels on figures and tables, are lost. So the figures are impossible to read.

Answer: Thank you very much for your suggestions, we have corrected this mistake.
References


