

February 6, 2014

Dear Editor,

Please find enclosed the following documents:

1. Edited manuscript (file name: Edited Manuscript_ESPS Manuscript 6610)
2. Edited references (file name: Edited References_ESPS Manuscript 6610)
3. Edited table (file name: Edited Table 1_ESPS Manuscript 6610)
4. Copyright Assignment (file name: Copyright Assignment_Merchant and Li_ESPS Manuscript 6610)
5. Copyright Assignment (file name: Copyright Assignment_Kim_ESPS Manuscript 6610)

Title: Racial and Ethnic Disparities in Gastric Cancer Outcomes: More Important than Surgical Technique?

Authors: Shaila J. Merchant, MD, Lily Li, BS, and Joseph Kim, MD

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6610

Thank you for reviewing our manuscript. We have read the comments of the reviewers and have responded to each item as seen below.

Reviewer #1:

1. *Please change ref. 11 with a more recent reference on cancer trends*

We have replaced Reference #11 with a more updated reference

(American Cancer Society. Cancer Facts and Figures 2014. Available from: URL: <http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-041770.pdf>

2. *Please define "proximal" and "distal" cancers*

We have added definitions of proximal and distal gastric cancers (Page 2: Line Numbers 37-38)

“When considering disease presentation and location (proximal – cardia, fundus; distal – body, antrum, pylorus), Asian patients are more likely to be younger at initial diagnosis and to have a higher proportion of distal gastric cancers^[14,15]”

3. *In the discussion on molecular mechanisms, please spend a few more words to explain the role of E-cadherin in metastatic spreading*

We have added some additional detail regarding E-cadherin and its role in metastatic disease (Page 6: Line Numbers 129-130)

“These findings are relevant because abnormal E-cadherin expression is associated with adverse features in gastric cancer such as loss of cell-cell adhesion (a more common feature of diffuse-type gastric cancer)^[41,42] and increased *c-erbB2* expression may correlate with depth of invasion and metastasis^[43]”

4. *The authors should mention that different genetic background in different ethnic populations may affect cancer outcomes. They could give a few key examples of genetic polymorphisms in gastric cancer-related genes that show differential rates in Western vs. Eastern ethnic groups.*

We have added additional information on ethnic variations in gene polymorphisms and their role in susceptibility to gastric cancer (Page 7: Line Numbers 135-141)

“Different genetic backgrounds in various ethnic populations may alter susceptibility to developing gastric cancer. More recently, there has been a plethora of information pertaining to genetic polymorphisms in gastric cancer. Various genes, including but not limited to, CD14^[45], glutathione S-transferase T1^[46] and XRCC3^[47] have been shown to alter gastric cancer susceptibility in ethnic groups, particularly Asians and Caucasians. These molecular studies suggest that differences in tumor biology among various ethnic groups exist and may contribute to racial disparities in gastric cancer outcomes.”

Reviewer #2:

1. *The authors should communicate more details about their investigations under item “our research observations”*

We have added some additional detail regarding our own studies under the section “Our Research Observations” (Page 9: Line Numbers 176-190)

“Even more intriguing is the observation that there was no improvement in 5-year survival for patients with increased lymph node retrieval. Our results support the presence of persistent racial and ethnic differences despite controlling for technical factors

We subsequently compared outcomes among the different Asian ethnic groups and discovered differences in gastric cancer survival among Asian ethnicities^[59]. Again using the Los Angeles County Cancer Surveillance Program database, we showed stark survival differences between Korean, Chinese, Japanese, Filipino and Vietnamese populations, with the greatest difference between Koreans and Filipinos, who had the best and worst overall survival, respectively. Korean patients were least likely to have nodal or distant disease and had a lower rate of proximal tumors; conversely, Filipino patients had amongst the highest rates of nodal and distant disease as well as proximal gastric cancers. These results suggest that there are differences in gastric cancer presentation and survival among Asian ethnicities and that combining diverse Asian ethnic populations as one single race may be grossly inappropriate.”

All authors have participated in the manuscript revision and have approved the final submitted version. This manuscript has not been copyrighted or published previously and is not under consideration elsewhere. Additionally, none of the authors has a conflict of interest to declare.

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

Sincerely yours,

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