Reviewer’s report

Title: The prognostic significance of vascular invasion in patients with resectable gastric cancer: a large retrospective study from southern China

Version: 2  Date: 19 January 2015

Reviewer: Zongming Eric Chen

Reviewer’s report:

In this retrospective study, the authors analyzed prognostic impact of lymphovascular invasion (LVI) (focusing on cancer specific survival (CSS) and disease free survival (DFS)) in 1148 patients from Southern China with gastric adenocarcinomas, who received surgical resection and clinical follow up. LVI was detected by simple microscopic evaluation of H&E sections of the tumors and scored as present or absent. Statistical analysis of the data showed that the presence of LVI in the tumor sections correlated with many known histological features of poor prognosis including large tumor size, poor differentiation, deep invasion, nodal involvement, and high TMN stage, etc. Interestingly, a multivariate analysis of the data also indicated that LVI was an independent adverse predictor of DFS and CSS.

1. An obvious strength of the study is its large number of patients with long clinical follow up data. There is a good opportunity to make new discoveries and draw important conclusions from this cohort. However, the presented data fail to show any exciting novelty. The only new finding is the authors’ claim of LVI as an independent adverse predictor of DFS and CSS. Yet, this result is less convincing, particularly in the context that the same analysis did not reveal nodal metastasis status as a statistically significant factor (Table 2). The authors should provide necessary explanation.

2. From a tumor biology perspective, LVI in the primary tumor is presumably the beginning of systemic dissemination of cancer cells via either lymphatic or vascular channels. Therefore, in patients with positive lymph nodes for metastasis, LVI is an inevitable event. The absence of identifiable LVI in these patients’ tumors is merely a reflection of not enough sampling. Therefore, to study LVI impact in these patients is of little clinical significance and may confuse data analysis by creating unexpected bias.

3. On the contrary, the impact of LVI in patients without nodal metastasis is of great clinical significance and interest. If the authors can draw a definitive conclusion form this respective study by focusing their analysis on comparing DFS and CSS in patient groups with or without nodal metastasis, it will provide new evidence for risk stratification of potential recurrence and prediction of survival. It will be useful addition to the current TMN staging system.

4. It is quite encouraging but also surprising to see the plotted survival curves (Figure 2 and 3) are much better compared to the published SEER data (with greater than 20% survival in 100 month follow up period even for Stage 3 and 4
patients with or without LVI). The authors may want to discuss the potential causes for the difference. In addition, it will make the data more meaningful and clear to interpret if the authors would show separate curves for each stage rather than to combine two stages in one curve. The two curves for tumors without vascular invasion in figure 2B and figure 3C have unexpected drop at the end presumably due to data entry error in the analysis. Please check and correct.

5. Since the authors did not attempt to separate lymphatic vs. vascular invasion, a term of lymphovascular invasion (LVI) should be used and replace the vascular invasion (VI) that is used in the current text to avoid confusion.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

nothing to declare.