Reviewer's report

Title: Overexpression of Cystatin SN positively affects survival of patients with surgically resectable esophageal squamous cell carcinoma

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Reviewer: Ismail Sert

Reviewer's report:

In this study, the authors analyzed the cystatin SN expression in surgically resected ESCC tissue by immunohistochemistry and determined its effect on survival.

They concluded that their study is the first study analyzing the cystatin SN expression on ESCC tissue. The study data is interesting in terms of this situation. But there are some points should be answered in the manuscript before making decision for publishing.

MAJOR COMPULSORY REVISIONS:

1. The subject posed by the authors is well defined.

2. The title and abstract accurately convey what has been found.

3. Manuscript adheres to the relevant standards for reporting and data deposition.

4. The methods are appropriate and well defined. But there is one point to be answered.

The authors analyze the cystatin SN expression in surgically resected ESCC tissue by immunohistochemistry techniques. There is no information about the confirmation of the results by using quantitative methods like RT-PCR. Because immunohistochemistry is a subjective method, the results should be confirmed by using RT-PCR in randomly chosen 5-10% of the cases. This is a limitation of the study and should be mentioned in limitations part.

5. In the section of methods, authors said that the data regarding the tumor (t stage, n stage, surgical margin status,....) were collected. But there is no information about the surgical margin status in tables and section of the results. Surgical margin statuses are very important for esophagus malignancies. Margin effect on recurrences cannot be underestimated.

6. In the discussion part, the authors said that “In the studies mentioned above, cystatin SN, which was proved to contribute to cell proliferation, has been reported as an oncogene in colorectal and gastric carcinoma.[6,21] Howere, in our study, we found that ESCC patients with positive expression of cystatin SN had significantly longer DFS and OS than those with negative cystatin SN expression. These findings indicate that the biology character of cystatin SN in
different cancers might be different."

Here, the authors explained the reverse effect of cystatin SN in esophageal carcinoma with biology character of cystatin SN in different cancers. This explanation is not satisfying. How could a marker as an oncogene in gastric and colorectal cancer be a positive predictor of survival in esophageal cancer? Are there any other samples like this among other CST superfamily members?

7. The writing is acceptable and fluent but there are some misspelling or writing errors like resectabel, indicatd, conclusion, howere, The manuscript should be checked once more in terms of typing mistakes.

8. In the part of patients' characteristics, it is written that 79 patients received systemic chemotherapy. Although, some studies claims that chemotherapy has a positive effect on survival and some doesn’t, their survival rates should be given.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests