

In this randomized controlled study, the efficacy and outcome of Extensive Intraoperative Peritoneal Lavage (EIPL) in advanced gastric cancer patients were analyzed. And it was found that EIPL application is associated with both reduced postoperative early complications like ileus and abdominal abscess and better outcomes in overall survival (OS) and recurrence-free survival (RFS). This study, in some circumstances, is similar to the article titled "Combined Surgery and Extensive Intraoperative Peritoneal Lavage vs Surgery Alone for Treatment of Locally Advanced Gastric Cancer. The SEIPLUS Randomized Clinical Trial" published in "JAMA Surgery" by Guo J et al. However, the presence of data such as OS and RFS in the median 30-month follow-up period in this study and univariate and multivariate analyzes of factors affecting overall survival makes this study valuable and acceptable for publication. But some revisions are needed to be made and some questions are needed to be answered by the authors.

1. The word "data" has been used twice in line 154. This sentence needs revision.

Response: Thank you for your suggestion. The error has been corrected. And the sentence is completed and corrected (Line 154).

2. What exactly is "upper-middle-low" expressed as tumor location? Can the upper localization be for gastroesophageal junction tumors? if so, shouldn't neoadjuvant chemotherapy (NAC) be considered in some of those patients?

Response: Thank you for your suggestion. Tumor location was classified into five subgroups according to the anatomy of the stomach: gastric cardia, fundus of stomach, body of stomach, gastric antrum, pylorus. Among them, upper means cardia and fundus of stomach. Middle means body of stomach. Low means gastric antrum and pylorus. To prevent the influence of esophageal cancer on the results of this study, gastroesophageal junction tumors were not included into our research. I have added this explanation into our manuscript (Lines 166-171).

3. Complications such as post-operative ileus, abscess, leakage, and bleeding are mentioned in the manuscript. In this study, the authors found that ileus and abscess were seen statistically significantly less in the EIPL group. However, it should not be ignored that there may be other factors that may affect these complications. For example, type of surgery (total-subtotal), pre-op nutritional status of patients, additional disease status, etc. It would be appropriate to discuss these facts in the discussion section. Also, Guo J. et al. found similar outcomes and complication rates in their multicenter study (The SEIPLUS Randomized Clinical Trial). This study should be discussed more in the discussion section.

Response: Thank you for your suggestion. In the manuscript, we have analyzed and discussed the impact of some factors on surgical complications, including

post-operative ileus, abscess, leakage, and bleeding. Regarding other factors you mentioned that may influence complications, we have also taken into consideration and analyzed these factors.

As for the factors of type of surgery, when the proximal resection margin ranged from 3 to 5 cm, there was no significant difference between distal gastrectomy and total gastrectomy for the 5-year OS of gastric cancer patients(20), so our study concluded that EIPL can reduce the possibility of perioperative complications including ileus and abdominal abscess, so the technique of EIPL may be beneficial for perioperative complications and make patients more comfortable after the operation, and this conclusion was consistent with previous study(21).

4. Has any patient in the study ever been considered unresectable because of invasion from T4 tumors to surrounding tissues? What methods were used for the diagnosis of recurrence? Is pathological diagnosis or radiological diagnosis accepted for recurrence? Were all patients' had adenocarcinomas?

Response: Thank you for your suggestion. We have a relatively strict and complete set of inclusion criteria. Patients with cT3 or cT4 and M0 were included in our study. 150 patients with gastric carcinoma in total were enrolled in the research. At the time of statistical analysis, all patients were found to be pT3 or pT4 and pM0. And no one was considered unresectable. Diagnosis of recurrence is made by abdominal ultrasound, CT, MRI, gastroscopy and pathology tests. We got their follow-up data through telephone and outpatient visits. After preoperative and postoperative pathological examination, all patients had gastric adenocarcinomas (Lines 179-183).

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In the 4th paragraph of the discussion part, it was stated that the pre-op NLR level was lower in the non-EIPL group compared to the other group. however, in Table 2, the results are similar between the groups, and there is no significant difference. Also in this paragraph, it was stated that the postoperative NLR levels were low in the EIPL group, but it is seen that there is no statistically significant difference between groups in Table 3. So, this paragraph or tables 2 and 3 need revision.

I have revised this.

6 It is recommended to add descriptions to the tables. Long versions of abbreviations such as EIPL, CEA, and NLR... are recommended to be added to the table descriptions.

Response: Thank you for your suggestion. Long versions of abbreviations have been added to the table descriptions. (Lines 202-203, 212-213, 225-226, and 229-230)

7 In the discussion section, on line 283, Kuramoto et al.'s publication is cited as the eighth reference. But in the references section, Kuramoto et al.'s publication appears to be the ninth reference. References should be revised.

Response: Thank you for your suggestion. The error has been corrected. (Line 302) And all the reference section is checked.

8 There are no mortality data in this study. It would be appropriate to include this data as well if possible.

Response: Thank you for your suggestion. The 3-year survival rate of the EIPL group was 38.4%, and the 3-year survival rate of the non-EIPL group was 21.7%. and for the all patients, the 1- and 3-year OS rates were 71.0% and 26.5%, respectively.

Review2

1. There are too many words in the author's abstract, and the key points of the article are not well summarized.

Response: Thank you for your suggestion. The abstract section has been simplified. And the key parts of the article have been reorganized and summarized. (Lines 25-64)

2. What is the meaning of β in Supplementary Tables S5 and S6?

Response: Thank you for your suggestion. In Cox proportional hazards model, the meaning of β is partial regression coefficient which denotes the degree of influence of each independent variable on the random variable.

3. The predicted results and the accuracy of the model should be validated by random cohorts or external cohorts.

Response: Our study include three centers, the external population includes 50 gastric cancer patients, we will verify our results with more patients from more centers in the future

4. The statistical analysis section should explain in more detail the processing and analysis of the data.

Response: Thank you for your suggestion. In the statistics section, we have provided a detailed description of the methods used to process and analyze the data. (Lines 173-193)

5. In the Discussion, comparisons should be made with findings from recent years.

Response: Thank you for your suggestion. In the discussion section, we have introduced three RCTs ongoing currently and compared to our study to explore the long-term efficacy of EIPL in advanced gastric cancer. (Lines 303-326)

6. The format and language of the article should be further revised.

Response: Thank you for your suggestion. The format and language of the article have been revised.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade C (A great deal of language polishing)

Scientific Quality: Grade C (Good)

(2) Company editor-in-chief:

1. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Response: Thank you for your suggestion. The title was shorted to meet the requirement for title.

2. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

3. Please provide the original figure documents.

4. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

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