

Response to reviewer 1:

Question 1: Abstract: a. Aim: The authors must provide an explicit statement of questions being addressed regarding participants, interventions, comparisons, outcomes, and study design (PICOS). Results: please, the I2 must be included in this section.

Answer 1: We have modified the aim part and provided the I2 with corresponding P values in the results. (page 2, line 14-19)

Question 2: Introduction a. In this section, also, the authors must provide an explicit statement of questions being addressed with reference to PICOS. b. The authors must describe the differences between their aim and the findings of other meta-analyses published. This would add value to their study.

Answer 2a: We have provided the statement (page 3, line 26-28). **2b:** We have described the differences between our aim and their findings. Actually, the main difference is the tumor type. (page 3, line 21-25)

Question 3: Results: a. Some findings have high heterogeneity, such as overall survival (I2=85.7) and TNM stage III/IV EEGJA patients(I2=73.1). these must be assessed by meta-regression.

Answer 3: The meta-regression analysis were further conducted. Unfortunately, we did not find the source of significant heterogeneity. And the results of meta-regression analysis for OS have been provided in the “results” part (page 7, line 17-21).

Question 4: Methods: a. The authors must indicate if a review protocol exists. Also, they must state that the PRISMA guideline was performed. b. The inclusion criteria must be described before Literature retrieval. c. The type of studies included must be described. d. The authors must be stated the process for selecting studies in a separated section. e. The authors must clarify the method of data extraction from reports. They must describe who performed data extraction as described in the Quality assessment. f. A brief description of the Newcastle-Ottawa scale is needed. g. The authors must describe which outcomes were measured. Some variables were not described, such as overall survival, disease-free survival, disease-specific survival. Also, these must be described.

Answer 4a: Actually, no review protocol exists. We have indicated that this systematic review and meta-analysis were conducted according to the PRISMA guideline. (page 4, line 4-5) **4b:** The inclusion criteria have been adjusted to the correct position (page 4, line 7-14). **4c:** The type of included studies has been described in the methods part and also the results part (page 4, line 9-10). **4d:** This section has been added (page 4, line 26-27). **4e:** We have described the method of data extraction and also the name of investigators (page 5, line 1-3). **4f:** The brief description of NOS was provided in the “quality assessment” part (page 5, line 14-16). **4g:** This has been added in the “data extraction” part (page 5, line 8-11).

Question 5: Discussion: a. The authors must describe the differences between their meta-analysis and another meta-analysis published. This would add value to their study.

Answer 5: Actually, this is the first meta-analysis to explore the clinical role of SRC in EEGJA patients. Other similar meta-analyses were about gastric and colorectal carcinomas and we have described the differences in the introduction part (page 3, line 21-25).

Response to reviewer 2:

Question 1: “Esophageal carcinoma is one of the most common malignancies worldwide with an increasing incidence in recent decades [1-3]” precise data required and update data on epidemiology

Answer 1: The precise data and update data on epidemiology have been added (page 2, line 27-29).

Question 2: “Despite of the great progress we have made in the surgical and adjuvant therapies” language is below par

Answer 2: This sentence has been changed to “Although we have made great progress in the surgical and adjuvant therapies of esophageal cancer in recent years” (page 3, line 1-2)

Question 3: “Nie et al. included 19 studies involving 35,947 cases and demonstrated that gastric carcinoma patients with SRC tended to be younger [weighted mean difference (WMD)=-3.88, P=0.001] and predominantly female [odds ratio (OR)=1.60, P < 0.001]”. Irrelevant data for prognosis?

Answer 3: Actually, the topic of this meta-analysis is about the association of SRC with the clinicopathological parameters and prognosis of EEGJA patients. Thus, this sentence is mainly to describe the relationship of SRC with some clinicopathological parameters and the following sentence is to describe the association between the SRC and prognosis in gastric carcinoma.

Question 4: “Besides, early-stage gastric cancer patients with SRC had a better overall survival (OS) [hazard ratio (HR)=0.57, P=0.002], but advanced stage patients with SRC had a worse prognosis (HR=1.17, P < 0.001)”. Seriously ? Early stage has better prognosis than advanced stage? That’s the finding? Provide a better clinical point?

Answer 4: Yes, the actual results are as described and we also provided some detailed information (page 3, line 12-16). The original findings of this meta-analysis are as follows “There was no difference in overall survival (OS) between SRC and non-SRC patients in the total population (HR: 1.02, P=0.830). Early gastric cancer with SRCs was associated with better OS (HR: 0.57, P=0.002), while advanced gastric cancer with non-SRCs was associated with a worse prognosis (HR: 1.17, P<0.001).”(DOI: 10.7150/jca.21017).

Question 5: “Besides, Tan et al. manifested that the presence of SRC was an independent prognostic risk factor in colorectal cancer patients, despite of the proportion ($< 50\%$: 2.182, $P=0.005$; $> 50\%$: 1.699, $P=0.016$)”. Who manifested ? Use a professional language editing service. Language below par

Answer 5: We have modified this sentence to make it clearer and appropriate (page 3, line 16-17).

Question 6: “However, in esophageal and esophagogastric junction adenocarcinoma (EEGJA), the clinical significance of SRC remains unclear because of the inconsistent reports” Cite the articles with conflicting reports

Answer 6: The relevant articles have been cited (page 3, line 25).

Question 7: “The PubMed, Web of Science and EMBASE electronic databases”. SCOPUS ? Why was it left out?

Answer 7: Actually, for this type of meta-analysis, the SCOPUS database is not commonly searched. The PubMed, EMBASE and Web of Science are more common. Besides, in the similar meta-analysis we discussed in the introduction, only the PubMed and Web of Science databases were searched.

Question 8: “ when the HR with 95% CI for prognosis was not directly reported in articles the Kaplan-Meier survival curves were provided for calculation” .Language below par

Answer 8: This sentence has been modified (page 4, line 12-14).

Question 9: “exclusion criteria were” Language barrier was overcome or was it a filter ?

Answer 9: We have added the language restriction in the inclusion criteria (page 4, line 14)

Question 10: “duplicated or severely overlapped data”. Meaning?

Answer 10: If the included patients were duplicated or severely overlapped with another study, then this study should be excluded. We also modified this sentence to make it clearer (page 4, line 22-23).

Question 11: “Then, 17 full texts were assessed for eligibility after eliminating 21 publications”. How many people performed the review? If more than one, then was kappa coefficient carried out?

Answer 11: As mentioned in the methods part, two independent authors performed the review. However, the kappa coefficient was not carried out.

Question 12: “The pooled results indicated that SRC was more likely to occur in esophageal adenocarcinoma rather than esophagogastric junction adenocarcinoma ($RR=0.76$, 95% CI: 0.61-0.96, $P=0.022$; $I^2=49.4\%$, $Pheterogeneity=0.160$) (figure 2)”. Compared to?

Answer 12: We have changed this sentence to “The pooled results indicated that SRC was more likely to occur in esophageal adenocarcinoma rather than esophagogastric junction adenocarcinoma” (page 6, line 22).

Question 13: “Interestingly, Chirieac et al. manifested that SRC predicted”. Again the term manifested being use in an inappropriate fashion

Answer 13: We have changed the “manifested” to “demonstrated” (page 8, line 1).

Response to editor:

Abbreviations: All abbreviations have been carefully checked and modified.

Original pictures: all original pictures have been provided.

Article highlights: this section has been added at the end of the main text.

References: The PMID and DOI numbers have been added and all authors have been listed.

Response to revision-review

Question: This statement needs a reference “This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines”.

Answer: The reference has been cited for this statement. (page 5, last line)