

Respond to reviewers' comments

Reviewer #1:

N0. 1: This is an interesting article. The topic is novel. The inclusion of cuproptosis in this study is important, but more studies are needed to prove the role of these genes in esophageal cancer and also other cancers. It is also difficult how to link these genes to the most common types of esophageal cancers either squamous or adenocarcinomatous.

Answer: We fully agree with the reviewer's comments. Currently, there is fewer studies on cuproptosis in some malignancies, particularly esophageal cancer. Future research may investigate the connection between pan-cancer and genes linked to cuproptosis. We'll give it careful consideration because this is a worthwhile avenue of study as well. We discussed the limitations on our study in the discussion part. Further examination of squamous cell carcinomas and adenocarcinomas individually was challenging because our total sample size was only 151 individuals, including 74 adenocarcinomas and 77 squamous cell carcinomas. We will further investigate this finding using studies on samples of esophageal adenocarcinoma or esophageal squamous cell carcinoma as this study is merely a preliminary investigation. It is regrettable that more mechanism study hasn't been done. Future research will focus on the mechanism behind the connection between cuproptosis-related genes and esophageal cancer.

N0. 2: language editing is needed.

Answer: Thank the reviewer for correcting the manuscript's language mistakes. Based on the reviewer's remarks, we carefully revised the article. Using the QuillBot (<https://quillbot.com/>), we also performed sophisticated polishing. After that, Professor Yu Hua reviewed, checked, and validated that there were no grammatical issues.

Reviewer #2:

N0. 1: The authors analyzed the relationship between cuproptosis-related genes and esophageal cancer prognosis. The results are of interest to the reader. However, I have a question about the statistical method in Table 2. Why not use Cox proportional hazards models to compare clinicopathological characteristics and survival outcomes? And there are some minor points. P8, L9-10: "receiver operating characteristic" has already appeared on P7 L14 and is abbreviated as ROC. Table1: Table 1 mentions DFS. If this isn't a mistake, how did you define DFS, especially for stage IV cancer? P9, L23: "regression" is duplicated. P12, L5-16: The first paragraph of the Discussion session can be moved to the Introduction session.

Answer: I appreciate the reviewer's comments. In the Table 2, the chi-square test was used to investigate the preliminary connection between clinicopathological characteristics and prognosis. However, in Table 4, the association between clinicopathological characteristics and prognosis was assessed using univariate COX

regression analysis and multivariate COX regression analysis. According to the author's comments, several of the manuscript's abbreviations are incorrect and have been changed. "DFS" should be changed to "PFS". P9, L23: "regression" has been deleted. "P12, L5-16: The first paragraph of the Discussion session" repeats the description in the introduction, and we delete it according to the reviewer's suggestion.