

June 11th, 2022

Dear Prof. Lian-Sheng Ma,

Thank you very much for your timely handling of our manuscript entitled “***CT-Based multiscale and multiphase Imaging Signature for the Quantitative Assessment of Patients With Carcinoma of the Esophagogastric Junction: Initial Differentiation between Squamous Cell Carcinoma and Adenocarcinoma***” (Original Article, ID: 76424). We appreciate all the comments from the reviewers and revised the manuscript.

Thank you again and we look forward to hearing from you.

With best regards,

Sincerely,

Jianbo Gao MD, PhD

Responses to Reviewers' Comments

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Comments The following points should be stated and answered clearly in the manuscript: Can these CT criteria replace upper endoscopy and biopsy for histopathological diagnosis? Can we recommend chemotherapy or advice certain type of operation depending only on these CT parameters with no or inconclusive histopathological diagnosis? If upper endoscopic biopsies were inconclusive can we depend on these CT parameters, or should we repeat the biopsy or recommend endoscopic ultrasound deeper biopsies? If these CT parameters can not replace tissue diagnosis, then what is the real benefit of this study? All these points should be stated and answered clearly in the discussion section and conclusions.

Response: We thank the reviewer for taking the time to assess our work and provide these valuable suggestions. Histopathology biopsy was a commonly used clinical method, and these radiomics features were considered to be complementary to histology biopsy but not a complete substitute for histopathology at this time. Repeat biopsy or endoscopic ultrasound deeper biopsies should be recommended if upper endoscopic biopsies were inconclusive or if it conflicts with the results suggested by radiomics features. Radiomics can provide an adequate reference if the patient has contraindications and low tolerance to endoscopic biopsy. We have added to the above points in our discussion and conclusions.

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Du et al. analyzed CT-based multiscale and multiphase imaging for determination of squamous cell carcinoma of the esophagogastric junction

from adenocarcinoma of the esophagogastric junction. Overall, the manuscript is significant contribution and I recommend that it be accepted for publication.

Response: Thank you very much for your patient review.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors describe a CT-based model for diagnosing the subtype of gastroesophageal junction neoplasms. This is an expanding area of research in gastrointestinal tumors, that is of significant scientific interest. Description of the methods used and of the results is very accurate and well-illustrated. The discussion and conclusion sections are supported by the results. The authors have published a similar article in 2019 (DOI: 10.1097/RCT.0000000000000826), but have greatly increased the study population and expanded on the radiomics model ever since. On page 4 line 3 there is a typing error ("contraindications or low tolerance").

Response: Thank you very much for your patient review. Thanks a lot for this kind suggestion and we are sorry for making this mistake. We corrected the error in the INTRODUCTION.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Interesting and well written paper.

Response: Thank you very much for your patient review.

Science editor:

1 Conflict of interest statement: Academic Editor has no conflict of interest. 2 Manuscript's theme: The topic is within the scope of the journal. 3 Academic misconduct: No academic misconduct was found. 4 Scientific quality: The authors submitted an

applied radiomics techniques to predict the pathological type of carcinoma of the esophagogastric junction (CEGJ), and established radiomics models for discriminating squamous cell carcinoma and adenocarcinoma of the CEGJ before operation based on CT images by a retrospective study. They concluded that radiomics method could help open up a new field for noninvasive diagnosis and personalized management of CEGJ. The manuscript is qualified. (1) Advantages and disadvantages: The reviewers have given positive peer-review reports. One of them raised some issues which need to be responded positively. (2) Main manuscript content: The authors state the purpose of the study clearly, and it is an expanding area of research in gastrointestinal tumors, that is of significant scientific interest. Description of the methods used and of the results is very accurate and well-illustrated. However, Several points need to be revised according to the detailed comments listed below. (3) Table(s) and figure(s): There are 2 tables and 6 figures, well illustrated. (4) References: A total of 25 references are cited, including 16 published in the last 5 years. There are 3 self-cited references of the authors. The cited references are overall sufficient and reasonable. 5 Language evaluation: The language quality is good. 6 Medical ethics: The authors had properly reported a certification of institutional ethics approval. 7 Specific comments: Can CT criteria replace upper endoscopy and biopsy with histopathological diagnosis? Can we recommend chemotherapy or advice certain type of operation depending only on these CT parameters with no or inconclusive histopathological diagnosis? If upper endoscopic biopsies were inconclusive can we depend on these CT parameters, or should we repeat the biopsy or recommend endoscopic ultrasound deeper biopsies? If CT parameters can not replace tissue diagnosis, then what is the real benefit of this study. All these points should be stated and answered clearly in the discussion section and conclusions.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Response: Thank you very much for your patient review. We have answered the reviewers' comments in detail.

Finally, we would like to thank the Editor and reviewers again for the constructive and detail-oriented comments, as well as your patience with our study!