Peer Review File

Reviewer A

In the present study, the authors investigated the prognostic significance of tumor stroma ratio (TSR) in clear cell renal cell carcinoma patients. The greatest concern is that the merit of using TSR in addition to the classical prognostic factors is unclear. Furthermore, the authors should describe the method of TSR measurement in more detail, which is one of the most important points in this manuscript. My specific comments are as follows.

1.Please describe how TSR was calculated in more detail. How was the percentage of tumor cells determined? What was concretely measured for that?

Reply: Thanks for your question. We evaluated TSR serially in a minimum of 10%, such as 10% for TSR between 0% and 10%, 20% for TSR between 10% and 20%, and so on until 100%. Five 100× visual fields were selected for evaluation, and the highest value was taken as the final TSR score of the patient.

Changes in the text: We have added it to the text (see Page 4, line76-81).

2. Please also show some photomicrographs with a concrete TSR value.

Reply: Thank you very much. In order to simplify the operation and standardize the scoring criteria, we selected 10 images as a reference for different tumor stroma proportion scores.

Changes in the text: We have added these to the text (see Page 4, line82).

Supplement Figure1：
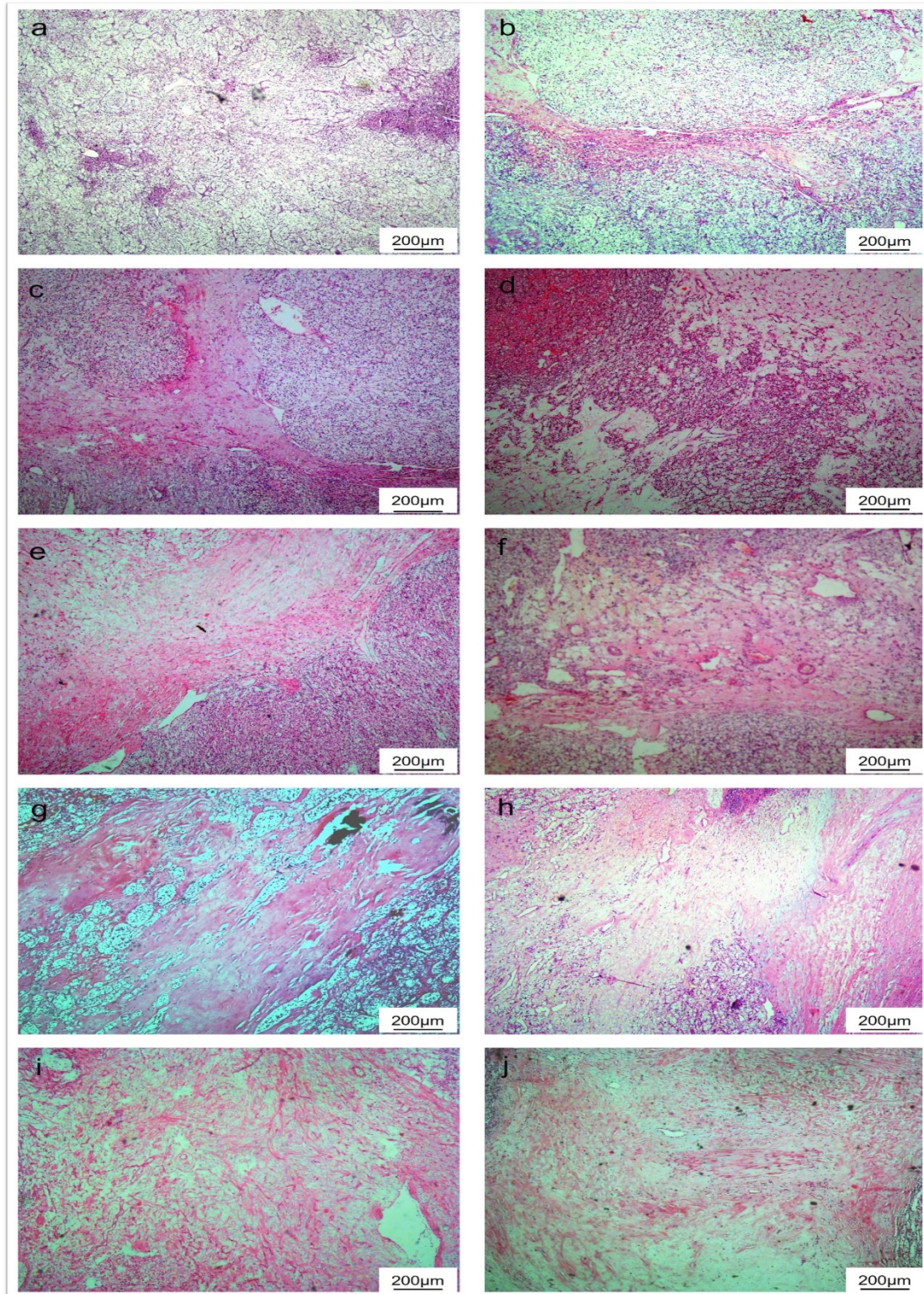
Different TSR scores. a: TSR score of 10%; b: TSR score of 20%; c: TSR score of 30%; d: TSR score was 40%; e: TSR score was 50%; f: TSR score was 60%; g: TSR score was 70%; h: TSR score was 80%; i: TSR score of 90%; j: The TSR score was 100%.

3. The authors should show the merit of introducing TSR as a new prognostic factor. I

feel the prognosis of RCC patients can be easily predicted using the currently known factors. Is TSR really necessary?

Reply: Thank you very much. The evaluation of TSR has the advantages of simplicity, no additional cost, and high reproducibility. If further research shows that TSR is indeed a new independent prognostic factor for various solid tumors, TSR can be used as a routine measurement indicator included in tumor pathological examination, so as to better evaluate the risk of patients and develop more practical and effective individualized treatment plans.

Changes in the text: We have added it to the text (see Page 8, line154-159).

4. Unclear how the authors are going to use the present result in clinical settings. Please create nomograms, which include TSR.

Reply: Thank you very much. In order to use the present result in clinical settings as advised, we create nomogram plot to demonstrate the value of TSR.

Changes in the text: We have added it to the text (see Page 6, line124-125)

Supplement Figure 2：Nomogram for predicting OS of ccRCC patients.
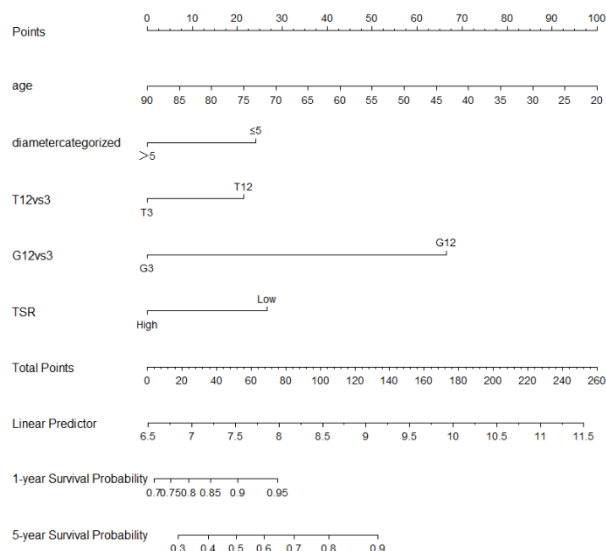
5. In multivariate analysis, please use all the parameters used in the univariate analysis. In the tables, there are many vacant cells, which should be filled by performing the analysis as recommended.

Reply: Thanks for your advice. We added some data in "Table"

Changes in the text: see Table 2,3,4.

L. 104, "urinary ultrasound": What is this?

Reply: Thank you. "Urinary system ultrasonography", We have corrected the

description.

Changes in the text: see Page3, line60.

Reviewer B

Here are my observations for improvement and assessment of its novelty:

Novelty and Interest:
* The study presents novel insights into the prognostic value of tumor-stroma ratio in ccRCC, a topic that has not been extensively explored in existing literature.
* It adds valuable information to the field of oncology and could be of interest to researchers and clinicians focused on renal cell carcinoma.
* The methodology, utilizing a retrospective analysis of clinical and histopathological data, provides a new perspective in the study of ccRCC prognosis.
* However, the novelty would be more pronounced if the paper positioned its findings within the broader context of existing research, showing how it fills a specific gap in knowledge.

Reply: Thank you very much. We appreciate for your comments, and hope that this manuscript will meet with approval.

Areas for Improvement:
* Clarity and Structure: The paper could benefit from a clearer structure, especially in the Methods and Results sections. It's important to ensure that the study's design, methodology, and statistical analyses are clearly articulated.

Reply: Thank you very much. We have further improved the clarity and structure of content

Changes in the text: see Page 4, line76-81.

* Detailed Literature Review: The Introduction could be expanded to provide a more comprehensive review of existing literature, particularly focusing on studies related to tumor-stroma ratio in clear cell renal cell carcinoma (ccRCC).

Reply: Thank you. We review the existing literature of ccRCC. The TSR has been reported in a variety of solid tumors, such as colorectal carcinoma, breast cancer, gastric cancer, lung cancer etc. but there been not reported the role of TSR in ccRCC patients so far.

Changes in the text: see Page 8, line150-153.

* Discussion of Results: The Discussion section should more thoroughly explore the implications of the findings, comparing them with existing studies and highlighting

their unique contributions to the field. In light of your study's focus on the prognostic value of tumor-stroma ratio in clear cell renal cell carcinoma (ccRCC), it might be beneficial to reference recent advancements in the treatment of complex renal masses, as discussed in an article with PMID: 38024426. This systematic review evaluates the outcomes of robot-assisted partial nephrectomy (RAPN) in various complex scenarios of renal cell carcinoma.

Reply: Thanks for your advice. We have read the paper (Pandolfo SD, Cerrato C, Wu Z, et al. A systematic review of robot-assisted partial nephrectomy outcomes for advanced indications: Large tumors (cT2-T3), solitary kidney, completely endophytic, hilar, recurrent, and multiple renal tumors. Asian J Urol. 2023;10(4):390-406.) in detail and refined the Discussion section as your advised.

Changes in the text: see Page 10, line196-202.

* Limitations and Further Research: While the paper mentions some limitations, a more detailed discussion on this, including potential biases and suggestions for further research, would strengthen the study.

Reply: Thanks for your advice. We will continue to advance this study and continue to enroll a larger sample of patients to minimize limitations.

Changes in the text: see Page 10, line207-208.

Overall, the paper holds significant interest for the medical research community, particularly in the field of oncology. With improvements in clarity, structure, and a more detailed discussion of its findings in the context of existing literature, it could make a valuable contribution to the understanding of ccRCC.

Reply: Thank you very much. Thank you for your recognition, we will continue to work hard to obtain greater results to report to you in future.