# Peer Review File

**Reviewer A**

In this paper the Authors reported a Survival nomogram and risk classification system for patients with adrenocortical carcinoma. A comprehensive and extensive literature review of the NCBI database PubMed was also carried out.

The article was well conducted and it is interesting in its fields. It is a well-structured paper, written in good English and the References are up dated.

Minor issues:

In the "discussion" section I suggest to better analyze the role of laparoscopic tranperitoneal andrenalectomy and of retroperoneoscopy. Therefore the following papers should be considered:

Conzo G, Pasquali D, Colantuoni V, Circelli L, Tartaglia E, Gambardella C, Napolitano S, Mauriello C, Avenia N, Santini L, Sinisi AA. Current concepts of pheochromocytoma. Int J Surg. 2014;12(5):469-74. doi: 10.1016/j.ijsu.2014.04.001. Epub 2014 Apr 12. PMID: 24727002.

Single center experience with laparoscopic adrenalectomy on a large clinical series.Conzo G, Gambardella C, Candela G, Sanguinetti A, Polistena A, Clarizia G, Patrone R, Di Capua F, Offi C, Musella M, Iorio S, Bellastella G, Pasquali D, De Bellis A, Sinisi A, Avenia N. BMC Surg. 2018 Jan 11;18(1):2. doi: 10.1186/s12893-017-0333-8.

Long-term outcomes of laparoscopic adrenalectomy for Cushing disease. Conzo G, Pasquali D, Gambardella C, Della Pietra C, Esposito D, Napolitano S, Tartaglia E, Mauriello C, Thomas G, Pezzolla A, De Bellis A, Santini L, Sinisi AA. Int J Surg. 2014;12 Suppl 1:S107-11.

**Comment:** In the "discussion" section I suggest to better analyze the role of laparoscopic tranperitoneal andrenalectomy and of retroperoneoscopy.

**Reply**: Thanks for your suggestion. In the "discussion" section of our paper, we have incorporated an analysis of the role of laparoscopic tranperitoneal andrenalectomy and of retroperoneoscopy. The overall revisions are as follows: "Surgery is currently the main curative treatment for ACC. Even in advanced stages with metastatic ACC patients, surgery has the potential to potentially improve patient survival rates. For localized ACC patients, laparoscopic approaches can serve as a possible alternative to open adrenalectomy. Additionally, for the treatment of benign-appearing adrenal tumors with a diameter of ≤ 6 cm, minimally invasive adrenalectomy has become the preferred surgical approach." Additionally, we have consulted literature provided by you, which is authoritative within our specialized field. This has significantly enhanced the overall structure and enriched the content of our manuscript.

**Changes in the text**: See Page 24-25, line 311-317.

**Reviewer B**

The authors report an interesting study with impact for clinical management. However, there are some issues which need to be clarified and improved for publication.

Major comments

1) In multivariate analysis, risk actors can be included which add to each other rather than be redundant. Including both T, N, M and tumor stage is redundant as these are different views on the same risk factors. Please revise.

2) According to the methods section, patients with missing data on chemotherapy/radiotherapy were excluded. However, in table 1, 2, and 3 the left column indicates patients with "unknown" information on radiotherapy and chemotherapy. Please revise.

3) The results stated in paragraph 3.2, particularly in lines 186-191, are not concordant with the data presented in table 3. Please clarify.

4) Resolution of figure 6 is insufficient and figures are barely comprehensible with the provided figure legend. Please revise.

5) Figure 7 depicts the web-based calculator to predict OS. However, the patient presented raises questions as the data entered are inconculsive: T1N0M0 and distant tumor stage? Please comment.

6) In the results section as well as the discussion section (e.g., lines 304-306) the authors use "clinical net benefits". Please define.

Minor comments

1) Sentence incomplete (line 90)

2) Please thoroughly review the manuscript and figure legends for spelling / grammatical errors.

3) Figure 4 is hardly identifiable. Please provide with higher resolution.


**Major comments:**

**Comment 1**: In multivariate analysis, risk actors can be included which add to each other rather than be redundant. Including both T, N, M and tumor stage is redundant as these are different views on the same risk factors. Please revise.

**Reply 1**: We sincerely appreciate your valuable comments. Due to distinct perspectives on the same risk factor represented by T, N, M, and tumor staging, we individually incorporated them into a multivariable regression analysis. Based on all patient data from the SEER database, the C-index for the two models was 0.711 (95% CI 0.690–0.732) and 0.709 (95% CI 0.688–0.730), indicating that the model incorporating T, N, and M demonstrated greater discriminatory power in predicting OS. Consequently, we proceeded with subsequent research processes based on this analysis results.

**Changes in the text**: See Page 11-12, line182-202.


**Comment 2**: According to the methods section, patients with missing data on chemotherapy/radiotherapy were excluded. However, in table 1, 2, and 3 the left column indicates patients with "unknown" information on radiotherapy and chemotherapy. Please revise.

**Reply 2**: Thank you for your suggestion. Due to oversight in the writing process, there were irregularities in the formatting of the tables. We have rectified these issues in accordance with your guidance, and once again, we appreciate your valuable Comment.

**Changes in the text**: See Page 8, line160; page 10, line173; page 12, line 202.

**Comment 3**: The results stated in paragraph 3.2, particularly in lines 186-191, are not concordant with the data presented in table 3. Please clarify.

**Reply 3**: Thank you for your valuable comment. The results stated in paragraph 3.2, particularly in lines 186-191, primarily focus on the interpretation of the outcomes of a multivariate regression analysis. In this section, we mainly explain the results of Figure 2. Due to unclear descriptions in the original manuscript, misunderstandings arose. We have corrected the figures and tables accordingly.

**Changes in the text**: See Page 11-12, line188-202.

**Comment 4**: Resolution of figure 6 is insufficient and figures are barely comprehensible with the provided figure legend. Please revise.

**Reply 4**: Thanks for your suggestion. We have made modifications to Figure 6, including enhancing the image resolution and converting it to the TIFF format. The original images have been uploaded in the supplementary files. We have also corrected the figure legend, providing more detailed descriptions, including explanations for the coordinate axes, the significance of each curve, and an elucidation of net proceeds. These adjustments aim to facilitate a clearer understanding for other readers perusing the article.

**Changes in the text**: See Page 20, line 255-271.

**Comment 5**: Figure 7 depicts the web-based calculator to predict OS. However, the patient presented raises questions as the data entered are inconculsive: T1N0M0 and distant tumor stage? Please comment.

**Reply 5**: Thank you for your prompt reminder. Due to an oversight in our writing, we inadvertently used an example that theoretically could not occur. We have rectified this error. In conjunction with our new web calculator, we have removed information regarding the staging of distant tumors from the example. Once again, we appreciate your valuable comment, which has greatly benefited us.

**Changes in the text**: See Page 21, line 278-283.

**Comment 6**: In the results section as well as the discussion section (e.g., lines 304-306) the authors use "clinical net benefits". Please define.

**Reply 6**: Thank you for bringing to my attention the deficiencies in our manuscript. In order to clarify, we have provided a definition for "clinical net benefit". Furthermore, we have explained the implications of net benefit being either positive or negative. When net benefit is positive, it means that under the given conditions, the model's predictions result in an overall

benefit to patients. Higher positive net benefit values indicate a more favorable prediction by the model. Conversely, when net benefit is negative, it indicates an overall loss.

**Changes in the text**: See Page 20, line 258-266.


**Minor comments**

**Comment 1**: Sentence incomplete (line 90)

**Reply 1**: Thank you for your alert. Following your notification, we identified a grammatical error in this sentence and have made the necessary revisions.

**Changes in the text**: See Page 4, line 88.


**Comment 2**: Please thoroughly review the manuscript and figure legends for spelling / grammatical errors.

**Reply 2**: Thanks for your suggestion. We conducted a thorough examination of the manuscript for spelling and grammar errors and made the necessary corrections, indicating the changes in red font.

**Changes in the text**: See Page 6, line 112; page 7, line 141; page 15, line 219,228,230; page 22, line 286,291 et al.


**Comment 3**: Figure 4 is hardly identifiable. Please provide with higher resolution.

**Reply 3**: Thank you for your valuable comment. We have made modifications to Figure 4, including enhancing the image resolution and converting it to the TIFF format. The original images have been uploaded in the supplementary files.

**Changes in the text**: See Page 18, line 242.