Peer Review File

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Reviewer A

This study has attempted to come up with a convenient nomogram based to predict mortality risk in 30 days using "objective" first lab value (assuming since admission to palliative care unit). Patients were excluded if they are already planned for chemotherapy or RT. As authors have already identified the major limitation, there are layers of potential selection biases in the study population. Are there admission criteria to the palliative care unit followed by national guideline? What would mean by "terminal cancer"? How these physicians determine "terminal cancer"?. How dose cancer diagnosis in this study population represent the general population based cancer statistics in China? Certain cancer are not known for hypercalcemia of malignancy (such as prostate cancer) or organ metastasis (CNS cancer) are not seen in the list of cancer diagnosis. Ultimately, does this nomogram help identifying patients who are less likely to live beyond 30 days yet to undergo chemotherapy or radiotherapy? It would be challenging to test this model without rigorous inclusion and exclusion criteria for tested population.

Comment: Are there admission criteria to the palliative care unit followed by national guideline?

Reply: Thank you for the detailed review. There lack of standard admission criteria to the palliative care unit around the world. WHO has defined the “Palliative care “ as an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness. NICE guideline states that palliative care involves providing integrated ongoing support from the diagnosis of a life-limiting condition (conditions that are expected to result in an early death, including cancer). Thus, people who have chronic diseases such as cardiovascular diseases, cancer, chronic respiratory diseases, AIDS, kidney failure and dementia are suitable for palliative care. Further more, in Chinese condition, the most of the patients in palliative care units are those who diagnosed as advanced cancer. Considering the data availability and research gap , we choosed advanced cancer patients as the research object.

Changes in the text: We have further clarified the admission criteria and palliative care unit.(see Page 5, line 103-109)

Comment: What would mean by "terminal cancer"?

Reply: Thanks for your question. It means “advanced cancer”. We have changed the “terminal cancer” to “advanced cancer” through the whole manuscript.

Comment: How these physicians determine "terminal cancer"?

Reply: I'm sorry that my omission caused you any confusion. The physicians assessed the patients by The TNM Staging System. Only the patients who were diagnosed with cancer of any type and stage III or IV were considered.

Changes in the text: We have provided more detailed description about how physicians determine participats in "2.2 Patients" (see Page 6, line 106-109)

Comment: How dose cancer diagnosis in this study population represent the general population based cancer statistics in China?

Reply: Thank you. The population included in present study is representative to a certain extent. According to Global Cancer Statistics 2020, the most common types of cancer in China were lung cancer, colorectal cancer, gastric cancer, breast cancer, and liver. The lung cancer, liver cancer, stomach cancer, esophageal cancer and colorectal cancer had the highest death rate. The cancer diagnosis in our study covered the most common and most deadly types of cancer. However, due to the limited number of population and single research unit, the generalizability of the model is restrained. Further validation is required in a prospective, multicenter and large sample study.

Comment: Certain cancer are not known for hypercalcemia of malignancy (such as prostate cancer) or organ metastasis (CNS cancer) are not seen in the list of cancer diagnosis.

Reply: Thank you for your detailed review for your advise gave the chance to enrich the content of the article**.** There are a small number of patients who are diagnosed with prostate cancer or CNS cancer. We have put them in "others" category under "Primary cancer diagnoses".

Changes in the text: We have provided the detailed note about "others" under the Table 1.(see Page 11, line 182-184)

Comment: Ultimately, does this nomogram help identifying patients who are less likely to live beyond 30 days yet to undergo chemotherapy or radiotherapy?

Reply: Thanks, its a good question. It might be suitable for patients who are less likely to live beyond 30 days yet to undergo chemotherapy or radiotherapy. However, accuracy may be a challenge. In present study, we constructed the nomogram based on the characteristics of participants who did not receive chemotherapy or radiotherapy, for chemoradiotherapy could affect survival time. A more specific and targeted model could be developed if some variables like frequency of chemoradiotherapy, dosage, intensity and chemotherapy regimens are to be considered. Prognosis estimation can help assess overall survival (OS), provide early palliative care and reduce torment brought by overtreatment or improper treatment. Although the enrolled patients are those who have already gave up chemoradiotherapy, they also have a potential to receive treatment in the future, especially Chinese family members always hope the patients to be cured positively. We could still provide early palliative care, help make advanced care planning and relieve anxiety associated with prognostic uncertainty based on prediction results.

Changes in the text: We have specified the using of nomogram in Discussion. (see Page 24, line 293-297)

Comment: It would be challenging to test this model without rigorous inclusion and exclusion criteria for tested population.

Reply: Thanks for your sincere advice. We have tried our effort to clarify the inclusion criteria and applicable situation of the nomogram.

Changes in the text: (see Page 5, 24, line 102-106, line 293-297)

Reviewer B

The manuscript describes the nomogram for prognostic prediction in patients with cancer undergoing palliative care. Basically, I feel the approach is interesting but the details of the explanation of the results seem insufficient as commented below:

Comment: Page 1, abstract: As this nomogram cannot completely predict the accurate prognosis probably because the inter-patients' variability of several factors as shown by the wide range of the bars in Figure 6. I wish to add some comments of such bosspble variability in such nomogram. I.e., a limitation or an important notice by the authors in using the nomogram had better been added.

Reply: Thanks for your sincere advice. We have supplied the detailed notice about calibration of the nomogram in "3.3 The construction and evaluation of nomogram" and under the Figure 6 (see Page 19, 22, line 234-240, 268-275). Meanwhile, We have specified the using of nomogram in Discussion. (see Page 24, line 293-297)

Comment: The authors used only the Lab data such as WBC, ALT. How the authors think using so-called patient-oriented-outcome (PRO) such as QOL evaluation by patients themselves?

Reply: Thank your. Patient-oriented-outcome (PRO) such as QOL, performance score, physical signs and symptoms are all important predictive indicators without doubt, and nearly all of them have been proved to be related with OS. However, the assessment results might be labile, for it could be influenced by evaluators' experience and patients' personal perception. Meanwhile, the retrospective nature of the study made it difficult to distinguish the quality of QoL evaluation. Prospective study design and standard evaluation process are needed in the future.

Comment: Page 2, bottom: Please add some explanation about the palliative care conditions in the inluded patients. E.g., using opioids, pain severality etc., if any.

Reply: Thanks for your sincere advice. We have added the service the palliative care unit provided in 2.2 Patients.

Changes in the text: see Page 5, line 103-105

Comment: There seems no data of albumin and CRP. These are important from the viewpoint of nutritional status, why not included these?

Reply: Thank you. Albumin has been included in our study. However, no statistical corelation with OS has been found in our study. We have considered to put CRP into our model. Unfortunately, through reviewing the medical records, we found that not all patients had CRP value at first admission to palliative care. It emphasizes the necessity of prospective study design to include more blood indicators.

Comment: Page 4, Section 3.3: Descriptions of the result given by Figures 3-7 are too simple for readers to understand.

Reply: Thanks for your sincere advice. We have tried our effort to more detailed descriptions about the nomogram (see Page 18, line 213-223), ROC curve (see Page 21, line 262-264), overall survival curves (see Page 20, line 254-258), calibration (see Page 19,22, line 234-237, 268-275) and DCA curve (see Page 19, 23, line 237-240, 279-285).

Comment: Figure 3: For example, if a patient had “Ca>2.65, NEUT>7, Urea<=7.6, GOT<=40” hen total point is 100+80+0+0=180, and the probability is 0.1. Is this correct?

Reply: Yes, it is correct. The total point 180 shows that the 30-days survival probability is 10%. I'm sorry that my omission caused you any confusion. We have added some illustration about how to calculate the score according to patients’ blood test result. (see Page 18, line 213-223)

Comment: Figure 3: It is not clearly described how the value 80 (etc.) was determined in case, e.g., GOT>40. Why 80?

Reply: The scores of Point line were calculated by computer according to regression coefficient of each value. Nomograms transforms the complex regression equation into a visual graph, which makes the results of the prediction model more readable. The basic principle of the nomogram is to build a multi-factor regression model (such as Cox regression), assign scores to each value according to its regression coefficient, and present the score in appropriate proportions. The Point line represents the single score of each variable under different values.

Changes in the text: We have added more instructions about nomogram in “3.3 The construction and evaluation of nomogram”. (see Page 18, line 213-223)

Comment: Figure 4: The ROC curves did not necessarily show that the prediction accuracy is enough. Add some descriptions for the figure.

Reply: Thank you for your detailed review. We have added more description for ROC curves.

Changes in the text: see Page 21, line 262-264

Comment: The explanation of the bars should be added in the captions.

Reply: We have added more explanation about each bars.

Changes in the text: the nomogram (see Page 18, line 213-223), ROC curve (see Page 21, line 262-264), overall survival curves (see Page 20, line 254-258), calibration (see Page 19,22, line 234-237, 268-275) and DCA curve (see Page 19, 23, line 237-240, 279-285)

Comment: More detailed explanations would be helpful for authors.

Reply: Thank you very much for your time involved in reviewing the manuscript and your very encouraging comments on the merits. We have tried our effort to provide more detailed descriptions about inclusion criteria (see Page 5, line 103-109), palliative care unit service (see Page 5, line 103-105), applicable situation of the nomogram(see Page 24, line 293-297), more detailed interpretation about each bar. (All changes are shown in red font)