

Peer Review File

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Reviewer A

1. I congratulate the authors on their attempts to identify prognostic indicators for gastrointestinal cancer.

Reply: We thank the reviewer for this positive comment.

2. I am left hanging by their data in that no actual survival information is provided. The comparisons are interesting but are of no value to me as I evaluate my own activity in the management of gastrointestinal cancer.

3. Try and make the narrative review a working document that has relevance to my practice of gastrointestinal cancer.

Reply: We appreciate and understand the relevance of comments 2 and 3. Thank you for bringing this to our attention. These two comments are quite related, and so we addressed them in this reply. To help expound on the clinical relevance of our review, we have included examples of the use of the publically available reviewed calculators for colorectal cancer. We inputted some of our own colorectal patient variables from 5 years ago (identified at random), and calculated OS using the MD Anderson and MSK calculators as well as included the actual outcomes of the patients. Different results were obtained with each calculator, but both performed reasonably well. It is our hope that use of these examples showcase how these prognostic tools can be used in clinical practice to provide patients with reasonable estimates of survival, but also demonstrate their limitations.

Changes in the text: This has been specifically added and addressed in Pages 8-9, Lines 170 – 182.

Reviewer B

This article is a narrative review evaluating the relationship between nomograms and prognosis in gastrointestinal cancer.

The paper specifically mentions monograms for prognosis of colorectal cancer and esophageal cancer.

The English is plain, and the text is easy to understand as the nomograms are categorized by category.

The article is worth reviewing because there are few papers like this one, but there are some questions and corrections that need to be made.

Please reply to them.

Reply: We thank the reviewer for these initial positive comments.

1, Relationship between the degree of progression of cancer and monograms

Cancer diagnosis is usually evaluated by staging based on the UICC. Especially in L125-135(Ref.17,31,32,11), there are several reports that state that the original monogram is superior as a prognostic evaluation system in comparison with the UICC. In this section, please write in the text not only the name of the score but also each of the items on which the evaluation was based.

Reply: Thank you for this comment. We agree with this comment that TNM is the current main system for prognostication. As requested, we have included in the text the items used by the other prognostic tools as information for the reader, which is summarized here:

1. Ref. 17 (Duan) – Gender, Tumor length, T stage, N stage, Number of chemotherapy cycles.
2. Ref 31 (Shao) – Grade, T Stage, Modified N Stage, CRP/Alb and NLR (Neutrophil lymphocyte ratio).
3. Ref 32 (Weiser)
Recurrence free survival – AJCC ypT (postoperative pathological tumor stage), # of positive nodes, DTAV (distance from the anal verge), venous invasion, PNI (perineural invasion)
Overall Survival – Age, AJCC ypT (postoperative pathological tumor), # of + nodes, DTAV, venous invasion, venous invasion, PNI
4. Ref 11 (Diao) – Age, (< 60, greater than or equal to 60 – <80, or greater than or equal to 80), Marital status, T stage, M stage, Surgery (Local excision/partial proctectomy vs total proctectomy vs no surgery), Chemotherapy, Radiotherapy.

These references do not designate a specific name for their tools, but rather are simply referred to based on the leading author.

Changes in the text: This has been specifically added and addressed in Pages 9-10, Lines 186-206.

2, Regarding the number of cases used to create the monogram

In order to create a monogram, it is necessary to have a statistically sufficient number of cases. Please indicate the approximate number of cases examined in each paper for the creation of the monogram. Also, please tell us whether each paper statistically calculates the basis for the number of cases.

Reply: We thank the reviewer for this comment and agree that the requested information should provide additional scrutiny in the examination of these prognostic tools. We have thus added the number of cases used to create and validate these tools as follows. However, because these calculators are developed based on retrospective data, none of them had a power calculation, which we have also included in the text as information for the reader.

1. Ref. 17 (Duan)
Internal validation: n = 328
External validation n = 76
2. Ref 31 (Shao)
Primary cohort: n = 633
Validation: 283
3. Ref 32 (Weiser) – MSK Cohort
Model training group – 710
Validation group – 359
SCC Cohort: Chemoradiotherapy validation group - 200
Short course radiotherapy validation group – 131
Total number of patients – 1400
4. Ref 11 (Diao)
Training set: n = 534
Validation set: n = 272

Changes in the text: This has been specifically added and addressed in Pages 9-10, Lines 188-210.

3, About biomarkers and monograms

The author describes biomarkers as a prognostic evaluation system (L146-153, Ref. 33-36). I thought that the evaluation of nomograms was created by multiplying multiple factors, but it seems that biomarkers are independent evaluation criteria in the beginning. Were the biomarkers in these papers multiplied by other factors? Or is the evaluation based on the biomarker alone?

In the references pertaining to biomarkers, the relevant tools utilized biomarkers as independent evaluation criteria, which we verified in each of the papers. We appreciate this comment as we think that the reviewer astutely highlights the need to include different variables within prognostication tools. We propose that future prognostic tools incorporate demographic, pathologic, and biomarker variables to strengthen the accuracy and utility of these tools. All of these changes have been addressed in Pages 10 -12, lines 212, 244-245, and 249-252.

Minor revise

L121 and L123 adjuvant!

I think the "!" is not necessary! is unnecessary.

Reply: We apologize for this error and thank the reviewer for identifying this. It has been corrected.