Author’s response to reviews

Title: Controlling nutritional status (CONUT) score as a preoperative risk assessment index for older patients with colorectal cancer

Authors:
Yuka Ahiko (yahiko@ncc.go.jp)
Dai Shida (dshida@ncc.go.jp)
Tomoko Horie (fmutmk@yahoo.co.jp)
Taro Tanabe (tatanabe@ncc.go.jp)
Yasuyuki Takamizawa (ytakamiz@ncc.go.jp)
Ryohei Sakamoto (ryosakam@ncc.go.jp)
Konosuke Moritani (kmoritan@ncc.go.jp)
Shunsuke Tsukamoto (shtsukam@ncc.go.jp)
Yukihide Kanemitsu (ykanemit@ncc.go.jp)

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Author’s response to reviews:

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Controlling nutritional status (CONUT) score as a preoperative risk assessment index for older patients with colorectal cancer

Please find enclosed our revised manuscript entitled, “Controlling nutritional status (CONUT) score as a preoperative risk assessment index for older patients with colorectal cancer,” which we are submitting again for publication in BMC Cancer.

We believe our manuscript has been improved substantially. Our point-by-point responses to the Editor and Reviewers’ comments are provided below.

We look forward to hearing from you at your earliest convenience.

Sincerely yours,

Dai SHIDA, MD, PhD
Department of Colorectal Surgery, National Cancer Center Hospital,
5-1-1 Tsukiji, Chuo-ku, Tokyo 1040045, Japan
Telephone: +81-3-3542-2511     Fax: +81-3-3545-3567
E-mail address: dshida@ncc.go.jp

Response to the Editor comments
1. Please change the Introduction heading to Background.
   Thank you for your suggestion. We changed the Introduction heading to Background.

2 - The Availability of data and materials section refers to the raw data used in your study and presenting tables and figures is not sufficient to state that all data is contained within the manuscript and additional files. Please only use this statement if you have indeed provided all raw data on which your study is based. We strongly encourage all authors to share their raw data, either by providing it in a supplementary file or depositing it in a public repository and providing the details on how to access it in this section. If you do not wish to share your data, please clearly state this in this section along with a justification. Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Thank you for your suggestion. We modified this section as follows (page 18, line 4 - 6); The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

3 - Please remove this heading: 'Conflicts of interest and Source of funding:'
Any text may be included in the Competing interests section.
Thank you for your advice. We removed this section.

Response to the Reviewer’s comment.

Reviewer 1: Prof. Nora Manoukian Forones
The study is retrospective but has a high number of patients, that make the results interesting. Thank YOU!
The authors didn't include any nutritional status of the patient as BMI or nutritional risk factor as percentage of weight lost before surgery. Although these aspects were not included in the the research, they have to be mentioned as a limitation of the study as well in the discussion the reason why they did not include these parameters.
The results, the discussion, the references and the tables and figures are been adequate.
Thank you for the comments.
Regarding BMI as nutritional status of the patients, we already included BMI in the multivariate analysis of OS (please see Table 2). On the other hand, we did not include BMI in the multivariate logistic regression analyses of postoperative complications because BMI was not an independent factor for postoperative complications by univariate analysis (p = 0.648). However, as the reviewer’s comment, BMI was reported as an independent factor for postoperative complications in some reports. Thus, in this revised manuscript, we included BMI into the variable of logistic regression analyses of postoperative complications.
We added BMI into modified Table 3, and we added the description in the Results section (page 13 line 3 -4).
We did not investigate percentage of weight lost before surgery.
Reviewer 2:
Table 2: I’d recommend to take the lowest category of each score as reference and compare the higher categories with the lowest category.
Thank you for your suggestion.
According to the comments, we newly created Table 2 by taking the lowest category of each score as reference and comparing the higher categories with the lowest category.

Could the authors add a list of complication definitions as a supplement?
Thank you for the comments.
According to your suggestion, we added the description in the Methods section (page 6 line 13 -16), and also newly provided a list of complication definitions as a supplement (Supplementary Table 1).

Normally, complications graded Clavien Dindo 3 and higher are considered severe/serious complications. Could the authors add an analysis regarding these complications?
Thank you for the comments.
We added analysis of severe/serious complications (Clavien-Dindo 3 and higher) and provided these results as Supplementary Table 2. The results were similar to those of complications graded Clavien Dindo 2 and higher, which we showed as Table 3.

A previous study showed that the appropriate cutoff of the CONUT score to predict postoperative major complications would be between 4 and 5. Could the authors add an additional analysis using this principle?

Thank you for the comments.


In this study, we set the cutoff of the CONUT score between 3 and 4, when we investigated association between CONUT score and postoperative complication. That is because, for analyses of OS and the CONUT score, we divided patients into three groups by CONUT score, that is, 0-1, 2-3, ≥4 (not ≥5). Moreover, the proportion of the patients with ≥5 CONUT was only 4.5 %, whereas that of ≥4 CONUT score was 9% as shown in Table 1. Taken these results together, it does not seem valuable to set cutoff between 4 and 5.

Setting a cutoff between 4 and 5 does not change the results. (OR= 2.17; 95% CI (1.09-4.30); p= 0.028)

Were patients with higher tumor stage also the patients with poorer CONUT scores? It would be helpful to describe patient characteristics stratified for CONUT categories.
Thank you for the comments.

Yes, patients with higher stage were the patients with higher CONUT score (p= 0.045). We modified
Table 1 and described patient characteristics stratified by CONUT category. We also added this description in the Results section (page 9 line 11 – 13, line16 - 17).

How was BMI added to the multivariate model?
Thank you for the comments.
As for OS, we already included BMI in the multivariate analysis (please see Table 2 and its footnotes).
As written in the Method section, multivariate analysis using the Cox proportional hazards model was performed separately for each of five indices (page 8 line 7 -11). And HRs (adjusted for sex, BMI, lymph node metastasis, Stage, CEA, and CA19-9) of OS in each index were calculated (please see Table 2 and its footnotes). As for BMI, BMI was an independent prognostic factor for OS. We added the description in the Results section (page 11 line 7 -9).

As for postoperative complications, we did not include BMI in the multivariate logistic regression analyses of postoperative complications because BMI was not an independent factor for postoperative complications by univariate analysis (p= 0.648). However, as the reviewer’s comment, BMI was reported as an independent factor for postoperative complications in some reports. Thus, in this revised manuscript, we included BMI into the variable of logistic regression analyses of postoperative complications.

We added BMI into modified Table 3, and we added the description in the Results section (page 13 line 3 -4).

Could the authors add tables including the Cox proportional hazard models?
Thank you for the comments.
Please see the response above. The current Table 2 and its footnotes (describing the COX proportional hazard models as ‘adjusted for’) seems to be easy to understand.

Did the authors consider to measure skeletal muscle mass and adiposity on abdominal CT scans? This has recently also been described as an important nutritional and physical status parameter.
Thank you for the comments.

In the present study, we focused on CONUT score as a novel nutritional evaluation index, gaining much attention in recent years, which can be calculated from blood test data and is excellent in objectivity and simplicity. Thus, to measure skeletal muscle mass and adiposity on abdominal CT scans is beyond purpose of this study.

On the other hand, we agree that skeletal muscle mass is an important nutritional and physical status parameter, since it seems to be associated with survival and postoperative complications in colorectal cancer. So, we will try to do another research including this parameter in the future.