Reviewer's report

Title: The prognostic significance of the postoperative prognostic nutritional index in patients with colorectal cancer

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Reviewer: Jesse Joshua Smith

Reviewer's report:

The paper by Shibutani et. al entitled 'The prognostic significance of the postoperative prognostic nutritional index in patients with colorectal cancer' is a well-written paper describing use of the postoperative prognostic nutritional index (PNI--serum albumin and lymphocyte derived) in 'predicting' outcomes in colorectal cancer patients. The paper is truly a pilot study for this putative biomarker and falls short in prognostication due to the fact that there is no validation cohort.

1. Overall considerations:
   a. The authors defined their question well but the final execution of their findings is flawed with no validation cohort.
   b. Methods seem appropriate other than missing the validation step for their proposed biomarker.
   c. These pilot data seem sound
   d. The figures and data seem genuine
   e. I see no problem with compliance with relevant standards of report and data deposition
   f. The discussion and conclusions are well written but a major limitation (no validation cohort for a biomarker) was not mentioned nor was it addressed as a potential weakness.
   g. The authors are building on similar work in other GI cancers and seem to acknowledge that work sufficiently.
   h. The title and abstract overstate the findings given the lack of a validation cohort.
   i. The paper is well written but lacks in the substance needed to make this a valid biomarker paper.

2. Major compulsory revisions:

I cannot accept this paper as is, but if a validation cohort mirrors these findings then I would reconsider my current stance. Declaration of prognostic significance carries the burden of proving PNI as a durable biomarker in colorectal cancer patients and their current data supports a pilot study finding but falls short of proving the robust nature of PNI as an independent predictor of outcomes in
colorectal cancer patients. On page 7 line 5, the authors state 'Moreover, the postoperative PNI was a stronger predictor of survival than the preoperative PNI. In addition, the combination of the preoperative and postoperative PNI enabled a more accurate stratification of the risk for a poor prognosis." I think this statement could hold if the postoperative PNI were properly validated. Until tested in an independent cohort then the strength of many of the statements in the paper needs to be tempered. For example, on page 8, line 16: I would argue that the authors missed the major limitation and flaw with the current body of work--no validation of their interesting findings in a validation cohort precludes publication at this time in my view. If the authors do not have access to a validation cohort then they might consider breaking their group into a testing and validation cohort.

3. Minor essential revisions--Some specific questions/thoughts for the authors:
   a. on page 5 line 5 (why is there only 106 and 23 patients (high and low PNI)?--were their only pre-op values for 129 patients of the 186?
   b. Declaration of prognostic significance carries the burden of proving PNI as a durable biomarker in colorectal cancer patients and their current data supports a pilot study finding but falls short of proving the robust nature of PNI as an independent predictor of outcomes in colorectal cancer patients.
   c. On page 7 line 5, the authors state 'Moreover, the postoperative PNI was a stronger predictor of survival than the preoperative PNI. In addition, the combination of the preoperative and postoperative PNI enabled a more accurate stratification of the risk for a poor prognosis." I think this statement could hold if the postoperative PNI were properly validated. Until tested in an independent cohort then the strength of many of the statements in the paper needs to be tempered.
   d. page 7, line 8 contains a typo--'clinically' should be 'clinical'
   e. page 7 line 17: 'lymphopenia creates a favorable microenvironment for micrometastatic growth'--it seems that this needs a reference
   f. also need to label Fig 2 as the preoperative PNI and Fig 3 as the postoperative PNI

4. Discretionary revisions: none

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

My competing interests: none
I declare that I have no competing interests.