Reviewer’s report

Title: Perioperative dynamics and significance of plasma-free amino acid profiles in colorectal cancer

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Reviewer: Stephen Mcsorley

Reviewer’s report:

Thanks to the authors and editor for inviting this review. The authors present a small observational study examining the impact of surgical resection of CRC on concentrations of PFAAs which have been identified as being associated with the presence of CRC in the AICS scoring system. The authors report that resection of the primary tumour in patients without metastatic disease results in a reduction in AICS in the majority of patients, suggesting that these levels of PFAAs are driven by the tumour, rather than themselves being causally implicated in the disease process. Although the study is small, the analysis is appropriate, and the conclusions drawn reasonable. The authors identify the main limitations of small numbers and the significant variation in timing of postoperative blood sampling. I have a few comments;

1. The authors suggest that levels of AICS reflect the presence of the tumour, explaining the reduction in the postoperative period. Is there any additional evidence to support this? In particular, have such bloods been drawn from any patients who went on to have disease recurrence? If AICS was found to rise again in this scenario then both the hypothesis, and the case for the use of AICS as a prognostic and then predictive measure would be strengthened. If this has not yet been tested in CRC, is there any evidence from other solid tumours in the literature?

2. Following on from the first comment, both the preoperative AICS values, and fall after surgery were stage independent. If PFAAs are produced by the tumour or host-tumour interactions, is there any evidence of relationship with tumour burden outside of TNM stage?

3. As the authors state in the discussion, the local and systemic immune response is increasingly recognised to drive many tumour-host interactions, being prognostic in most solid tumours. Furthermore, and of particular importance in the context of PFAAs, systemic inflammation is recognised to significantly perturb commonly measured micronutrients and plasma proteins. Were any measures of local or systemic inflammation measured in these patients before and after surgery, e.g. NLR, mGPS? This would be important as the host inflammatory response may both be a confounder of PFAAs and/or be a key underlying process relating them to the tumour.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
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