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Associate Professor Monjur Ahmed & Professor Rosa Rodriguez
Editors-in-Chief
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To Associate Professor Ahmed, Professor Rodriguez & Assistant Professor Kasi,

Thank you for your review and consideration of the paper '*Should we resect colorectal cancer in patients over the age of 85?*'.

We thank both yourselves and the peer reviewers for their feedback and kind comments on the paper, it has been very helpful in strengthening the paper.

We have addressed each point from the peer review process below. An updated copy of the manuscript with suggested changes has now been submitted.

Kind regards

Dr David Flynn (on behalf of all authors)

Reviewer 1:

Authors should include the number of patients from each assessed group in the abstract

Thank you for this suggestion and oversight on our part. I agree that placing the number of patients in the abstract gives necessary information in the abstract. This has been amended.

The authors need to include the limitations of this study. (single institution study, etc.).

We agree that the limitations of the study need to be addressed and should be mentioned within the manuscript. This is an oversight on our part. An analysis of the limitations of the study has been included within the discussion section of the manuscript.

The references used in the manuscript is not very up-to date in some cases. Some recommendations: Hashida H, Mizuno R, Iwaki K, Kanbe H, Sumi T, Kawarabayashi T, Kondo M, Kobayashi H, Kaihara S. Laparoscopic Surgery for Colorectal Cancer in Super-Elderly Patients: A Single-Center Analysis. Surg Laparosc Endosc Percutan Tech. 2020 Nov 23.

Ueda Y, Shiraishi N, Kawasaki T, Akagi T, Ninomiya S, Shiroshita H, Etoh T, Inomata M. Short- and long-term outcomes of laparoscopic surgery for colorectal cancer in the elderly aged over 80 years old versus non-elderly: a retrospective cohort study. BMC Geriatr. 2020 Nov 4;20(1):445.

Thank you for the suggestions of these articles- they provide excellent contextual and comparative data for our study while also being more up to date than several of the other references used. Both references bear similar methodologies and cohorts to this study which make them relevant and appropriate studies to reference. I have made specific reference to the articles within the discussion.

Reviewer 2:

The BMI data in table I need to be double checked

Thank you for bringing this to our attention. The data in the BMI section of table 1 has been corrected and is reflected in the updated manuscript.

Reviewer 3:

In the abstract, should start with an introduction

Thank you for this comment- we agree that greater background and context to the study should be included within the abstract. We have expanded the abstract introduction to give a greater context to the study. This is reflected in the updated manuscript.

Under Methods, should explain the time period selected and also the total number of patients in that cohort

We agree that this should have been included within the abstract. This change has been made and is reflected in the updated manuscript.

Similarly under Results, there was no mention of the number of cases, n=?.

We have updated and revised the abstract to include this important information.

Introduction, second paragraph, line 4 selected... Comments, age >85 group is still within age >80 group

Thank you for this comment. The point we are trying to make is that other studies have examined patients within wider age brackets, even if they do include those in the 'oldest old' category. Within literature, there is a paucity of information specifically regarding colorectal cancer surgery outcomes in those over 85 exclusively. Including patients under 85 in the analysis obscures the result of how those in the oldest age bracket really perform following colorectal cancer surgery.

Under Materials and methods, demographic and comorbidity characteristics, any use of Charlson Comorbidity Index?

The use of the Charlson Comorbidity Index (CCI) was discussed between the authors of the paper as a means of stratification. However, it was felt that analysing the patients with more detailed and granular comorbidity data over the CCI was more applicable in this context. Very few papers within literature have analysed the specific comorbidities of each patients within this demographic. It was the consensus of the authors that this data would be more beneficial to the publication over a CCI score for this reason.

The font for Table 1 is very small for reading and can improve

Thank you for this comment. We agree that the font is small and difficult to read. The font size has been increased for all tables.

Under Results, Patient demographics, since the two groups have little comorbidity difference and one would expect similar surgical outcomes, have you look into frailty index between the two groups instead?

The authors of the paper did discuss the role of frailty index as a means of stratifying outcomes, however for analysis, it was decided that investigating specific co-morbidities was under-reported in literature and would be of greater benefit to literature.

The analysis of specific comorbidities helped us to elicit more in-depth detail about our population. The role of a frailty index in this population was thought (amongst the authors) to be a new avenue of investigation for future studies.

Although both groups of patients are similar in comorbidities, we could not assume that their surgical outcomes would be similar (hence why the study focussed on the role of age specifically in surgical outcomes).

Any comments on the use of ERAS in colorectal surgery at your unit?

The Enhanced Recovery after Surgery program at The Prince Charles Hospital can be split into pre-operative and post-operative planning.

Pre-operatively, patients are reviewed by the anaesthetic and allied health team and given strict instruction for pre-operative management. These include fasting from midnight before the operation, appropriate steps for bowel preparation, insertion of anaesthetic blocks pre-operatively and anti-emetic management for post-operative nausea and vomiting. Physiotherapists and dieticians assess the patients and advise of their goals post-operatively in elective cases.

Post-operative management for ERAS includes strict fluid balance with hourly urine output monitoring, early mobilisation (day 1), early IDC removal, early feeding and up titration of diet and aggressive pain management.

The ERAS employed at our institution is a reflection of accepted practice and evidence-based medicine to help reduce post-operative stay and accelerate recovery.

Under Discussion, how would you address the limitation of your study including selection bias at the outset on those patients who were not offered upfront surgery and any suggestion to improve future studies?

Thank you for this comment. This issue was raised by the authors when discussing the data and outcomes from the study.

This paper outlines a retrospective analysis of patients over 85 who underwent colorectal cancer resection. Within the study, only patients who were deemed surgical candidates or accepted surgery were included within the study. Patients who were deemed too comorbid or did not accept surgical intervention were thereby excluded from the study.

It is difficult in a retrospective study to alter selection bias. In this case, blinding or randomisation would not be feasible for this methodology. Within this cohort an acknowledgment of the limitation and making readers aware of the limitation is the most important aspect of our findings. The results of this study should reflect outcomes of patients deemed candidates and not a reflection of all people over the age of 85 with colorectal cancer. Similar studies have acknowledged this limitation and discussed the difficulty in limiting selection bias in this methodology.

Future studies could include prospective, multicentre, randomised trials which would help to decrease selection bias and confounding factors.

Those who were offered surgery would have been fitter and therefore unlikely to show statistical difference between the 2 different age groups but more importantly to select

those fit enough to undergo surgery regardless of age. Would you not consider Charlson comorbidity index and frailty index essential in the elderly cohort in selecting those suitable for surgery?

Thank you for this comment- you raise a very interesting point about the study. The aim of the study was to investigate and review the outcomes of patients over the age of 85. We were looking to see whether the outcome from their surgery are equitable to those who are younger, thereby validating the role of surgery in the older population.

Those selected for surgery were done so at the discretion of the surgeon. There was no specific criteria for selection other than appropriate clinical fitness for surgery. Both the CCI and frailty index are appropriate and important tools for stratifying elderly patients. However, they were not used in this instance as the selection of those undergoing surgery was already undertaken in this retrospective cohort.

The use of CCI and fragility scores are invaluable in determining the fitness of patients and their use in selecting those suitable for surgery is a future avenue for research within this cohort.

Reviewer 4:

Nil

Editor

However, its methods, results and other aspects need to be modified, and its references need to be adjusted appropriately. The questions raised by the reviewers should be answered:

Thank you for this comment. The comments made by the reviewers have been very helpful in strengthening the paper. The points raised by the reviewed have been incorporated into the manuscript and appropriately amended.

The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement

Both of these statements have been provided to the publisher along with the updated manuscript.

I found no "Author contribution" section. Please provide the author contributions;

Thank you for bringing this to our attention. We have amended the manuscript to reflect the contributions by various authors.

I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text; and

Thank you for bringing this to our attention. The “article highlight” has been added and updated on the revised manuscript.

Please write the “Conclusion” section at the end of the main text

Thank you for this bringing this to our attention. We have modified the manuscript to include a formal conclusion at the end of the main text.

JOURNAL EDITOR-IN-CHIEF (ASSOCIATE EDITOR) COMMENTS TO AUTHORS

Some spelling errors should be corrected. 1. Research background The global population is living longer than every before. It should be ever before. 2. analysed. It should be analyzed. 3. we also aught to investigate the viability of laparoscopic surgery in the over 85 population. It should be ought to --- 4. rarely utilised. It should be utilized.

Thank you for this bringing this to our attention. The spelling errors have been corrected.