ROUND 1

Name of Journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 69622

Manuscript Type: ORIGINAL ARTICLE

Title: Predicting the outcome of closed-loop small bowel obstruction by preoperative characteristics

Authors: Masja K Toneman, Bente M de Kok, Frank M Zijta, Stanley Oei, Gijs JD van Acker, Marinke Westerterp, Anne EM van der Pool

Dear editor,

Please find enclosed the resubmitted and revised manuscript for the original article titled: Predicting the outcome of closed-loop small bowel obstruction by preoperative characteristics. Manuscript NO: 69622.

We have read thoroughly all the reviewer comments and we have taken all comments into consideration. The feedback questions are answered from the next page onwards.

With my best regards,

On behalf of all the authors,

Masja K. Toneman

Reply to the reviewers

Reviewer #1:
Scientific Quality: Grade D (Fair)
Language Quality: Grade A (Priority publishing)
Conclusion: Major revision
Specific Comments to Authors: Thanks for inviting me to read this study. The aim study was to describe clinical, CT imaging, and blood results differences in patients with Closed-Loop Small Bowel Obstruction (CL-SBO).
Also, to describe the clinical predictors of ischemia perioperative. Patients with CL-SBO were classified into three groups (ischemia perioperative): viable bowel, reversible ischemia, and irreversible ischemia. The authors describe that the most of patients are old and have an ASA classification > 3.
The authors did not describe the clinical predictors of these outcomes since they did not use measures of association, such as RR or OR. Moreover, they did not performer an ordinal logistic regression that allowed the calculation of an OR.
Thanks for your feedback. We additionally performed a logistic regression and added it to the paper.

I have additional comments:
Abstract: • The authors must describe the abbreviations used, such as CT.
Based on your request we described all abbreviations.

Methods: • I do not understand why this study was not approved by a Bioethics Committee. This must be clarified.
The study was evaluated by the Bioethics committee, however they declared that the law on medical scientific research concerning humans was not applicable, due to the non-invasive and retrospective nature of the study.
Clarified this in the paper as follows:
The regional Medical Ethical Testing Committee evaluated the study protocol and declared that the law on medical scientific research concerning humans was not applicable because of the non-invasive and retrospective nature of the study. The

scientific board of our hospital approved the study, and the need for written informed consent was waived. However, every patient file was checked for notes of refusal to participate in scientific research.

Results:

• **Some data could be summarized in a table.**

According to your request, the text is shortened and an extra table is added.

• **How many radiologists did CT imaging assess? is there agreement between them?**

Original reports were used for this study. All these original reports are from experienced radiologists in our centre specialized in abdominal radiology. (Added in the manuscript)
No independent radiologists were asked to examine these reports again.
Unfortunately, also our study showed that the agreement of the findings of the radiologists compared with the peroperative findings in terms of ischemia was low (which corresponds to the literature).

• **Why were 32 patients use to evaluated postoperative complications? This could be a selection bias.**

This was misunderstood, 32 patients of the total 148 patients in our cohort had postoperative complications. We adjusted the text to clarify this.

• **There are no findings of clinical predictors of ischemia perioperative. The authors did not perform an ordinal logistic regression.**

According to your request we additionally performed a logistic regression and added it to the paper.

• **The tables must be improved.**

Based on your request, the tables were improved.

o All data must include two decimals.

Based on your request, all data in the tables and tekst (apart from the patient numbers) are transformed. Also p-value was transformed to two decimals.

o Abbreviations must be described.

According to the guidelines, all abbreviations are described now.

o The measurement units of each variable must be written.

According to the guidelines, all measurement units are provided.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The manuscript needs editing by a language expert to improve language usage.

According to your request, the manuscript was edited by Filipodia to improve language usage.

This retrospective study is to evaluate the preoperative characteristics of patients with closed loop small bowel obstruction (CL-SBO) and the postoperative outcome, based on the perioperative viability of the small bowel (viable, reversible ischemia or irreversible ischemia).

The authors conclude that patients with higher age or ASA classification have increased risk for irreversible ischemia due to CL-SBO; postoperative morbidity is increased in this patient group. The study design is good and the manuscript is well written.

However, the reason to exclude the patients with an abdominal surgery history comprising bariatric surgery or surgery with Roux-en-Y reconstruction is unknown.

This may cause the relatively high percentage (42%) of patients without history of abdominal surgery in this study. Please explain it.

Based on your request the exlusion of this patient group was explained. This is stated in the manuscript as follows:

Patients with Roux-and-Y surgery were excluded because of the difference in clinical presentation with intermittent and subacute pain, and difference in perioperative aetiology, *i.e.* small bowel herniation through an iatrogenic defect created in the mesentery[16, 17].

Peritonitis represents a crucial sign of bowel ischemia, but the related signs were missing in the presenting clinical symptoms in this study. Please provide the data.
We provided additional data about abdominal guarding.

Please describe the complications in details. The reasons of re-exploration (grade IIIb complications) in the viable bowel and the reversible ischemia groups are unknown. Were these cases related to delayed bowel necrosis or perforation? If so, the accuracy of intra-operative assessment of bowel viability is questionable.
Based on your request, an paragraph with the description of the re-exploration was provided.

The total references number (21) is low. 38% (8/21, lower than 50%) of the cited references represent publications from the recent 5 years. PMID and DOI numbers are missing in the reference list.
Not all authors of the references were listed.
More referencers were added. The additional PMID and DOI information was added following the guidelines.

Table 2 should be Table 2a. *We adjusted this.*

Table 2b is not completely shown in the Microsoft Word format. *Tables were adjusted.*

The language quality is grade B.
Please visit the following website for the professional English language editing companies that we recommend: https://www.wjgnet.com/bpg/gerinfo/240. All

authors must provide their personal ORCID registration number. Please visit the ORCID website at https://orcid.org/ for more information.

According to your request, the manuscript was edited by Filipodia to improve language usage.

The "Author contributions" section is missing. Please provide it after "The institutions" section.

We provided the author contribution section.

Toneman MK, de Kok BM, Zijta FM, Oie S, van Acker GJD, Westerterp M and van der Pool AEM designed the report; Toneman MK collected the patient's clinical data; Toneman MK analyzed the data and wrote the paper; de Kok BM, Zijta FM, Oie S, van Acker GJD, Westerterp M and van der Pool AEM revised the paper for important intellectual content; van der Pool AE supervised the report.

The "Supportive foundations" section is missing. Please provide it after the "Author contributions" section.

*We provided the supportive foundation section***.**

Supported by a grant from the Haaglanden Medical Centre Research Foundation to Toneman M to conduct this study.

The "Acknowledgements" section is missing. Please provide it after the "Conclusion" section in the main text.

*We provided the acknowledgements***.**

We would like to thank the Haaglanden Medical Centre Research Foundation for contribution to this study.

As a retrospective study, the authors offered Institutional Review Board Approval Form, STROBE Statement, and Biostatistics Review Certificate. Signed Informed Consent Form was waived by the scientific board of the single centre.

Conflict-of-Interest Disclosure Form and Copyright License Agreement are missing.

Both forms are attached in the revison.

Finally, all the issues raised by the peer reviewers should be addressed.
Language Quality: Grade B (Minor language polishing)
Scientific Quality: Grade B (Very good)

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Surgery, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

ROUND 2

SPECIFIC COMMENTS TO AUTHORS

Thanks for inviting me to read this study. I thank the authors that have considered my comments. They have satisfactorily addressed all my comments and questions, and the article has been significantly improved.

However, the findings of logistic regression must be improved, and the confounding must be assessed. These would allow us to ensure that their findings are true.

Many thanks for the feedback that the article is improved. And thanks for providing the current feedback. Hereby are our answers and revisions to the text.

I have some comments:

• Abstract: Please, include OR findings in your abstract. Since this study aims to describe predictors of perioperative outcome and viable bowel.

According to the suggestions, we revised the result section of the abstracts and added the OR findings.

• Methods:

why was not a multivariable regression performed?

The results from the univariate analysis show only two significant factors, that is ASA classification and age. To perform a multivariate analysis with two factors seems not useful, therefore the multivariate analysis has not been performed.

o please, the ethical approval must be described with the section named "patients and study design".

We changed the location of the section describing the ethical approval to the section 'patients and study design'

o The authors have already carried out a logistic regression; however, the main limitation of cohort studies is the selection bias, which has independent effects on the outcome. This effect is known as confounding. Has there been a systemic effort to identify and measure potential confounders?

In order to limit the selection bias, all operation reports were screened by 2 surgeons, without any difference in interpretation of the inclusion criteria. The patient who did not have a closed loop obstruction were not included. Patients with no signs of decolouration (i.e. ischemia) were included in the viable group, patients with signs of decoloration but without resection were included in the reversible ischemia group, and patients with a resection due to ischemia were assigned to the irreversible ischemia group. Described by the following paragraph;

'The small bowel was considered viable when the affected region between the two sites of obstruction did not show signs of discoloration before the obstruction was released. Reversible ischemia required that a discoloured portion of the small bowel regained normal colour within 5 min after surgical release and repositioning of the bowel. If there was no evident return to viable bowel in 5 min, but a clear increase in colour did occur, we waited a maximum of 20 min, as previously described[17]. If recoloration did not occur after release of the obstruction, the ischemia was considered irreversible and the affected bowel was resected.'

• Results:

o Table 1. There are two approaches to identify imbalance confounders between both groups. The first is to use the significance test (chi2, t-test), these are sensitive to sample size. The second is to use standardized difference, this is not sensitive to sample size. Please, the authors must perform this last.

This is the table describing the baseline characteristics of the three groups. Because the analysis is performed on three groups, standardized difference is not performed.

o Please, include all variables studied in multivariable logistic regression; such as clinical symptoms, blood results; and, intervals between onset of symptoms and computed tomography and surgery in the three study groups. For last, describe how the best model was selected (AIC Akaike information criterion, BIC Bayesian information criterion, or REML redidual maximum likelihood); and, these must be stated in your findings and methods.

The results from the univariate analysis show only two significant factors, that is ASA classification and age. To perform a multivariate analysis with two factors imposes to be not useful, therefore the multivariate analysis has not been added.

o The authors must describe which statistical analyses were performed for assessing the goodness of fit of their model, such as the Hosmer-Lemeshow test, R2 for logistic regression.

We performed the Chi-Square goodness of fit test, which resulted in a $p<0.001$ and the judgement to reject the null hypothesis. Indicating a suited goodness of fit.

o Table 2. Please, 95% CI must be included in all variables.

In table two, all 95%CI intervals are included now.

o Please, include a table that includes unadjusted OR and adjusted OR by age, ASA, or each variable that has a standardized difference greater than 0.1. These findings could be reported as supplementary material. This will allow ensuring that there is no confounding.

The standardized difference has not been analyzed, therefore the unadjusted OR is not mentioned.