

Manuscript title: Definition of colorectal anastomotic leakage: consensus survey among Dutch and Chinese colorectal surgeons.

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To the Editors of the World Journal of Gastroenterology,

Thank you for considering our manuscript for publication in World Journal of Gastroenterology. We are grateful for the constructive criticism of the reviewers and agree on many points. We have intended on answering the questions raised by the reviewers and have adapted the manuscript according to their comments, which has improved the paper significantly. Please find a comprehensive list of all changes below; changes within the manuscript have been highlighted.

We hope that the editorial board will appreciate our work and accept the paper for publication. This last version of the manuscript has been approved by all authors.

We are looking forward to your reply.

On behalf of all authors,

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Reviewer 03475726

Major comment:

The reviewer suggests that there might be a bias in the selection of the surgeons in the different countries. The reviewer worries that the Dutch surgeons might be highly specialized colorectal surgeons with academic interest, and that also upper GI-surgeons and HPB-surgeons were included in the Chinese population. The reviewer therefore suggests that the two populations of surgeons are not comparable according to: background, number of colorectal procedures performed annually, and their attitude to read scientific literature.

Answer major comment:

As this might have been confusing at first, we have tried to clarify this further in the materials and methods section in the manuscript: the Dutch colorectal surgeons were identified via the contacts section from the Coloproctology division of the Dutch Society of Gastrointestinal Surgery and were sent an individual email following this. This division (the Taskforce Coloproctology) includes all – junior and senior, academic and non-academic - colorectal surgeons in the Netherlands.

Despite the fact that the Chinese DXY has more than four million registered users covering varied field in the medical industry including clinical doctors, pharmacological and life-science researchers, we selectively sent the survey invitation only to colorectal surgeons. Although in some hospitals these surgeons do both upper and lower GI surgeries, in most cases, the participants mainly focus on colorectal operations. Moreover, more than half of the participants in the survey were senior surgeons. Given the fact that the Chinese survey covers most provinces in China, we believe both populations are still sufficiently representative of the colorectal surgeons in the two countries.

Minor comment 1:

The invitation letter and instructions to fill the questionnaire should be included in the supplementary materials.

Answer minor comment 1:

The invitation letters for both countries were written in Chinese and Dutch respectively, and no additional instructions were provided on how to fill out the questionnaire. Instead, details about the scoring systems can be found included in the English version of the questionnaire in the manuscript.

Minor comment 2:

Furthermore, the reviewer correctly states that with regards to clinical manifestations predictive of CAL, the use of parameters derived from the Dutch Leakage Score might have led to reach a greater agreement between Dutch surgeons compared to Chinese colleagues.

Answer minor comment 2:

It is indeed possible that the Dutch surgeons are more likely to consider the parameters of the DULK-score (or Dutch Leakage-score) as more important signs of colorectal anastomotic

leakage in the postoperative phase, as the DULK-score was constructed and validated in a multicenter study in the Netherlands. It is highly plausible that some of the participating surgeons in this consensus study were involved in the development of this score. However, it is unknown whether this group is sufficiently large enough to skew the data. Furthermore, the use of the scoring system has not remained limited to the Netherlands, as a French research group validated both the original and modified DULK-score. A short remark has been added regarding the origin of the DULK-score in the limitation part of the Discussion section of this manuscript (highlighted in yellow).

Minor comment 3:

The fact that 40% of Chinese surgeons interviewed expressed disagreement about high levels of CRP as predictive of CAL is indeed interesting. This might be the spy of different usage of this laboratory test and this question should have been preceded by the question: Do you routinely use CRP?

Answer minor comment 3:

In hindsight, the question 'Do you routinely use CRP', could have been indeed very helpful in understanding the different views regarding the predictive ability of this laboratory test. However, as we conducted this research as a collaboration between Dutch and Chinese researchers and surgeons, we feel that by our combined experiences, we are able to explain a large part of the differences observed in the study.

Reviewer 03647716

Major comment:

The reviewer suggests to more clearly express that this manuscript is indeed comparing the views between surgeons in the east and west. The reviewer further stresses that the 'state of the art' should be discussed in more detail.

Answer major comment:

We feel that both China and the Netherlands are good representatives for the east and the west, respectively, and we agree with the reviewer that this comparison should be highlighted in the manuscript. Therefore, we have added a short section about the aim of the study in the introduction section. We were unsure what the reviewer intended with stating that the 'state of the art' should be discussed. We assumed that the reviewer was referring to what definition we suggest to use as a result of the findings in this study. However, we feel that the proposal of any definition at this point would not be helpful to the scientific and clinical community. Instead, as is stated in the discussion section of the manuscript, the construction of a new definition of colorectal anastomotic leakage requires an extensive literature review (which is currently being conducted by the authors), followed by a Delphi-based consensus by a large panel of experts. The results of this Delphi analysis will hopefully follow this manuscript shortly.