

Dear Editor and Reviewers,

Thank you for the time taken to review our manuscript as well as the positive and constructive comments given. Our point-by-point response is provided below in blue:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The article is well structured, according to the guideline provided by the journal. I have a few questions to the authors, on which they can elaborate a little bit in the text: How was the transanal pullthrough for sigmoid cancer performed when you have the full length of the rectum preserved?

The double-ring wound protector is inserted into the bowel from the anus with the internal ring fully past the rectal stump. The external ring is then opened against the perineum to shorten the length of the channel. As the reviewer pointed out, this is particularly important for high anterior resections for sigmoid cancer where the entire rectum is preserved. We have added a comment in the revision to emphasize this point.

Patients 3,4,7 and 8 all had sigmoid cancer but transvaginal NOSE was performed only in patient 3. What was the selection criteria for transvaginal NOSE?

Transanal NOSE is always preferable over transvaginal NOSE to avoid an additional vaginal incision. Transvaginal NOSE was used if the maximum tumour was larger than 3-5 cm, based on the international NOSE surgery consensus by Guan et al 2019 [Reference 12]. The vagina was chosen for retrieval of larger specimens due to the increased elasticity of the vagina compared to the anus – this is reflected in the revised manuscript.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Thank you to have submitted your manuscript. Below the report. The title reflect the main subject of the manuscript. The abstract summarize and reflect the work described in the manuscript and the key words reflects the focus of the manuscript. The manuscript describes the methods in adequate details. The contributions of the study tends to demonstrate the benefit of reduced port laparoscopic colorectal surgery with natural orifice specimen extraction compared to conventional laparoscopic colorectal surgery that could represent a natural progression towards scarless surgery. The tables are sufficient, of good quality and appropriately illustrative of the paper contents. About the discussion: the manuscript interpret the findings adequately and

appropriately, highlighting the key points concisely, clearly and logically. The findings and their applicability and relevance to the literature are stated in a clear and definite manner.

We thank the reviewer for his or her positive comments.

Observations/Remarks The sample is small: are the Authors sure that it is sufficient to achieve your conclusions?

While we are aware of the limited sample size, to our knowledge no previous study has looked at reduced port colorectal resection together with NOSE. Moreover, for the comparator group we increased the ratio of propensity-matched patients to 4x the studied cohort to increase the robustness of the comparison. This important limitation has been mentioned in the last paragraph of the discussion, and the need for larger studies to draw definitive conclusions is also mentioned at the end of the manuscript.

The absence of the figures make difficult to be sure about the clearly description of the surgical technique.

We agree with the reviewer and have added additional figures to the revised manuscript, including intra-operative photos to better demonstrate the surgical technique.

About method surgical technique it is mandatory to specify how many patients required an ileostomy: this is crucial about the holy grail of no scar surgery; probably it is better to pull out this patient if that is the only one.

Two patients had defunctioning ileostomy performed, and we have reflected this in the revised Table 1. However, we do not agree that these patients should be taken out of the study. Reduced port surgery and NOSE surgery are incremental and progressive steps towards the holy grail of scarless surgery; they are not yet considered scarless surgery. It is important therefore to show that these techniques (3-port surgery and NOSE) can be performed for low anterior resection to pave the way for future operative innovation to achieve truly scarless surgery.

About follow up it is not correct to report information about recurrence because the shortness of observation. About this parameter we need longer follow up.

We agree with the reviewer that we will need longer a follow-up period to report meaningful data concerning recurrence. However, we included this information very briefly (our cohort had a median follow up of 1 year), for completeness, as previous authors have questioned if the NOSE procedure would increase early local recurrence due to tumor cell seeding. We therefore felt it would be useful to demonstrate that this was not observed in our limited series.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: 1. Well written, the study seems reasonable statistically, but the number of patient enrolled seem a bit small.

We acknowledge this limitation of the study. To our knowledge this is the first study of reduced port with natural orifice specimen extraction surgery for colorectal cancer with a propensity matched cohort, showing good results. There, we believe our results will be a valuable addition to the literature and of interest to colorectal surgeons.

2. Are there any methods that you used to evaluate the success rate of NOSE before surgery?

Tumor size is an important criterion for NOSE surgery. Our size selection for NOSE was based on the international consensus on colorectal NOSE surgery by Guan et al. 2019 [Ref 12] – tumor size of 3cm for transanal NOSE and 5 cm for transvaginal NOSE. As stated in the discussion, while tumor size can be estimated on preoperative imaging, the decision to proceed with the NOSE procedure can often only be established intraoperatively, due radiological limitations on assessment of peritumoral desmoplastic reaction and mesocolic or mesorectal bulkiness, which may add considerably to the overall specimen diameter.

Moreover, while absolute diameter is an important consideration, the relative size of the specimen to the width of the pelvic outlet as well as the laxity of the chosen bodily orifice may be more crucial in determining the success or failure of the procedure. This can be assessed or approximated on physical examination pre-operatively, e.g. by per rectal or per vaginal examination.

We thank all the reviewers once again for their effort and time.

Sincerely,

The authors

8 October 2022