

Dear Editor,

Thank you for carefully reviewing our manuscript previously titled "**Short-term efficacy of natural orifice specimen extraction surgery for low rectal cancer using a prolapsing technique based on propensity score matching (Manuscript NO. 42956)**" for possible publication in *World Journal of Clinical Cases (WJCC)*. We are grateful to you and your reviewers for their constructive critique. Those comments are valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied the reviewers' comments carefully and have made corrections which we hope be approval. We have revised the manuscript, highlighting our revisions in yellow, and have attached point-by-point responses detailing how we have revised the manuscript in response to the reviewers' comments below.

Thank you for your consideration and further review of our manuscript. Please do not hesitate to contact us with any further questions or recommendations. We are looking forward to hearing good news from you.

Yours Sincerely,

Dr. X.-H. LIN, Department of Clinical Laboratory, Translational medicine center, Huaihe Hospital Affiliated to Henan University, 115 Ximen Street, Kaifeng City, Henan Province, China

Dr. J.-H. HU, Department of General Surgery, Huaihe Hospital Affiliated to Henan University, 115 Ximen Street, Kaifeng City, Henan Province, China

Review 1: This is an interesting retrospective comparative study on efficacy of NOSES for low rectal cancer using a prolapsing technique. The authors concluded that NOSES for low rectal cancer has advantages in reducing postoperative pain, shortening the length of the postoperative hospital stay, and improving patient satisfaction in terms of a more aesthetic appearance of the abdominal wall. The study is well-written and suitable for publication.

[Answer: Thank you very much for your valuable comments and consideration of our manuscript. We will spare no effort to continue the research in this field in future.](#)

Review 2: This paper is interesting. There are no major and few minor concerns. Regarding the latter, minor language polishing is needed. For example, page 2, second line of Methods. Change "Our" to "our". Page 3, third line of Introduction. Change "From the recent, rapid development " to "From the recent rapid development". The authors should check their paper carefully for grammar and punctuation mistakes.

[Answer: Thank you very much for your suggestion. The sentences you mentioned have been corrected. In addition, we have checked and confirmed the grammar and punctuation of the manuscript.](#)

Review 3: The article is aimed to compare the short-term clinical efficacy of natural orifice specimen extraction surgery (NOSES) using a prolapsing technique and the conventional laparoscopic-assisted approach for low rectal cancer. The title is "Short-term efficacy of natural orifice specimen extraction surgery for low rectal cancer using a prolapsing technique based on propensity score matching". 1. This is a case-control study. 2. A sample size of the study is relatively small. 3. Please review the literature and add more details. 4. Please add the limitations of the study in the discussion section. 5. What are the new knowledges from this study? 6. Finally, please recommend the readers "How to apply this knowledge for routine clinical practice?"

Answer: Thank you very much for your valuable comments and consideration of our manuscript. This is indeed a case-control study in which the sample size is not large enough.

The shortcoming of the study was that the study was a retrospective case-control study with insufficient sample size.

The Discussion part has been modified according to your comments, please see the highlighted part of the manuscript. In this clinical study, we investigated short-term efficacy of natural orifice specimen extraction surgery (NOSES) for low rectal cancer using a prolapsing technique based on propensity score matching. Our study provided the interesting evidence that NOSES of low rectal cancer can achieve satisfactory short-term efficacy and has advantages in reducing postoperative pain, shortening the length of the postoperative hospital stay, and improving patient satisfaction in terms of a more aesthetic appearance of the abdominal wall.

Surgical indications must be strictly controlled when performing this operation. Otherwise, prolonging the operation time will also increase the incidence of surgical complications. We will spare no effort to continue the research in this field in future.

Review 4: This manuscript reports on the short-term clinical efficacy of natural orifice specimen extraction surgery (NOSES) using prolapsing technique and the conventional laparoscopic-assisted approach for lower rectal cancer. The results obtained with 52 patients revealed that NOSES of the low rectal cancer can achieve satisfactory short-term efficacy and has advantage in reducing postoperative pain, shortens the hospital stay, and improves the patient satisfaction. This is well presented and amply documented presentation.

Answer: Thank you for your recognition of our work. Thank you!

Review 5: A quite good idea and usefull for the future but i think the way they decided to manage with the study display direct signs of low quality. For the first all these case controls where the patient is free to decide the procedure he/she is being operated with , suffers of big bias. A new procedure gives always better objective results. Randomised is best. For the second,there is no references about the PSM matching score sysstem. How about the accuracy of this test to

try to balance the baseline data between the groups.?? Then comes the problem with the pictures that are too small to follow the procedure even if the describing is with much details. A quite obvious misunderstanding is in the field of statistical analyses where quality variables are tested with t-test or Fischer. Maybe the mean categorical variables otherwise no possible to test quality variables with quantity tests. At the end how was evaluated the patients post op quality of Life? Which test? No references.

Answer: Thank you very much for your valuable comments and consideration of our manuscript. It is undeniable that the level of evidence in retrospective case-control studies is not as good as RCT, and we are actively preparing for prospective randomized controlled trials.

The PSM is a statistical method for evaluating the effect of non-randomized control data, which makes the covariates of the groups comparable and reduces the influence of confounding factors on the research results. The propensity value is the probability that each subject is assigned to an exposed or control group under a range of observable covariates. But PSM still has its limitations, as you said, RCT is the best. And we will spare no effort to continue the research in this field in future.

For postoperative quality of life, we mainly evaluated postoperative gastrointestinal function in patients, because all patients were low rectal cancer, so the LARS rating scale was chosen. We have uploaded additional materials in the review system.

Review 6: Masroor et al. is an IRB approved case control study designed to establish association of HbA1C, marker of glycemic control and various grades of fatty infiltration in NAFLD patients. A cohort of 300 individuals were recruited randomly, amongst 150 cases had NAFLD and another 150 patients as controls having no fatty infiltration were identified. NAFLD cases were further classified according to the disease severity. Detailed physical examination was done including BMI measurement, fasting blood glucose (FBS) determined enzymatically and HbA1C by TINIA method. ANOVA was applied to find out differences in the levels (FBS), HbA1C and BMI of healthy individuals and NAFLD patients with various grades. The F statistics depicted significant differences in the mean levels of FBS ($F=10.36$, $p<0.01$), HbA1C ($F=15.64$, $p<0.01$) and BMI ($F=33.70$, $p<0.01$) of healthy individuals and patients with NAFLD. Moreover, post hoc test revealed that HbA1C levels were significantly higher in patients of NAFLD having grades II and III compared grade I. Spearman correlation applied to analyze the relationship of HbA1C and BMI with fatty liver revealed that HbA1C is significantly correlated with BMI ($r=0.274$, $p<0.001$) and with the grades of fatty Liver ($r=0.432$, $p<0.001$). They concluded that the study provides substantial evidence that high HbA1C level is significantly associated with presence of NAFLD. Furthermore, the study also shows that its levels are significantly associated with severity of NAFLD. This is a good paper, but I am missing concrete purpose of this bio-finger signature finding. Is it for diagnostic

or prognostic or both? What is the significance of this biosignature in clinical setting?

Answer: Thank you for taking time carefully reviewing our manuscript, I read your comments carefully, which is not related to the content of my manuscript. I want to confirm that is this the review of my manuscript?

Review 7: Overall a well written and conceived manuscript. What needs to be done is a review of the literature regarding outcomes of natural orifice specimen extraction after laparoscopic resection to compare to the set of cases in this manuscript. This can be done using citation number 5 and others like it (there are several in the literature). In addition, what are limitations of the technique? Can the size of the specimen be too large? Is obesity a problem for this technique? Did you learn other lessons about using this technique?

Answer: Thank you for taking time carefully reviewing our manuscript, Limitations of the technology, we have detailed in the text: The inclusion criteria were as follows: (1) low rectal cancer in which the margin was 4 to 6 cm proximate to the anal margin; (2) protuberant tumor with a circumferential diameter < 3 cm; (3) ulcerated tumor with less than 1/2 of the circumferential length of the rectal wall invasion; (4) no distant metastasis and preoperative examination showing the tumor in stage T 1-3 N0 M0; and (5) no history of abdominal surgery.

The exclusion criteria were as follows: (1) patients with a body mass index (BMI) > 35 kg/m²; (2) patients with sigmoid colon and mesangial hypertrophy; (3) sigmoid colon and its mesentery are not long enough to be pulled out through the anus; (4) patients complicated with obstruction, hemorrhage, or perforation and in need of emergency surgery; (5) patients undergoing neoadjuvant therapy; and (6) patients who received preventive terminal ileostomy.

Whether larger specimen can cause anal sphincter damage requires further study.

As I said, according to our experience, patients with a body mass index (BMI) > 35 kg/m² are not suitable.

European and American colorectal surgeons are more inclined to taTME, There are so many NOSES in china, Professor Wang Xishan from Beijing, China has established the China NOSES Alliance and the International NOSES Alliance. The NOSES database shows that China has carried out nearly 3,000 cases of colorectal cancer NOSES surgery, which may be related to Asian BMI, But I have to say that this is a new technology worth trying, which is more beneficial to patients.