

Manuscript NO: 60269

Manuscript Type: CASE REPORT

Title: Pure Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) right hemicolectomy for colon cancer: Case report and surgical video

Dear Editors,

We thank you for your careful consideration of our manuscript. We appreciate the positive and constructive comments and suggestions on our manuscript. We have carefully considered the reviewers' comments and suggestions, responded to these comments and suggestions point by point, and revised the manuscript accordingly. We hope that you will find the revised manuscript suitable for publication. Please do not hesitate to contact us with any questions or concerns regarding the manuscript.

Best regards,

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Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Congratulations for an excellent surgery and a concise presentation of an interesting case. This should certainly be published. My only concern regarding discussion is that information is missing on possible future patient selection. This was a case of underweight (BMI<18.5) female that was not particularly tall. Would higher BMI or smaller/larger height influence the possibility of transvaginal NOTES hemicolectomy or demand different instruments?

Response: We appreciate your positive comments. In accordance with your suggestion, we have added discussion on possible future patient selection in the "Discussion" section (Page 9, Line 11-17). In our opinion, as the surgery is still in the exploratory stage, the selection of patients should be strict. Patients with BMI< 30 kg/m², tumor size < 5cm, no previous abdominal history and clinically diagnosed cT₁₋₃N₀₋₁M₀ lesions according to the 8th Edition of AJCC Cancer Staging Manual may be selected for pure vNOTES. More studies are required to further evaluate the indications. Obese patients (BMI>30 kg/m²) are theoretically more difficult to perform the operation because of the small space in the abdominal cavity and experience on these patients is lacking. Patients with greater height need longer instruments. The use of a robotic system (such as the DaVinci SP) may be a good alternative.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: In the manuscript entitled "Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) right hemicolectomy for colon cancer: Case report and surgical video," the authors present a case of pure vNOTES for ascending colon cancer. I read your document with interest. There are a few comments. [1] I think it is better to emphasize that this case report is pure vNOTES throughout the title, abstract, main text. [2] There have been several reports of hybrid NOTES for colorectal cancer including the left or right-sided colon. I think that you should make a comparison between the pure NOTES and the hybrid NOTES for colon cancer in the discussion section. [3] You should describe the indications and limitations of pure NOTES for the right-sided colon in the discussion section. [4] How many cases of pure NOTES for right-sided colon cancer were performed at your institution? I think it is better to report it as Case series. [5] I think you should show the gravidity and parity in this case.

Response: We appreciate your positive and constructive comments.

[1] We have revised the title, abstract and main text as you suggested to emphasize that this case report is pure vNOTES.

[2] According to your suggestion, we have added a comparison between the pure NOTES and the hybrid NOTES for colon cancer in the "Discussion" section (Page 7, Line 28-31; Page 8, Line 1-6).

[3] According to your suggestion, we have added the indications and limitations of pure NOTES for the right-sided colon in the "Discussion" section (Page 9, Line 11-17).

[4] We have performed 3 cases of pure NOTES for right-sided colon cancer. Current case reported was the first case. As you suggested, we would conduct a case series study and a retrospective case-matching study after more experience is accumulated.

[5] The patient had an uneventful obstetric history (gravidity: 1, parity: 1). We have added it in the "Obstetric History" section according to your suggestion (Page 4, Line 26-27).

Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I'd like to congratulate the authors for demonstrating the feasibility of a vNOTES approach for resection of an ascending cancer with extracorporeal anastomosis in this patient. This technically challenging approach is performed well and the technique is obviously honed from many cases of doing single port abdominal surgery. I am glad to know the patient did well and was discharged without incident. I do however have some comments to make about this report, which perhaps the authors may want to include to some extent in the main paper: 1. Single port surgery is a technically challenging skill set, based on current instrumental limitations. Thus the subset of surgeons that will be able to even consider

to do this approach will be only a small handful and perhaps only a few would be able to do this on a regular basis. This limits the applicability of this topic to even the colorectal surgeons

2. I am concerned about the need to ligate the middle colic vessels in the view that this patient has an ascending colon cancer. Frequently we only ligate the middle colic artery when we deal with hepatic flexure and distal lesions - I understand that this has to be done for length to allow an extracorporeal anastomosis (if not the transverse colon cannot be delivered transvaginally) - however i am concerned that it is unnecessary ligation of a vessel that potentially may lead to anastomotic problems.

3. Based on the technique there are only 2 instruments being used in the surgery. This leads to a rather inadequate approach to traction and countertraction, and I feel there may be difficulties in more anatomically challenging patients (eg obese) to be able to do this safely. Furthermore with the close dissection of major vessels - any bleeding will be difficult to deal with if it occurs. Also the ability of performing an intracorporeal anastomosis will be very limited with only 2 instruments.

4. Perhaps the use of a robotic system (such as the DaVinci SP) may be a good alternative to attempt this procedure via a NOTES procedure. I wonder if the authors have any experience in this?

Response: We appreciate your positive and constructive comments.

[1] We completely agree with your opinion. The development of single-incision laparoscopic surgery for colorectal cancer is mainly limited by the technical challenges, including loss of triangulation, parallel coaxial effect, poor exposure, instruments collision, etc. The unique skill sets cannot be directly adapted from existing conventional laparoscopic surgery experience.

[2] As you said, in this case, the middle colic artery was ligated in order to allow an extracorporeal anastomosis. To ensure the blood supply of the anastomotic stoma in this case, we carefully examined the color and the marginal artery pulse of the transverse colon. In some patients, the blood supply to the transverse colon can be provided by branches of left colic artery. Usually, when we deal with ascending colon and ileocecal lesions, the right branch of the middle colic artery will be ligated and the left branch will be preserved. Intracorporeal anastomosis may be the best way to solve the problem of limited intestinal length, and we are conducting relevant studies.

[3] As we described in the "Discussion" section, before we performed this case, we have performed over 400 cases of single-incision laparoscopic colorectal cancer surgery (Page 8, Line 20-24). These operations were all performed by one surgeon using 2 instruments. The triangulation can be restored by using the internal instrument-cross and external hand-cross technique. In addition, using curved instruments and a flex laparoscope can effectively avoid instrument collisions. For anatomically challenging patients, an additional Trocar was usually added. Therefore, as the surgery is still in the exploratory stage, the selection of patients should be strict (Page 9, Line 11-17). Patients with BMI < 30 kg/m², tumor size < 5cm, no previous abdominal history and clinically diagnosed cT₁₋₃N₀₋₁M₀ lesions according to the 8th Edition of AJCC Cancer Staging Manual may be selected for pure vNOTES. If serious blood vessel or organ injury occurs, we will immediately add additional Trocar(s) or convert to laparotomy. Performing intracorporeal anastomosis is very difficult with only 2 instruments and we are trying to solve the problem with suspension technology.

[4] The DaVinci SP system is a promising way to perform the NOTES procedure. However, relative experience is insufficient due to inadequate equipment in our center. We certainly looking forward to try once it is installed.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Song et al. showed us a case report of vNOTES right hemicolectomy for colon cancer. The paper was well written and the video was good. I listed a few small points to improve the quality of this paper: 1. In the abstract, BACKGROUND section, the authors pointed out that the NOTES for CRC is a complex procedure and rarely used in clinical practice for the technical challenges including loss of triangulation, in-line orientation, and instrument collision. However, to our opinion, its limited application are not only due to technical challenges, but also to ethical concerns. 2. Based on a case with short-term outcomes, the authors could not draw a conclusion as "vNOTES right hemicolectomy, performed by well-experienced surgeons, overcomes the technical challenges of pure NOTES and is feasible for colon cancer.". As we known, a phase 2 clinical trial in China is carrying out to prove the feasibility and safety of hybrid NOTES application in colon cancer. 3. There are some repeated contents, such as time to drink water and soft diet. 4. As we known, Fu et al. have presented a video article of hybrid NOTES for a case with sigmoid colon cancer in Surgical Oncology. 5. Ethical concerns should be mentioned in the DISCUSSION section. The advantages of intracorporeal anastomosis should also be discussed.

Response: We appreciate your positive and constructive comments.

[1] We have added ethical concerns in the "BACKGROUND" section as you suggested (Page 2, Line 5-6).

[2] According to your suggestion, we have revised the conclusion.

[3] According to your suggestion, we have deleted repeated contents.

[4] We have watched the surgical video of Fu et al. It was an excellent surgery. However, there are many differences between pure NOTES and hybrid NOTES. We have added a comparison between the pure NOTES and the hybrid NOTES for colon cancer in the "Discussion" section (Page 7, Line 28-31; Page 8, Line 1-6).

[5] According to your suggestion, we have added the ethical concerns (Page 8, Line 26-29) and the advantages of intracorporeal anastomosis (Page 9, Line 3-10) in the "Discussion" section.

EDITORIAL OFFICE'S COMMENTS

(1) Science editor: The authors did not upload the video. "Dear editor, Where can I find the video of this case report? Thanks. "

Response: Thank you for your comments. We have uploaded the surgical video.

(2) Editorial office director: I have checked the comments written by the science editor.

Response: Thank you for the consideration of this paper and for your comments.

(3) Company editor-in-chief: I recommend the manuscript to be published in the World Journal of Clinical Cases. Before final acceptance, the author(s) must add a table/figure to the manuscript.

Response: Thank you for the consideration of this paper and for your comments. We have added two figures to the manuscript.