Outcomes of trans-anal natural orifice specimen extraction combined with laparoscopic anterior resection for sigmoid and rectal carcinoma
An observational study

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Abstract
Colorectal carcinoma is currently the third most frequent cancer worldwide. Conventional open surgery was replaced by laparoscopic anterior resection with total mesorectal excision for the treatment of sigmoid and rectal carcinomas; however, it needed an incision to harvest the specimen, which contributed to complications. In 2013, trans-anal natural orifice specimen extraction laparoscopic anterior resection (Ta-NOSE-LAR) to treat sigmoid and rectal carcinoma was performed in our hospital for the first time. The aim of this study was to investigate the outcomes of Ta-NOSE-LAR in sigmoid and rectal carcinoma.

Seventy-three patients diagnosed with sigmoid and rectal carcinoma were enrolled between September 2013 and June 2016. Thirty-five patients underwent Ta-NOSE-LAR, whereas the others underwent traditional laparoscopic anterior resection (LAR). We compared the operative data, postoperative complications, pathological evaluation results, and incision-related complications between the 2 groups.

Our result showed that the operative time, specimen length, tumor size, amount of total lymph nodes, and lymph node metastasis between the 2 groups were not statistically different. Further, without abdominal scaring for harvesting the specimen, the operative blood loss (49.29 ± 14.63 vs 69.29 ± 13.54 mL, \(P < .001\)) and post-operation hospital stay (5.77 ± 0.94 vs 6.76 ± 0.75 days, \(P < .001\)) of the Ta-NOSE-LAR group were less than those of the LAR group. Besides, the follow-up data showed that 2 patients were lost to follow-up, and 1 patient had liver metastasis 2 years after surgery in the LAR group, whereas the others showed no regional recurrence, distant metastases, or critical complications.

Ta-NOSE-LAR is a valuable and alternative surgical method to treat sigmoid and rectal carcinoma, with the advantages of being a scarless procedure and having a lower post-operation hospital stay duration.

Abbreviations: BMI = body mass index, CT = computer tomography, LAR = laparoscopic anterior resection, MRI = magnetic resonance imaging, NOSE = transanal natural orifice specimen extraction, NOTES = natural orifice transluminal endoscopic surgery, POHS = post-operation hospital stay, Ta-NOSE-LAR = trans-anal natural orifice specimen extraction laparoscopic anterior resection, TEM = transanal endoscopic microsurgery, TME = total mesorectal excision.

Keywords: laparoscopic, natural orifice specimen extraction, scarless, sigmoid and rectal carcinoma, trans-anal endoscopic microsurgery

1. Introduction
Colorectal carcinoma has the third highest incidence among cancers worldwide.\cite{1} Conventional open surgery has been gradually replaced by laparoscopic anterior resection with total mesorectal excision (LAR/TME) for sigmoid and rectal carcinomas, which is advantageous for patients.\cite{2-5} However, LAR/TME needs an incision to harvest the specimen, which contributes to complications such as wound infection, incisional hernias, and peritoneal implantation of tumor residues.\cite{6-10} Because of these associated complications, a scarless surgical design became a topic of focus. Some surgical centers have reported successful application of the transanal and transvaginal approaches in laparoscopic colorectal surgery.\cite{11,12} Recently, Kvasha et al.\cite{13} reported on the use of the transanal natural orifice specimen extraction (NOSE) technique in a porcine model, which was a good trial before application of this technique in human. We adopted the NOSE technique, to remove the sigmoid and rectum carcinoma specimen transanally; therefore, avoiding the creation of an abdominal incision.\cite{12,14,15} Since 2013, we began to perform trans-anal NOSE in combination with laparoscopic anterior resection (Ta-NOSE-LAR) to treat sigmoid and rectum carcinoma. This cohort study aimed to evaluate the outcomes of Ta-NOSE-LAR in the treatment of sigmoid and rectum carcinoma.
2. Methods

2.1. Ethics statement

All surgical procedures were approved by the Department of Surgery at the Beijing Friendship Hospital, Capital Medical University (Beijing, China), and the Beijing Friendship Hospital ethics committee (document number: BJFH-EC/2013-069). Written informed consent was obtained from the patients for the surgery and for publication of this cohort study and any accompanying images.

2.2. Patients

All data are presented in Tables 1–3, we can also share the raw data upon request. Seventy-three patients participated in this study and the inclusion criteria and did not fulfill the exclusion criteria.

The exclusion criteria were as follows: confirmed malignancy on colonoscopy and pathological examination; confirmed sigmoid and colorectal tumors of diameter ≤5 cm on computed tomography (CT); no sign of bowel obstruction or hemorrhage; no severe hepatic or kidney dysfunction or hemorrhagic tendency; no past history of abdominal surgery; no metastasis observed on CT or magnetic resonance imaging (MRI).

The exclusion criteria were as follows: suffering from severe diseases, such as cardiovascular diseases, myocardial infarction, or cerebrovascular diseases; cannot accept to accept medical and radiological therapy after the operation; pregnant or lactating women; history of other tumors within the past 5 years; history of organ transplantation.

This study was an observational study. For the patients indicated for Ta-NOSE-LAR, we explained the methods used in both Ta-NOSE-LAR and LAR in detail before the operation. The patients selected one of the methods, and that was the method used. We compared the outcomes of the 35 patients who selected Ta-NOSE-LAR and 37 patients who selected LAR, both of which were performed to treat sigmoid and rectum carcinoma at our hospital since June 2013. Table 1 lists information on the sex, age, body mass index (BMI), stage of the disease, and other factors.

2.3. Surgical technique

2.3.1. Ta-NOSE-LAR group. The patient was placed in the modified lithotomy position and under general anesthesia. An artificial pneumoperitoneum was established (CO2: 12 mmHg). Then, we adopted a 5-port technique: a 10-mm trocar for the camera was placed 1.5 cm superior to the umbilicus, 2 5-mm ports were placed in the upper right and lower left abdominal quadrants, and 1 12-mm trocar port was inserted in the upper-right and lower-right abdominal quadrants.

Abdominal part: First, we separated the splenic flexure to mobilize the distal part of the colon. Second, we completely exposed the sigmoid mesentery and inferior mesenteric vessels; then, we performed high ligation of the inferior mesenteric artery with Haemolocks (Fig. 1) and dissected the lymph node and performed skeletonization of the intestinal wall at the level of anastomosis. Next, according to the transanal endoscopic microsurgery (TEM) principle, we mobilized the mesorectum to the pelvic floor (4th–5th sacral vertebrae of peritoneal reflection). Third, we dissected the lateral colonic attachments along the White line of Toldt to mobilize the sigmoid, distal part of the descending colon, and upper rectum. Two mobile intestine Hem-o-locks were placed at the designated incision points of the proximal sigmoid section (Fig. 2), and we adopted the Endoscopic Linear Cutter-Straight to transect the distal rectum approximately 5 cm below the tumor (Fig. 3). Anal part: Two stitches were placed with 3–0 surgical thread on both sides of the distal rectum stump for traction. An enema with iodine saline solution was administered before placement of the TEM socket (Fig. 4). We adopted a harmonic anvil to open the distal rectum stump. Then, a laparoscopic specimen retrieval bag was inserted into the abdominal cavity using TEM tools, and the specimen was removed transanally (Figs. 5 and 6). The circular stapler anvil was fixed at the proximal sigmoid stump with purse string sutures, and then the TEM socket was removed and the distal rectum stump, closed with Endo-GIA. A circular stapler was inserted into the rectum through the anus (Fig. 7), and sigmoid-rectum anastomosis was performed by the laparoscopic surgery (Fig. 8). No additional abdominal incision apart from the 5 trocars punctures was needed for Ta-NOSE-LAR (Fig. 9).

2.3.2. LAR group. The modified lithotomy position, artificial pneumoperitoneum, and 5-port laparoscopic technique for the Ta-NOSE-LAR group were common to the LAR group as well, except the anal part operation. We performed all procedures using laparoscopic tools, but we left a 5-cm incision in the
Figure 1. High ligation of the inferior mesenteric artery with Haemolocks, the yellow arrow showed the mesenteric vessels, and the blue arrow pointed out the Haemolocks.

Figure 2. Two mobile intestine Haemolocks were placed at the designated incision points of the proximal sigmoid section, the blue arrow showed the mobile intestine clamp placed at the designated part of the sigmoid.

Figure 3. Endoscopic Linear Cutter-Straight to transect the distal rectum approximately 5 cm below the tumor, the yellow arrow showed the Endoscopic Linear Cutter-Straight, which transecting the distal rectum.
Figure 4. An enema with iodine saline solution was administered before the placement of transanal endoscopic microsurgery (TEM) socket (yellow arrow).

Figure 5. Laparoscopic-dedicated sample bag was inserted into abdominal cavity via TEM tools, the blue arrow showed the specimen bag and the yellow showed the TEM tool. TEM = transanal endoscopic microsurgery.

Figure 6. The specimen bag was removed transanally via the TEM (red arrow). TEM = transanal endoscopic microsurgery.
abdomen to remove the specimens. All patients underwent chemotherapy or radiotherapy after the operation.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 19.0, released by 2010 (IBM corp., Armonk, NY). P-values < .05 were considered statistically significant. Comparisons between 2 groups were performed with the independent samples t test, and the chi-squared test (or Fisher exact test when needed) was used for comparison of categorical data.

3. Results

Both Ta-NOSE-LAR and LAR were performed successfully without conversion to open surgery. The results (Table 2) showed that operative time is not statistically significantly different between the 2 groups (170.37 ± 32.91 vs 161.82 ± 8.10 minute, P = .13), proving that the extra anal procedure will not prolong the operation time. Additionally, the Ta-NOSE-LAR group had less blood loss (49.29 ± 14.63 vs 69.29 ± 13.54 mL, P < .001), a shorter post-operation hospital stay (POHS) (5.77 ± 0.94 vs 6.76 ± 0.75 days, P < .001), and no incision-related complications. Although the low blood loss was not a significant improvement in clinical practice, it could be considered a small improvement since an incision was not needed. Moreover, mastering Ta-NOSE-LAR could be a prerequisite for performing a natural orifice transluminal endoscopic surgery (NOTES), such as trans-anal total mesorectal excision. Ten patients in the LAR group had wound infection; Clavien–Dindo classification grade II and grade IIIa complication rates were 73% and 27%, respectively (Table 3).

![Figure 7](image1.jpg)

Figure 7. The surgeon fixed the circular stapler through the purse-string suture for reconstruction; the yellow arrow showed the circular stapler and the blue arrow showed the purse string suture.

![Figure 8](image2.jpg)

Figure 8. The image showed the sigmoid-rectum anastomosis, which we should pay attention to the mesentery was separated enough to perform anastomosis.

![Figure 9](image3.jpg)

Figure 9. The image showed great appearance and scarless after the Ta-NOSE-LAR. Ta-NOSE-LAR = trans-anal natural orifice specimen extraction laparoscopic anterior resection.

| Table 2 Perioperative information between 2 groups. |
|---------------------------------------------------|
| Ta-NOSE-LAR (n = 35) | LAR (n = 38) | P-value |
|----------------------|-------------|---------|
| Operative time, min  | 170.37 ± 32.91 | 161.82 ± 8.10 | P = .13 |
| Blood loss, mL       | 49.29 ± 14.63 | 69.29 ± 13.54 | P < .001 |
| Specimen length, cm  | 16.00 ± 4.11 | 15.96 ± 4.55 | P = .97 |
| Tumor size, cm       | 3.05 ± 0.92 | 3.25 ± 0.99 | P = .32 |
| Amount of harvest lymph node | 14.57 ± 6.72 | 13.36 ± 7.29 | P = .39 |
| Amount metastatic lymph node | 1.51 ± 2.67 | 1.16 ± 2.67 | P = .52 |
| POHS, d              |             |         | P < .001 |
| Mean                 | 5.77 ± 0.94 | 6.76 ± 0.75 |         |
| Range                | 3–8         | 6–9     |         |
| pTNM-staging-T       |             |         | P = .55 |
| T2                   | 15          | 19      |         |
| T3                   | 11          | 19      |         |
| pTNM-staging-N       |             |         | P = .29 |
| NO                   | 20          | 17      |         |
| N1                   | 15          | 21      |         |

LAR = laparoscopic anterior resection, POHS = post-operation hospital stay, Ta-NOSE-LAR = trans-anal natural orifice specimen extraction laparoscopic anterior resection.
No severe complications such as anastomotic leakage, anastomotic stenosis, or abdominal abscess were observed in both groups. In the LAR group, 2 patients were lost to follow-up and 1 patient had liver metastasis 2 years after the surgery. Other patients showed no severe complications until April 2018.

4. Discussion

Laparoscopic surgery recommended for minimally invasive colorectal surgery has changed surgical concepts and approaches in the surgical field since its advent in the early 1990s.[16–18] However, the suggestion that the laparoscopic approach is minimally invasive may not be very accurate as a 5-cm long incision is still needed to collect the specimen. Some studies have reported[12,19,20] successful outcomes with laparoscopy in terms of specimen extraction, as with this approach, an abdominal incision is not required.

As the results of our analysis showed, the major difference between the Ta-NOSE-LAR and LAR was that the Ta-NOSE-LAR was a scarless procedure; with Ta-NOSE-LAR, an abdominal incision that could cause infections and hernias was not required. Additionally, because an abdominal incision was not required, Ta-NOSE-LAR also decreased intraoperative blood loss and the post-operation hospital stay (POHS). Although this may not be a huge improvement in terms of reduced blood loss and AOHs, Ta-NOSE-LAR is an essential technique to have mastered before a surgeon can start performing natural orifice transluminal endoscopic surgery (NOTES), because NOTES is a truly scarless surgery (complete absence of scars, including the one caused by the trocar incision). However, we recommend that this technique should be performed by a veteran laparoscopic surgeon as all operations involve laparoscopy. In routine clinical practice, Ta-NOSE-LAR can be an alternative surgical style to treat the sigmoid and rectal carcinoma, and it can also be effective in avoiding incision-related complications.

It must also be noted that the Ta-NOSE-LAR approach has some limitations: the tumor size and depth of tumor invasion were important factors affecting the management of Ta-NOSE-LAR, because the longest diameter of a TEM socket was 5 cm, and the trans-anal nature orifice specimen extraction technique is thus not suitable for tumors with a diameter larger than 5 cm. Moreover, this technique can only be used when the tumor invasion level does not exceed T4[21] (tumor invades the visceral peritoneum or invades adjacent organs or tissues), and it is important to confirm negative surgical margins and provide enough operation space to mobilize the sigmoid, distal part of the descending colon and the upper rectum without the interference of the tumor. The trans-anal endoscopic microsurgery socket was essential because it provided a safe and steady platform for anvil installation and sample extraction; however, one limitation was that the patient experienced archostenosis and anal stretch function abnormalities, which would cause problems with the TEM socket trans-anally. As Table 1 shows, the mean BMI of both groups was largely normal (22.64 ± 1.95 and 23.41 ± 1.60), and the patient BMIs were similar to those commonly seen in Asians. Thus, we need to enroll more patients with high BMIs to verify the effectiveness of Ta-NOSE-LAR in this group. The sample size is relatively small, and the study was observational; therefore, we need to increase the sample size and design a prospective study in the future.

In conclusion, adopting Ta-NOSE-LAR to excise tumors and extract specimens had several advantages, including the avoidance of scar formation, reduced blood loss, and reduced post-operation hospital stay. Moreover, we believe that minimally invasive surgery will be a key element in the treatment of all types of surgical diseases in the future.

Author contributions

Designed the study: Wang Jin and Zhang Zhong-tao.
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References

[1] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin 2017;67:7–30.
[2] Parker JM, Feldmann TF, Cologne KG. Advances in laparoscopic colorectal surgery. Surg Clin North Am 2017;97:547–60.
[3] Martinez-Pérez A, Carra MC, Brunetti F, et al. Pathologic outcomes of laparoscopic vs open mesorectal excision for rectal cancer: a systematic review and meta-analysis. JAMA 2017;152:e165665.
[4] Bertelsen CA. Complete mesocolic excision an assessment of feasibility and outcome. Dan Med J 2017;64 pii: B5334.
[5] Feinberg AE, Chesney TR, Acuna SA, et al. Oncologic outcomes following laparoscopic versus open resection of pT4 colon cancer: a systematic review and meta-analysis. Dis Colon Rectum 2017;60:116–25.
[6] Yamamoto S, Fujita S, Akasu T, et al. Wound infection after elective laparoscopic surgery for colorectal carcinoma. Surg Endosc 2007;21:2248–52.
[7] Pucciarelli S, Zorzi M, Gennaro N, et al. In-hospital mortality, 30-day readmission, and length of hospital stay after surgery for primary colorectal cancer: a national population-based study. Eur J Surg Oncol 2017;43:1312–23.
[8] Widmar M, Keskin M, Beltran P, et al. Incisional hernias after laparoscopic and robotic right colectomy. Hernia 2016;20:723–8.
[9] Radojkovic M, Gligorijevic J, Stojanovic M, et al. Laparotomy site implantation metastasis of carcinoma of the papilla of Vater. Scott Med J 2017;62:119–21.
[10] Mishin I, Ghidirim G, Vozian M. Appendiceal mucinous cystadenocarcinoma with implantation metastases to the incision scar and cutaneous fistula. J Gastrointest Cancer 2012;43:349–53.
[11] Han FH, Hua LX, Zhao Z, et al. Transanal natural orifice specimen extraction for laparoscopic anterior resection in rectal cancer. World J Gastroenterol 2013;19:7751–7.
[12] Franklin MEJr, Liang S, Russek K. Natural orifice specimen extraction in laparoscopic colorectal surgery: transanal and transvaginal approaches. Tech Coloproctol 2013;17(suppl):S63–7.

[13] Kvasha A, Hadary A, Biswas S, et al. Novel totally laparoscopic endolumenal rectal resection with transanal natural orifice specimen extraction (NOSE) without rectal stump opening: a modification of our recently published clean surgical technique in a Porcine Model. Surg Innov 2015;22:245–51.

[14] Knol J, D’Hondt M, Dozois EJ, et al. Laparoscopic-assisted sigmoidectomy with transanal specimen extraction: a bridge to NOTES? Tech Coloproctol 2009;13:65–8.

[15] Shimizu H, Adachi K, Ohtsuka H, et al. Totally laparoscopic resection for low sigmoid and rectal cancer using natural orifice specimen extraction techniques. J Surg Laparosc Endosc Percutan Tech 2017;27:e74–9.

[16] Zelhart M, Kaiser AM. Robotic versus laparoscopic versus open colorectal surgery: towards defining criteria to the right choice. Surg Endosc 2017;32:1–5.

[17] Devoto L, Celentano V, Cohen R, et al. Colorectal cancer surgery in the very elderly patient: a systematic review of laparoscopic versus open colorectal resection. Int J ColoRectal Dis 2017;32:1237–42.

[18] Kitano S, Inomata M, Mizusawa J, et al. Survival outcomes following laparoscopic versus open D3 dissection for stage II or III colon cancer (JCOG0404): a phase 3, randomised controlled trial. Lancet Gastroenterol Hepatol 2017;2:261–8.

[19] Kvasha A, Khalifa M, Biswas S, et al. Unlimited-length proctocolectomy utilizing sequential intussusception and pull-through: novel clean endolumenal note-assisted technique with transanal natural orifice specimen extraction without rectal stump opening in a porcine model. Surg Innov 2016;23:456–62.

[20] Andrés G, García-Mediero JM, García-Tello A, et al. The best option: Umbilical LESS radical nephrectomy with vaginal extraction. Actas Urol Esp 2015;39:188–94.

[21] de’Angelis N, Landi F, Vitali GC, et al. Multicentre propensity score-matched analysis of laparoscopic versus open surgery for T4 rectal cancer. Surg Endosc 2017;31:3106–21.