

Application of NOSES Combined with ERAS in the Treatment of Rectal Cancer

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Abstract

Background: In recent years, Natural Orifice Specimen Extraction Surgery (NOSES) has been developed rapidly, and the feasibility and advantages of Enhance Recovery after Surgery (ERAS) also have been recognized in colorectal cancer. How about combining NOSES with ERAS? In this article, we are trying to answer this question.

Methods: The 120 cases of rectal cancer patients who met the inclusion criteria from January 2018 to December 2019 were divided into three groups using the random number table method: traditional care control group (laparoscopic assisted surgery + traditional care), ERAS control group (laparoscopic adjuvant surgery + ERAS) and experimental group (NOSE + ERAS), 40 cases in each group, randomized controlled study was performed.

Results: There were no significant differences in surgical time, bleeding volume, number of detected lymph nodes, incidence of venous thrombosis in the lower extremities, anastomotic leakage, and abdominal infection among the three groups ($P > 0.05$). The total complication rate, incidence of incision-related complications, incidence of pulmonary and urinary tract infections, and postoperative pain NRS score in the NOSES+ERAS group cases were significantly lower than those in the other two control groups. Patients in the NOSES + ERAS group had higher satisfaction rates and shorter postoperative hospital stay than those in the other two control groups. The feeding time and exhaust time after surgery in NOSES+ERAS group and ERAS control group were earlier than those in traditional care control group. The above differences are statistically significant ($P < 0.05$).

Conclusion: The NOSES radical resection of rectal cancer under the guidance of ERAS achieved more minimally invasive cosmetic and functional, individualized treatment effect in laparoscopic surgery. There is a greater advantage that ERAS combined with the NOSES radical resection of rectal cancer which is worthy of popularization and with good application prospect.

Background

In recent years, with the advancement of economic, culture and medicine, patients' demands for quality of life and cosmetic effects after surgery have been increasing. Natural Orifice Specimen Extraction Surgery (NOSES) has been developed rapidly in the world; at the same time, the feasibility and advantages of Enhance Recovery after Surgery (ERAS) in colorectal cancer have been recognized by numerous scholars. How about combining NOSES with ERAS? In this article, we are trying to answer this question, and it is reported as follows:

Materials And Methods

General Information

The 120 cases of rectal cancer patients who met the inclusion criteria from January 2018 to December 2019 in the Central Hospital of Shaoyang were divided into three groups using the random number table method: traditional care control group (laparoscopic assisted surgery + traditional care), ERAS control group (laparoscopic assisted surgery + ERAS) and experimental group (NOSE surgery + ERAS), 40 cases in each group. All patients were clearly diagnosed with upper or middle rectal cancer, the distance from the tumor site to the dentate line is greater than 5 cm, tumor invasion depth T1-T3, and tumor circumference diameter < 5 cm; and patients with poor cardiopulmonary function, distant metastases, neoadjuvant chemoradiotherapy, or prophylactic stoma were excluded.

Surgical Method

All patients underwent D₃ lymph node dissection, proximal mesentery and distal rectal cut off under laparoscopy abide by TME (or TSME) principles. In the laparoscopic assisted surgery group, a 5–8 cm abdominal incision was needed to remove the tumor specimen and to connect the sigmoid to rectum by end-to-end anastomosis. In the NOSES group, there was no auxiliary incision, depending on the location of the tumor and the length of the sigmoid mesentery, NOSES II or IV was adopted to remove the specimen from the rectum as showed in the following figure.

Perioperative treatment plans

ERAS treatment plan

Strengthen pre-operative education and communication, and introduce the ERAS measures and treatment plans to the patients in detail; Regular diet as usual after admission, fasting 12 hours before surgery and oral mannitol catharsis cleans the intestines, and drink 300 ml of carbohydrates 2 hours before surgery; no gastric tube and no enema before operation; urinary catheter was indwelled after anesthesia and remove in 24 hours after operation; transabdominal fascia block anesthesia combined with general anesthesia; Restricted infusion during the operation, vasoactive drugs should be used to maintain blood pressure when blood pressure is lowered; warmed liquid and insulation blankets should be used to keep warm during the operation; postoperative rehydration should be limited within 2000 ml/day, and the amount of infusion should be gradually reduced as oral consumption increases; start drinking water 6 hours after surgery, start a full flow diet on the first day after surgery, and start eating semi-liquid food after venting the anus, but anastomotic leak must be ruled out; remove the pelvic drainage tube 3–5 days after operation according to the inflammatory index and the amount and color of the drainage tube; Postoperative intravenous analgesia, nonsteroidal analgesics if necessary; began to walk out of bed on the first day after surgery, and so on.

Traditional care plan

General education after admission; intestinal preparation started 3 days before surgery, mannitol was used for diarrhea one day before surgery, and enema was cleaned in the morning on the day of surgery; fasting was performed 12 hours before surgery, and water was absent 8 hours before surgery; nasogastric tubes and catheters were done in the ward; general anesthesia is used for anesthesia, and fluid rehydration is adopted when the blood pressure is low after anesthesia; there is no thermal insulation during the operation, The volume of fluid replacement is greater than 2000 ml/d after surgery; remove the abdominal drainage 7 days after operation; remove the stomach tube and drink water after venting anus, take a full liquid food the next day after exhausting, and a semi-liquid food after defecation; use morphine and dulidine to relieve pain; Voluntary out of bed activities for recovery.

Evaluation methods

Ceftriaxone was used to prevent infection for all patients during the perioperative period. The drainage tube ascites was cultured on the first day after operation. The data of surgical conditions (e.g. the operation time, incision length, blood loss, number of lymph node dissections), postoperative complications (e.g. the incidence of postoperative pulmonary infection, urinary tract infection, abdominal infection, anastomotic leakage, venous thrombosis of the lower limbs, and incision-related complications), and patient recovery (e.g. postoperative pain score, recovery time, exhaust time, postoperative hospitalization days, and patient satisfaction) from the three groups was compared and analyzed.

NRS pain grade score (digital scoring method) was used to grade the patients' postoperative incision pain: 0 for no pain; 1 to 3 for mild pain; 4 to 6 for moderate pain; 7 to 10 for severe pain. Patients can be discharged when they meet the following conditions: can enter a semi-liquid diet, have smooth defecation, can move freely, do not require intravenous infusion treatment, and oral pain medication can effectively relieve pain

Statistical analysis

SPSS 19.0 software was used for statistical analysis. The measurement data was expressed by ($\bar{x} \pm s$). The measurement data were analyzed by single factor analysis of variance and SNK-q test, and the count data by χ^2 test. $P < 0.05$, the difference is statistically significant.

Results

Surgical conditions

The operation of all patients were successfully completed without major bleeding and anesthesia complications. General information (age, gender, comorbidities, clinical stage, etc.) of the three groups was not statistically different. The incision length of the NOSES + ERAS group was significantly shorter than that of the two control groups, and the difference was statistically significant ($F = 23.798$, $P < 0.01$). There were no significant differences in surgical time, bleeding volume, and number of detected lymph nodes among the three groups ($F = 1.604, 1.835, 2.351$ respectively, all $P > 0.05$). The detailed data were showed in Table 1.

Table 1
Data of surgical conditions ($\bar{x} \pm s, n_1 = n_2 = n_3 = 40$)

Groups	Surgical time(min)	Incision length(cm)	Bleeding volume(ml)	Number of detected lymph nodes
Traditional care control	150.1 \pm 21.2	10.8 \pm 1.2 ^a	22.0 \pm 13.5	13.5 \pm 3.1
ERAS control	152.2 \pm 16.5	10.6 \pm 1.3 ^b	23.0 \pm 12.8	14.0 \pm 5.4
NOSES + ERAS	158.2 \pm 18.5	3.9 \pm 0.2	26.0 \pm 14.5	14.4 \pm 4.1
F value	1.604	23.798	1.835	2.351
P value	>0.05	<0.01	>0.05	>0.05
<i>Notes^a Comparison between NOSES + ERAS group and traditional care control group [P] 0.05</i>				
<i>^b Comparison between NOSES + ERAS group and ERAS control group [P] 0.05.</i>				

Postoperative Complications

Postoperative complications, abdominal infection, incision complications (incision infection, incision dehiscence, incision hernia, etc.), lower extremity venous thrombosis, pulmonary infection, abdominal infection, anastomotic leakage, were observed and recorded. The incidence of total complications in NOSES + ERAS group was significantly lower than that in the two control groups (7.5% VS 17.5% VS 57.5%, $\chi^2 = 9.46$, $P < 0.01$), and the rate of total complications in ERAS control group was also significantly lower than that in the traditional control group (17.5% VS 55%, $\chi^2 = 11.86$, $P < 0.01$); the incidence of incision-related complications in the NOSES + ERAS group was significantly lower than that in the two control groups (0% VS 10% VS 12.5%, $\chi^2 = 9.83$, $P < 0.01$); the incidence of pulmonary infection and urinary tract infection in patients in the NOSES + ERAS group and the ERAS group control group was significantly lower than that in the traditional control group (0% VS 0% VS 10% and 0% VS 0% VS 25%, $\chi^2 = 6.83, 16.97$ respectively, $P \leq 0.05$ and $P \leq 0.01$); There were no

statistically significant differences in the incidence of lower extremity venous thrombosis, anastomosis leaks and abdominal infections among the three groups ($\chi^2 = 1.43, 0.45, 0.87$ respectively, all $P > 0.05$). The detailed data as shown in table 2.

Table 2
Incidence of postoperative complications(% $n_1 = n_2 = n_3=40$)

Groups	Incision-related complications	Pulmonary infection	Urinary tract infection	Lower extremity venous thrombosis	Anastomosis leaks	Abdominal infections	Total complications
Traditional care control	5(12.5) ^a	4(10.0) ^{ac}	10(25) ^{ac}	1(2.5)	2(5)	1(2.5)	23(57.5) ^{ac}
ERAS control	4(10.0) ^b	0(0)	0(0)	0(0)	3(7.5)	0(0)	7(17.5) ^b
NOSES + ERAS	0(0)	0(0)	0(0)	0(0)	2(5)	1(2.5)	3(7.5)
χ^2 value	9.83	6.83	16.97	1.43	0.45	0.87	9.46
P value	<0.01	<0.05	<0.01	>0.05	>0.05	>0.05	<0.01
<p>Notes^a Comparison between NOSES + ERAS group and traditional care control group [P] 0.05]</p> <p>^b Comparison between NOSES + ERAS group and ERAS control group [P] 0.05.</p> <p>^c Comparison between ERAS control group and traditional care control group [P] 0.05.</p>							

Postoperative Recovery

Postoperative pain NRS score, postoperative feeding time, exhaust time, postoperative hospitalization time, and patient satisfaction were statistically analyzed. Postoperative pain NRS score in the NOSES + ERAS group were significantly lower than those in the two control groups (4.5 VS 5.6 VS 7.6 respectively, $F = 5.62, P < 0.01$), and the NRS score in the ERAS control group was also significantly lower than the traditional control group (5.6 VS 7.6, $q = 3.52, P < 0.05$). The postoperative feeding time and exhaust time of the NOSES + ERAS group and the ERAS control group were earlier than those of the traditional control group (1.2 VS 1.3 VS 2.8 and 2.0 VS 2.1 VS 2.9, $F = 4.37, 3.57$ respectively, $P < 0.01$ and $P < 0.05$), and there was no significant difference between the NOSES + ERAS group and the ERAS control group ($q = 2.74, P > 0.05$). The postoperative hospital stay time of the NOSES + ERAS group was significantly shorter than that of the two control groups (6.2 VS 7.3 VS 9.1, $F = 3.46, P < 0.05$), and the time of the ERAS control group was also significantly shorter than that of traditional control group (7.3 VS 9.1, $q = 3.54, P < 0.05$). Patient satisfaction in the NOSES + ERAS group was significantly higher than that in the two control group (95% VS 85% VS 70%, $\chi^2 = 6.86, P < 0.05$), and the ERAS control group also had higher satisfaction than the traditional control group (85% VS 70%, $\chi^2 = 6.43, P < 0.05$). As shown in Table 3.

Table 3
Postoperative recovery index($\bar{x} \pm s, n_1 = n_2 = n_3 = 40$)

Groups	NRS score	Feeding time(d)	Exhaust time(d)	Postoperative hospitalization time(d)	Cases of Satisfaction score/90(%)
Traditional care control	7.6 \pm 0.9 ^{ac}	2.8 \pm 1.2 ^{ac}	2.9 \pm 1.3 ^{ac}	9.1 \pm 2.5 ^{ac}	28(70) ^{ac}
ERAS control	5.6 \pm 0.9 ^b	1.3 \pm 0.5	2.1 \pm 0.6	7.3 \pm 1.5 ^b	34(85) ^b
NOSES + ERAS	4.5 \pm 0.8	1.2 \pm 0.4	2.0 \pm 0.5	6.2 \pm 1.8	38(95)
Statistical value	F = 5.62	F = 4.37	F = 3.57	F = 3.46	$\chi^2 = 6.86$
P value	<0.01	<0.01	<0.05	<0.05	<0.05
Notes ^a Comparison between NOSES + ERAS group and traditional care control group P 0.05					
^b Comparison between NOSES + ERAS group and ERAS control group P 0.05.					
^c Comparison between ERAS control group and traditional care control group P 0.05.					

Discussion

With the advancement of economic and medicine, patients' demands for quality of life and cosmetic effects after surgery are increasing. At the same time, higher requirements and challenges have been put forward to surgeons.

In the past 20 years, from traditional open surgery to conventional laparoscopic surgery to NOSES surgery, surgery has been developed rapidly. NOSES surgery uses conventional laparoscopic surgical instruments and familiar surgical paths to complete the radical resection of the tumor under laparoscopy, and then removes the specimen through the natural port and completes the digestive tract reconstruction [1]. There are only a few small puncture holes in the abdomen, without assistance incisions, and overcoming NOTES surgical instruments and technical obstacles, to obtain good cosmetic and minimally invasive results, and to maximize the benefits of conventional laparoscopic platforms. At present, it is believed that the NOSES radical resection of rectal cancer is mainly applicable to tumors with a depth of no more than T₃. Transanal specimens require a maximum peripheral diameter of less than 5 cm, and transvaginal specimens require a maximum peripheral diameter of less than 5-7cm. At the same time, we should fully grasp the operation specifications of specimen collection, and strictly abide by the principles of aseptic operation and no tumor [1, 2]. According to the location of the rectal tumor and the way of removing the specimen, rectal NOSES surgery is currently divided into five types of surgery: I, II, III, IV, and V [1, 4]. Because the anastomosis position of type I is very low, prophylactic colostomy is often required, and type III / V type requires a vaginal incision, which causes some patients and their families to be unacceptable. Transanal specimens are not restricted by gender, so they have become the most widely used method for specimen collection.

At present, the NOSES operation in our center is mainly type I and type II. In this study, compared with patients with traditional laparoscopy (traditional nursing control group and ERAS control group), NOSES surgery does not affect the radical dissection of the tumor, and does not increase the risk of surgery time, bleeding, abdominal infection and anastomotic leakage, but it has obvious advantages in terms of postoperative pain, incision infection, and postoperative

hospital stay. It not only achieves a radical resection of the tumor, but also greatly reduces the patient's trauma, postoperative wound pain, and stress response is reduced, and then to promote the patient's postoperative recovery.

On the other hand, with the long-term clinical observation of specialists and the introduction of evidence-based medicine theory, the feasibility and superiority of the application of the ERAS concept in colorectal cancer have been recognized by many scholars in recent years. Studies show that ERAS can reduce postoperative complications and the risk of death, reduce hospitalization costs and length of stay, improve patient compliance and satisfaction, and thus obtain good treatment results.^[4-7] In addition, Gustafsson and their team's studies have shown that ERAS can not only achieve satisfactory short-term effects, but also significantly improve the 5-year survival rate of patients with colorectal cancer after surgery, and the higher the compliance with the ERAS program, the more obvious the effect^[8]. In this study, postoperative complications such as lung infection and urinary tract infection in patients treated with ERAS were significantly lower than those in the traditional care group. At the same time, the incidence of postoperative anastomotic leakage was not increased, indicating that the application of ERAS is safe. The postoperative pain of patients treated with ERAS was significantly lower than that of the traditional care group, at the same time, patients with ERAS intervention had faster recovery, shorter hospital stays, and higher satisfaction, indicating that ERAS is more effective in promoting postoperative rehabilitation of patients with rectal cancer.

NOSE surgery and ERAS are mutually reinforcing. In this study, the patients in the NOSE + ERAS group were not significantly different from the traditional nursing control group and the ERAS control group in terms of surgical time, bleeding volume, degree of tumor resection (number of lymph node dissection), postoperative abdominal infection, and anastomotic leakage, which indicates that NOSE combined with ERAS does not affect the radicalness of the tumor and does not increase the risk of postoperative abdominal infections and anastomotic leakage. At the same time, patients in the NOSE + ERAS group were significantly better than the other two control groups in terms of postoperative pain score, postoperative hospital stays, and patient satisfaction, further indicating that NOSE surgery combined with ERAS treatment is more superior in the field of postoperative rehabilitation. NOSE surgery makes full use of the advantages of laparoscopic clear vision and convenient operation. At the same time, removing specimens from natural channels, NOSES is less invasive than traditional laparoscopic surgery, and can reduce incision infection, postoperative incision pain, reduce complications, thereby enable patients to get out of bed early, promote intestinal peristalsis of patients, and promote rapid recovery after surgery.

In summary, in the ERAS treatment plan for patients with rectal cancer, choosing the appropriate case for NOSES minimally invasive surgery will greatly reduce the incidence of postoperative complications and accelerate the recovery of patients. NOSE minimally invasive surgery conforms to the basic concept of ERAS, and is also a fundamental need for ERAS, the perfect combination of the two is worthy of clinical promotion and will benefit more patients. However, in the exploration process of NOSES combined with the ERAS, the indications should be fully evaluated and selected. Regardless of the ERAS treatment or the resected specimen removed through the natural orifice, the safety, tumor-free principle and sterility principle need to be fully considered.

Conclusion

This study revealed that the NOSES radical resection of rectal cancer under the guidance of ERAS achieved more minimally invasive cosmetic and functional, individualized treatment effect in laparoscopic surgery. There is a greater advantage that ERAS combined with the NOSES radical resection of rectal cancer which is worthy of popularization and with good application prospect.

Abbreviations

NOSES: natural orifice specimen extraction surgery; ERAS: enhanced recovery after surgery; TME: total mesorectal excision; TSME: tumor-specific mesorectal excision; NRS: numerical rating scale; NOTES: nature orifice transluminal endoscopic surgery.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

SL wrote the manuscript. BW, WY and XW collected data, wrote the manuscript, and contributed equally to the manuscript. KM, SL and XY revised the manuscript and provided comments on the structure and details of the article. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated during the current study are available in the <http://www.medresman.org/login.aspx>, and the number is ChiCTR-INR-19014175. The data is available from the corresponding author under reasonable request. The email of corresponding author is lisheng.136@163.com.

Ethics approval and consent to participate

We declare that this study has obtained the report of ethics board approval and informed consent obtained from each participant has been written before surgery. The study was approved by the ethics committee of Shaoyang Central Hospital, Hunan, China on Dec. 2018. The protocol number is 2018KT218.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

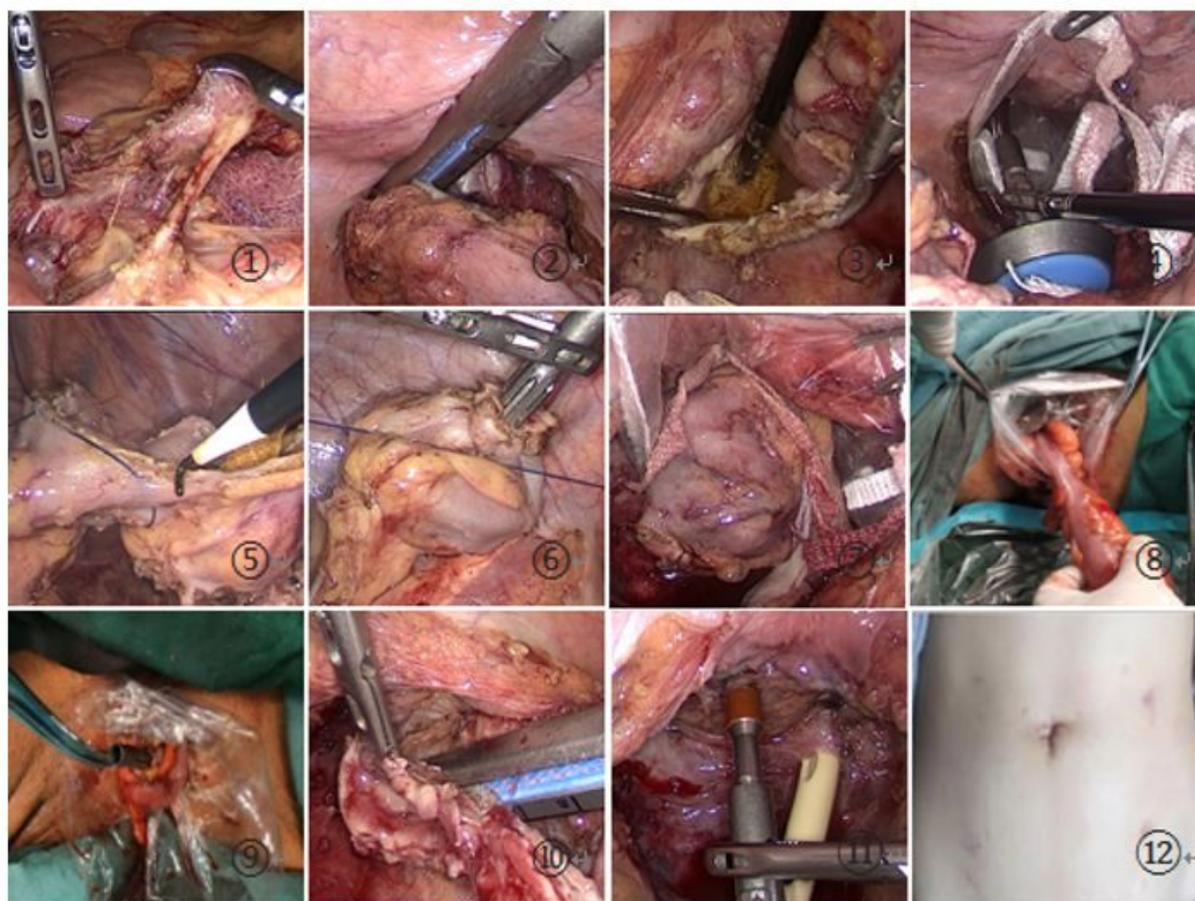


Figure 1

☒ D3 lymph node dissection under laparoscope, ☒ Disconnect the distal end of the tumor, ☒ Cut the stump of the rectum and disinfect it, ☒ Place the protective sleeve through the main operation hole and pull it out through the anus, and then insert the Stapler anvil into the abdominal cavity through the sleeve, ☒ Cut the sigmoid approximately 10cm from the proximal end of the tumor and sterilize it, ☒ The Stapler anvil is insert into the proximal sigmoid and fixed in a suture,

Remove the disconnected specimen through the anal protective sleeve, Pull out the uncut rectum and tumor through the anal sleeve, Resect the tumor and insert the sigmoid fixed with a Stapler anvil into the abdomen, The rectal stump is cut off and closed again, The rectum-sigmoid anastomosis is completed through the anus, There is no incision in the abdomen after surgery. The steps of NOSES operation are: NOSES, and NOSES-.

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