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Original Article

Efficacy of natural duct specimen extraction versus conventional laparoscopic surgery for rectal cancer: a single-centre retrospective analysis

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Abstract: Objective: Rectal cancer has a high incidence and its onset age is getting younger. Currently, conventional laparoscopic surgery can no longer meet the clinical requirements for surgical incisions. Natural orifice specimen extraction surgery (NOSES) is less invasive, but there have been few studies on the effectiveness of this procedure for rectal cancer. Therefore, this study aimed to explore the efficacy of NOSES and conventional laparoscopic surgery in rectal cancer treatment. Methods: In this retrospective analysis, we collected clinical data of 150 rectal cancer patients. Patients who received NOSES were included in a NOSES group and those underwent routine laparoscopic surgery were in a control group. Then, the observation group was matched with the control group at a ratio of 1:1 by using the propensity score matching method. We compared the surgical indicators, postoperative recovery indicators, physical indicators, pain, surgical stress-related indicators, inflammation indicators, immune indicators, quality of life, and postoperative complications between the two groups. Results: We found that compared with the control group, the NOSES group had a shorter exhaust start time, getting out-of-bed activity time, length of hospital stay, bowel sound recovery time, and gastrointestinal peristalsis time. The Pittsburgh Sleep Quality Index (PSQI) and Positive and Negative Affect Schedule (PANAS) scores decreased in both groups after surgery, with the NOSES group showing a more significant reduction. The Visual Analogue Scale (VAS) scores decreased in both groups, and the NOSES group had lower VAS scores. Additionally, the NOSES group exhibited a significant interaction effect with time (intergroup effect: F = 497.800; time effect: F = 163.100; interaction effect: F = 5.307). Superoxide dismutase (SOD) levels decreased and malondialdehyde (MDA) levels increased in both groups postoperatively; however, the NOSES group had higher SOD levels and lower MDA levels. All the above comparisons were statistically significant ($P < 0.05$). There was no statistically significant difference in the total complication rates between the NOSES group and the control group ($Z = -0.768$, $P = 0.442$; $\chi^2 = 2.333$, $P = 0.127$). Conclusion: Compared to conventional laparoscopic surgery, NOSES results in less pain and injury, a more stable mood, faster recovery, and comparable safety.

Keywords: Single-center, natural orifice specimen extraction, laparoscopic, rectal cancer, efficacy

Introduction

Rectal cancer is a malignant tumor originating from the mucosal epithelium of the rectum. It ranks third in incidence among men and second among women worldwide, with a concerning trend toward younger patients and more advanced diagnoses [1]. Clinically, early to mid-stage colorectal cancer is often treated with laparoscopic surgery, which offers effective therapeutic outcomes while being minimally invasive [2]. Given the benefits of minimally invasive surgery, surgeons are increasingly focused on minimizing bodily harm and preserving tissue function to accelerate patient recovery, all while ensuring the effectiveness of the surgery. Natural Orifice Specimen Extraction Surgery (NOSES) is a technique that uses natural orifices (such as the trachea, stomach, colon, or vagina) as surgical pathways, allowing specimens to be extracted without making incisions in the skin [3]. This approach minimizes postoperative pain, preserves the integrity of abdominal tissues, and promotes faster postoperative recovery [4]. Compared to traditional laparoscopic surgery, NOSES offers superior

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preservation of bodily functions and organs while ensuring complete tumor resection, thanks to its unique digestive tract reconstruction methods and surgical techniques. This results in enhanced minimally invasive outcomes [5]. The benefits of NOSES have garnered significant attention within the medical community, as it can notably improve the aesthetic outcomes, physical function, role function, emotional well-being, and overall physiological health of colorectal cancer patients [6]. Moreover, NOSES has been shown to significantly reduce the incidence of postoperative complications in colorectal cancer patients [7]. A meta-analysis further confirmed the positive prognostic and surgical safety outcomes of NOSES in colorectal cancer [8]. However, while NOSES has been explored in a limited number of studies for rectal cancer, there is still insufficient clinical evidence to fully validate its benefits in this context. Additionally, the impact of NOSES on patients' sleep quality, mood fluctuations, and stress response remains unclear. To address these gaps, we collected clinical data from rectal cancer patients and analyzed the efficacy of NOSES in improving sleep, mood, pain management, stress response, and overall safety.

Materials and methods

Source of research subjects

Clinical data from 150 patients with rectal cancer, admitted to Changde Hospital, Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City) between January 2022 and December 2023, were collected through retrospective analysis. The inclusion criteria were as follows: (1) a preoperative pathological report confirming rectal cancer [9]; (2) the lower margin of the tumor located 4-10 cm from the dentate line; (3) tumor transverse diameter ≤ 5 cm, involving ≤ 2/3 of the intestinal circumference; (4) pelvic magnetic resonance imaging (MRI) conducted before surgery, with a TMN stage of T1-2N0M0; (5) availability of complete clinical data and treatment index records. Exclusion criteria included: (1) complication with acute intestinal obstruction; (2) indications for surgery with previous NOSES or conventional laparoscopic surgery; (3) patients under the age of 18. This study was approved by the Ethics Committee of Changde Hospital, Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City).

Grouping

Patients who underwent NOSES were included in the NOSES group, while those who underwent routine laparoscopic surgery were included in the control group. The ratio between the NOSES group and the control group before matching was 63:87. The NOSES group was matched with the control group in a 1:1 ratio using a propensity score matching method. The matching was based on age, sex, body mass index, tumor diameter, and tumor node metastasis (TNM) stage. After matching by propensity score matching method, there were 56 cases in both the NOSES group and the control group. A total of 112 patients were included in the analysis.

Collecting treatment indicators

Treatment indicators were collected from patient records, including: surgical indicators (operation time, intraoperative blood loss, and number of lymph nodes dissected), postoperative recovery indicators (time to first exhaust, time to bowel sound recovery, time to gastrointestinal peristalsis, time to fluid intake, time to getting out of bed, and length of hospital stay), clinical indicators (Visual Analogue Scale (VAS) score, Pittsburgh Sleep Quality Index (PSQI) score, and Positive and Negative Affect Schedule (PANAS) score), surgical stress indixes (levels of superoxide dismutase (SOD) and malondialdehyde (MDA)), inflammation factors (levels of interleukin-6 (IL-6), IL-8, tumor necrosis factor α (TNF-α), and C-reactive protein (CRP)), immune markers, quality of life, and postoperative complications (incidence of anastomotic leak, ileus, abdominal infection, urinary system infection, pulmonary infection, and urinary retention).

The VAS [10] was used to assess pain on days 1, 3, and 7 after surgery, with higher scores indicating greater pain intensity. Sleep quality was evaluated using the PSQI [11], which ranges from 0 to 21 points. The score is divided into 4 levels, with each 5-point increment representing a higher level; higher scores indicate poorer sleep quality.

Negative emotions were assessed using the PANAS [12], which employs a 5-point scoring system across 20 items, with scores ranging from 1 to 5. The total score for each dimension is 50 points, with lower scores indicating better emotional status. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [13] was used to evaluate patients' quality of life, both 1 day before surgery and 7 days after surgery. The questionnaire consists of 30 items, with higher scores reflecting a better quality of life.

We collected 15 mL of blood intravenously 1 day before surgery and 7 days after surgery. The blood samples were placed in anticoagulant tubes and centrifuged at 3000 r/min for 20 minutes to collect the serum samples, which were stored in a refrigerator at -80°C for subsequent analysis. SOD levels were measured using colorimetry, while MDA levels were determined using the thiobarbituric acid (TBA) method. Serum concentrations of IL-6 were measured using an IL-6 ELISA kit (Wuhan Gilead Biotechnology Co., LTD., lot: J20252), and IL-8 levels were measured using an IL-8 ELISA kit (Shanghai Tongwei Biotechnology Co., LTD., lot: TW-E2518). Immunoglobulin A (IgA) concentrations were determined using an IgA ELISA kit (Shanghai Enzyme-linked Organisms, lot: mlsw_E1278), and immunoglobulin M (IgM) concentrations were measured using an IgM ELISA kit (Shanghai Tongwei Biotechnology Co., LTD., lot: TW-E2466). TNF-α and CRP concentrations were determined using an iChem-340 automatic biochemical analyzer and an immunosuppression assay, respectively.

Therapeutic methods

(1) Laparoscopic surgery: The patients were intubated under general anesthesia and placed in the lithotomy position. A 10-cm incision was made above the umbilicus using the "five-hole method". A trocar was inserted for endoscopic exploration, and pneumoperitoneum was established with an abdominal pressure of approximately 12 mmHg (1 mmHg = 0.133 kPa). The sigmoid colon was separated, sub-mesenteric blood vessels and surrounding connective tissue were removed, and lymph node tissue was excised. The bilateral ureters were fully exposed. Next, an incision of about 5 cm was made in the abdominal wall at the location of the tumor, and the corresponding surgical method was selected to resect the affected bowel. Pneumoperitoneum was then re-established, and staplers were placed in the proximal bowel. After the procedure, the abdominal cavity was carefully irrigated with sterile saline, and a drainage tube was routinely placed. The incision and trocar sites were closed. Routine antibiotics were administered postoperatively to prevent infection.

(2) NOSES: The patients were intubated under general anesthesia and placed in the lithotomy position. An artificial pneumoperitoneum was established with an abdominal pressure of approximately 12 mmHg, and four operative ports were set up. A 30° laparoscope was inserted through a 10 cm incision above the umbilicus to explore the abdominal cavity. The sub-mesenteric vascular root and surrounding connective tissue were separated and severed, and lymph node tissue was removed. The anterior sacral space was sharply dissected.

For high rectal cancer: The tumor was resected by severing the upper and lower intestinal tubes. The tumor specimens were extracted through the anus using a proctoscope, assisted by an incision protective sleeve. The anvil of the circular stapler was then inserted into the abdominal cavity through the anus, fixed at the end of the proximal intestinal tube, and the distal rectum was closed. The circular stapler was subsequently introduced into the anus to complete the end-to-end anastomosis.

For low rectal cancer: The mesorectum was freed laparoscopically down to the pelvic floor, and the proximal bowel tube was transected. The severed end of the bowel was held with oval forceps to facilitate eversion of the rectum. The distal bowel tube and tumor specimen were then removed. The anvil head was fixed at the proximal end of the bowel, and the distal rectum was closed extracorporeally before being returned to the body. The circular stapler was introduced into the anus to complete the end-to-end anastomosis.

Statistics process

Data were analyzed using SPSS 22.0 software. Quantitative data are presented as mean ± standard deviation ($\overline{x}$±s), and group comparisons were conducted using the t-test. For com-

Table 1. Comparison of matching factors after matching

Group	Gender (Male/female)	Age (year)	Body mass index (kg/m^2)	Diameter of tumor (cm)	TNM staging (I/II/III)
NOSES group (n = 56)	30/26	55.57 ± 6.38	24.11 ± 3.02	3.52 ± 0.43	28/19/9
Control group (n = 56)	28/28	55.84 ± 6.29	24.36 ± 3.08	3.47 ± 0.48	32/16/8
χ^2/t	0.143	0.226	0.434	0.581	0.583
P	0.705	0.822	0.665	0.563	0.747

Note: NOSES: natural orifice specimen extraction surgery; TNM: tumor node metastasis.

Table 2. Surgical indicators

Group	Operation time (min)	Intraoperative blood loss (mL)	Intraoperative blood loss
NOSES group (n = 56)	195.52 ± 42.33	55.26 ± 13.30	16.25 ± 4.16
Control group (n = 56)	210.48 ± 40.21	52.39 ± 15.15	15.39 ± 4.28
t	2.174	1.065	1.078
P	0.058	0.289	0.283

Note: NOSES: natural orifice specimen extraction surgery.

parisons of data across multiple time points, repeated measures ANOVA was employed. Qualitative data are expressed as frequencies (n) and analyzed using the chi-square (χ^2) test or the rank-sum test. The significance level was set at α = 0.05.

Results

Differences in matching factors after matching

After applying propensity score matching in a 1:1 ratio, 56 patients in the NOSES group and 56 patients in the control group were successfully matched. There were no statistically significant differences in the matching variables (gender, age, body mass index, tumor diameter, TNM staging) between the two groups after matching (P > 0.05). This indicates that the data between the two groups are balanced following propensity score matching (**Table 1**).

Surgical indicators

There were no statistically significant differences in operation time, intraoperative blood loss, or the number of lymph nodes removed between the NOSES and control groups (*P* > 0.05) (**Table 2**).

Postoperative recovery indicators

In the NOSES group, the times for exhaust start, getting out of bed, length of hospital stay, bowel sound recovery, gastrointestinal peristalsis, and fluid intake were (2.39 ± 0.55) days, (3.61 ± 0.52) days, (7.53 ± 2.25) days, (25.39 ± 4.48) hours, (9.22 ± 1.08) hours, and (47.53 ± 6.62) hours, respectively. In the control group, these times were (3.32 ± 0.50) days, (6.28 ± 0.84) days, (12.58 ± 3.39) days, (33.16 ± 4.52) hours, (13.25 ± 2.27) hours, and (48.35 ± 6.24) hours. Compared to the control group, the NOSES group demonstrated significantly reduced exhaust start time, time to get out of bed, length of hospital stay, bowel sound recovery time, and gastrointestinal peristalsis time (t = 9.363, 20.220, 9.288, 9.137, 12.000, respectively; all *P* < 0.001) (**Figure 1**).

Body indexes

Before surgery, there were no significant differences in PSQI and PANAS scores between the NOSES and control groups (P > 0.05). After surgery, both groups had lower PSQI and PANAS scores compared to preoperative values. However, the NOSES group exhibited significantly lower PSQI and PANAS scores than the control group (*P* < 0.05) (**Table 3**).

Pain

The NOSES group had lower VAS scores compared to the control group, and VAS scores generally decreased over time in both groups. The NOSES group showed a significant interaction effect with time, with the following statistical results: intergroup effect (F = 497.800, P < 0.001), time effect (F = 163.100, P < 0.001), and interaction effect (F = 5.307, P = 0.005) (**Figure 2**).

Surgical stress indicators

In the NOSES group, the preoperative SOD levels were (92.55 ± 7.41) U/mL and the postop-

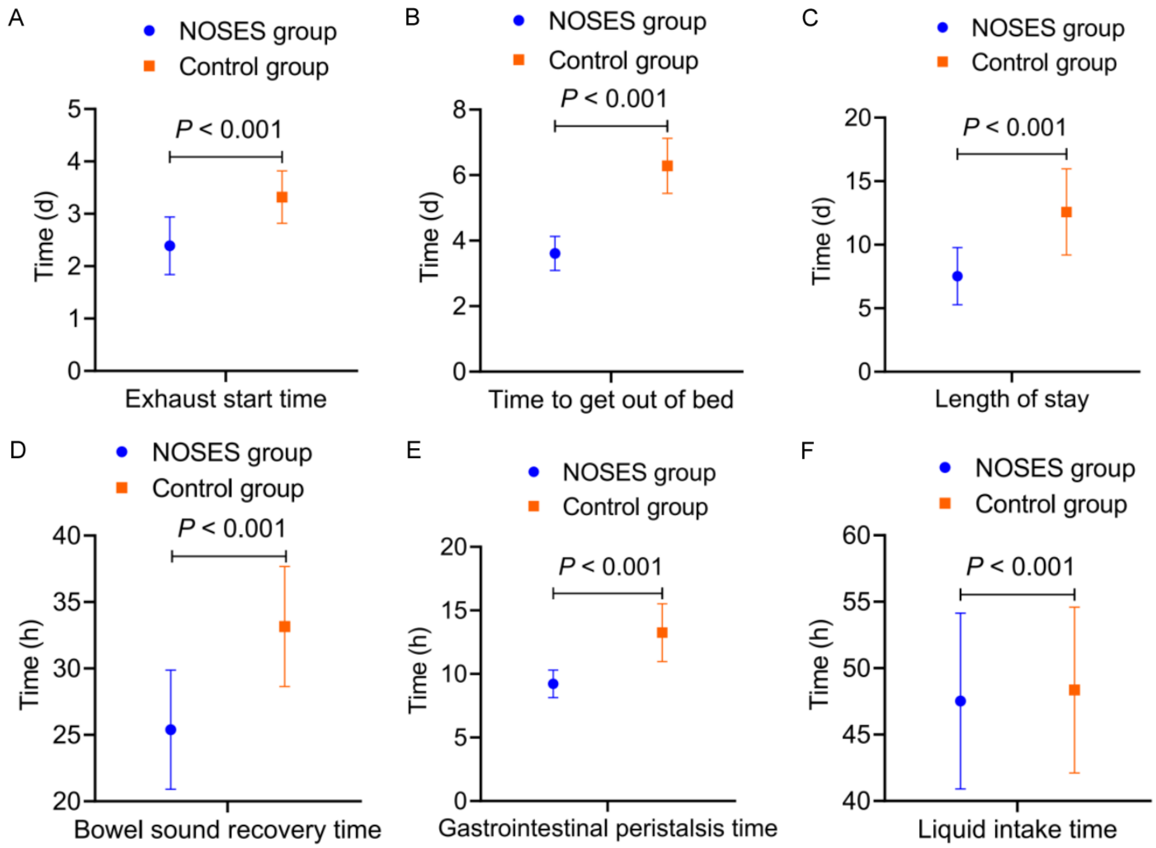

Figure 1. Postoperative recovery indicators. *Note*: A: Exhaust start time; B: Time to get out of bed; C: Length of stay; D: Bowel sound recovery time; E: Gastrointestinal peristalsis time; F: Liquid intake time. NOSES: natural orifice specimen extraction surgery.

Table 3. PSQI and PANAS score

Group	PSQI score (points)		PANAS score (points)	
	Preoperative	Postoperative	Preoperative	Postoperative
NOSES group (n = 56)	15.26 ± 3.20	7.85 ± 1.62[a]	43.22 ± 8.67	26.39 ± 6.68[a]
Control group (n = 56)	15.10 ± 2.86	10.84 ± 1.86[a]	45.30 ± 6.41	33.86 ± 7.52[a]
t	0.279	9.071	1.444	5.558
P	0.781	< 0.001	0.152	< 0.001

Note: [a]means compared with preoperative, *P* < 0.05. NOSES: natural orifice specimen extraction surgery; PSQI: Pittsburgh Sleep Quality Index; PANAS: Positive and Negative Affect Schedule.

erative levels were (69.22 ± 5.82) U/mL. In the control group, the preoperative SOD levels were (92.16 ± 6.59) U/mL and the postoperative levels were (62.52 ± 6.55) U/mL. The NOSES group's preoperative MDA levels were (5.39 ± 0.42) nmol/mL and postoperative levels were (7.11 ± 0.68) nmol/mL. In the control group, preoperative MDA levels were (5.28 ± 0.55) nmol/mL and postoperative levels were (7.92 ± 0.61) nmol/mL. There were no significant differences in SOD and MDA levels between the NOSES and control groups before surgery. After surgery, both groups showed decreased SOD levels and increased MDA levels. However, the NOSES group had significantly higher SOD levels and lower MDA levels compared to the control group (**Figure 3**).

Conventional inflammatory marks

There were no significant differences in IL-6, IL-8, TNF-α, and CRP levels between the NOSES

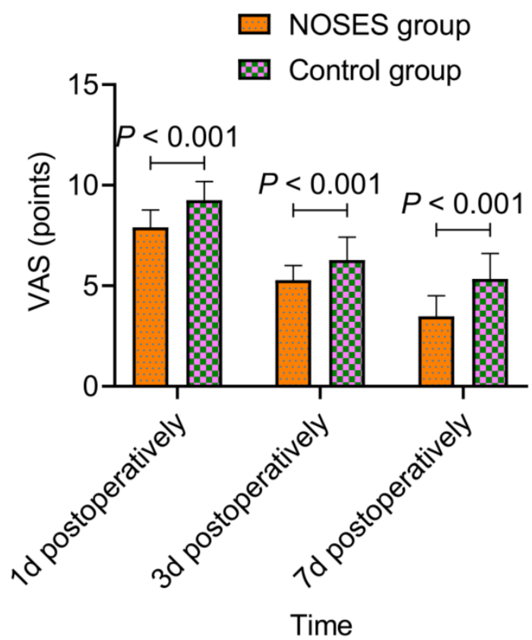

Figure 2. VAS score. NOSES: natural orifice specimen extraction surgery; VAS: visual analogue scales.

and control groups before surgery. After surgery, IL-6 levels increased in both groups compared to preoperative values (P < 0.05), while IL-8 levels did not change in the two groups before and after surgery (P > 0.05). There were no statistically significant differences in IL-6 and IL-8 levels between the NOSES and control groups (P > 0.05). Both NOSES and control groups showed reduced TNF-α and CRP levels after surgery compared to before surgery, with the NOSES group exhibiting lower levels of TNF-α and CRP than the control group (*P* < 0.05) (**Table 4**).

Immune indices

There were no significant differences in IgA and IgM levels between the NOSES and control groups before surgery (P > 0.05). Postoperatively, both groups showed increased levels of IgA and IgM compared to preoperative values. However, IgM levels were significantly higher in the NOSES group compared to the control group (*P* < 0.05) (**Table 5**).

EORTC QLQ-C30 score

The EORTC QLQ-C30 scores for the NOSES group were (63.23 ± 5.22) before surgery and (92.53 ± 8.02) after surgery, while the scores for the control group were (63.52 ± 5.39) before surgery and (79.18 ± 6.12) after surgery. There were no significant differences in EORTC QLQ-C30 scores between the two groups before surgery (P > 0.05). After surgery, both groups showed improved EORTC QLQ-C30 scores compared to preoperative values. However, the NOSES group had significantly higher EORTC QLQ-C30 scores than the control group (t = 9.903, *P* < 0.001) (**Figure 4**).

Postoperative complications and death

In the NOSES group, there was 1 case of anastomotic leak and 2 cases of urinary retention, resulting in a total complication rate of 5.36% (3/56). In the control group, there were 3 cases of anastomotic leak, 2 cases of ileus, 1 case of urinary system infection, 1 case of pulmonary infection, and 2 cases of urinary retention, yielding a total complication rate of 16.07% (9/56). There were no statistically significant differences in overall complication rates between the two groups (Z = -0.768, P = 0.442; χ^2 = 2.333, P = 0.127). Neither group experienced any deaths during the observation period.

Discussion

Colorectal cancer has a high incidence and is increasingly affecting younger age groups. Laparoscopic surgery is widely used for rectal cancer due to its minimally invasive nature, resulting in smaller scars and a lower risk of postoperative complications. As minimally invasive techniques continue to evolve, there are growing expectations for more systematic and advanced surgical approaches. NOSES is a technique that uses natural body cavities for specimen removal, eliminating the need for external incisions. This method has been successfully applied in colorectal cancer cases. It is important to investigate the impact of NOSES on treatment efficacy, sleep quality, mood, pain, stress response, and overall safety for patients with rectal cancer.

In this study, the NOSES technique involves specimen removal via the rectum and in vitro resection, followed by intracavity anastomosis. This approach eliminated the need for an auxiliary abdominal incision for specimen extraction, which effectively reduced surgical trauma, accelerates postoperative recovery, and short-

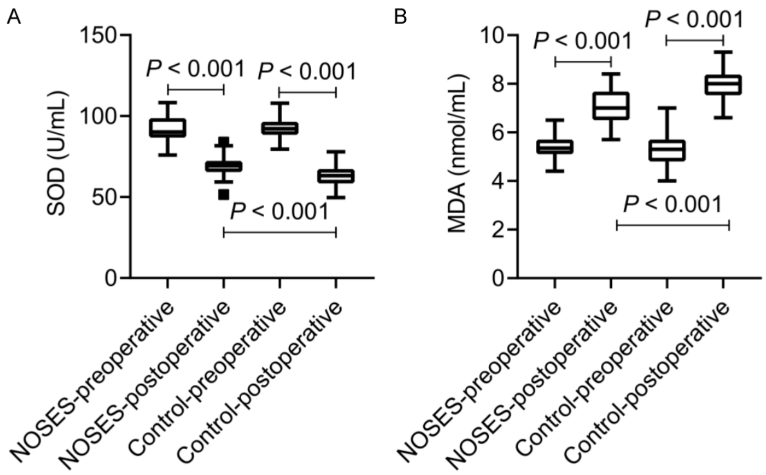

Figure 3. Levels of the SOD and MDA. A: Superoxide dismutase (SOD); B: Malondialdehyde (MDA). NOSES: natural orifice specimen extraction surgery.

ens the time to exhaust gas, get out of bed, and the length of hospital stay. It also reduced bowel sound recovery time and gastrointestinal peristalsis time. Hao et al. [14] demonstrated that improved postoperative recovery in colorectal cancer patients could reduce hospital stay duration and time to exhaust gas and get out of bed, which aligns with the findings of this study. Rectal cancer primarily affects the lower rectum, and patients often experience gastrointestinal symptoms such as diarrhea and constipation initially. As the disease progresses, symptoms may include blood in the stool, abdominal mass, and abdominal pain [15]. The discomfort from these abnormal bodily changes not only impacts patients' sleep quality but also contributes to negative emotions such as anxiety, restlessness, and irritability [16]. Sleep quality and quantity in colorectal cancer survivors are often linked to gastrointestinal issues [17]. Additionally, perioperative patients frequently experience sleep disorders [18]. These disorders can negatively affect subjective feelings and behaviors. For instance, rapid eye movement (REM) sleep is crucial for emotional regulation and memory consolidation, with alterations in REM sleep being associated with various psychiatric symptoms and disorders, including depression, mania, and suicidal thoughts [19]. The PSQI evaluates sleep quality, while the PANAS assesses emotional state. Our findings showed that PSQI and PANAS scores improved for all patients after surgery. However, patients who underwent NOSES had significantly lower PSQI and PANAS scores compared to those who had conventional laparoscopic surgery. This suggests that NOSES may substantially enhance sleep quality and mood in rectal cancer patients. We speculate that the less invasive nature of NOSES and the associated improved subjective experience may contribute to these benefits.

We also observed that postoperative pain tended to decrease over time in all patients. However, those in the NOSES group experienced less pain, likely due to the technique's more minimally invasive nature. Unlike conventional laparoscopic surgery, which requires additional incisions in the abdominal wall for specimen removal, NOSES involves making only a laparoscopic incision at the umbilicus. The procedure utilizes the rectum to remove the tumor and excise the specimen through this single access point. This approach minimizes tissue damage, preserves the integrity of the abdominal wall, and results in less pain for the patient. Zhao et al. [20] reported that transvaginal natural orifice specimen extraction in three-dimensional laparoscopic nephrectomy effectively reduced pain without affecting pelvic floor or sexual function. Conversely, Dobó et al. [21] found that NOSES for colon resection in rectal endometriosis did not significantly reduce VAS scores, which may be attributed to variations in disease types among patients.

The stress response is a non-specific defensive reaction to external stimuli. Key indicators for assessing this response are SOD and MDA, which reflect the extent of surgical injury [22]. SOD is a natural antioxidant enzyme that effectively neutralizes free radicals and protects cells from oxidative damage [23]. In contrast, MDA is a byproduct of lipid peroxidation and its levels in tumor tissues can indicate the degree of oxidative stress caused by the tumor [24]. Our study found that SOD levels decreased less and MDA levels increased less in patients underwent NOSES compared to those who underwent conventional laparoscopic surgery. This suggests that NOSES induces a lower

Table 4. Conventional inflammatory markers

Group	IL-6 (ng/L)		IL-8 (ng/L)		TNF-α (ng/L)		CRP (mg/L)	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
NOSES group (n = 56)	4.09 ± 1.62	29.55 ± 7.72[b]	2.61 ± 0.75	2.63 ± 0.82[b]	34.63 ± 5.02	51.26 ± 6.03[b]	5.28 ± 1.12	15.22 ± 3.73[b]
Control group (n = 56)	3.95 ± 1.58	28.53 ± 7.64[b]	2.57 ± 0.66	2.59 ± 0.72[b]	34.72 ± 5.11	61.39 ± 7.20[b]	5.34 ± 1.26	31.35 ± 6.28[b]
t	0.463	0.703	0.300	0.274	0.094	8.072	0.266	16.530
P	0.644	0.484	0.765	0.784	0.925	< 0.001	0.790	< 0.001

Note: [b]means compared with preoperative, $P < 0.05$. IL-6: interleukin-6; IL-8: interleukin-8; TNF-α: tumor necrosis factor α; CRP: C-reactive protein.

Table 5. Immune indices

Group	IgA (g/L)		IgM (g/L)	
	Preoperative	Postoperative	Preoperative	Postoperative
NOSES group (n = 56)	155.32 ± 8.46	137.23 ± 8.25[c]	175.19 ± 8.34	139.22 ± 10.58[c]
Control group (n = 56)	155.25 ± 9.03	137.19 ± 8.69[c]	174.87 ± 7.86	130.38 ± 11.24[c]
t	0.042	0.025	0.209	4.286
P	0.966	0.980	0.835	< 0.001

Note: [c]means compared with preoperative, $P < 0.05$. NOSES: natural orifice specimen extraction surgery; IgA: immune globulin A; IgM: immune globulin M.

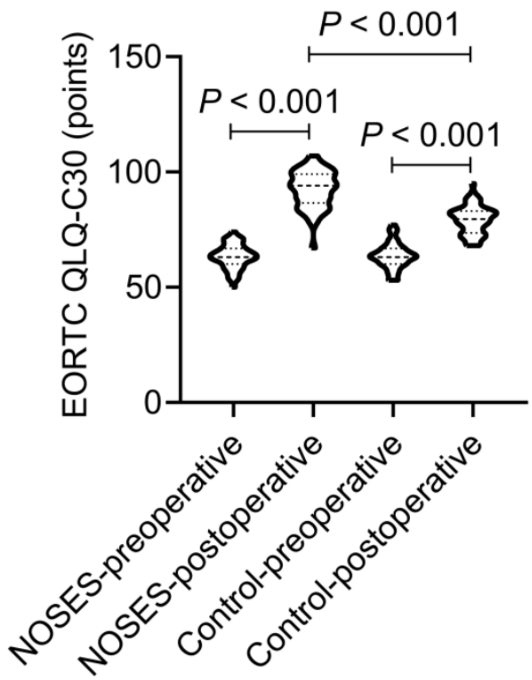

Figure 4. EORTC QLQ-C30 score. NOSES: natural orifice specimen extraction surgery; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of life Questionnaire.

stress response and results in less cellular damage, highlighting the advantages of this minimally invasive technique. NOSES not only shortens hospital stays and speeds up recovery but also reduces postoperative pain, thereby improving the overall quality of life for patients. Zhao et al. [25] investigated the clinical effects of NOSES combined with endoscopic anal surgery and reported that NOSES patients had better sleep quality (6.26 ± 1.16) and lower pain scores (2.95 ± 0.79) compared to those undergoing conventional laparoscopic surgery. These findings align with our study, reinforcing the benefits of NOSES in enhancing sleep quality and reducing pain.

Humoral immunity involves antibodies binding to tumor antigens, thereby activating the complement system and leading to cell lysis and opsonization, which together contribute to antitumor immune responses [26]. Cellular immunity, which is crucial for tumor defense, is reflected in immune indicators such as IgA and IgM. IgA primarily protects mucosal surfaces, while IgM has a potent role in complement activation and phagocytosis enhancement [27]. Surgical stress can impact both humoral and cellular immunity. Our study observed a decrease in postoperative levels of IgA and IgM in both groups, with a smaller reduction in IgM levels among NOSES patients. This suggests that NOSES may mitigate the immunosuppressive effects associated with surgery, thereby supporting immune function recovery and enhancing postoperative rehabilitation. Wang et al. [28] examined the short-term clinical effects and inflammatory responses of NOSES compared to traditional laparoscopic surgery for sigmoid colon and rectal cancer. They reported significantly higher IgA ($t = 3.30$, $P = 0.001$) and IgM ($t = 3.38$, $P = 0.001$) levels in the NOSES group compared to the control group, which differs from our findings. This discrepancy may be due to variations in disease types and their severities, indicating that NOSES might have different immune effects depending on the specific conditions treated. Further studies are needed to explore these variations and validate the findings across different diseases.

IL-6 is a crucial cytokine in immune response and inflammatory damage, serving as a sensitive marker for assessing tissue injury and traumatic stress response [29]. IL-8 is known for its role in neutrophil chemotaxis and activation, contributing to neutrophil-mediated tissue damage [30]. TNF-α promotes the production of various cytokines involved in the body's defense mechanisms, with its levels rising significantly during early inflammation [31]. CRP, an acute-phase protein synthesized by the liver, reflects the severity of the body's stress response and serves as a major indicator of inflammation [32]. Previous studies have highlighted a significant correlation between elevated IL-6 levels and the severity of tissue injury [33]. In our study, we found no significant differences in IL-6 and IL-8 levels between the NOSES and control groups. However, NOSES patients exhibited lower levels of TNF-α and CRP, suggesting a reduced risk of postoperative infection compared to those undergoing traditional laparoscopic surgery. This may be attributed to factors such as meticulous bowel preparation, accurate execution of key surgical steps, and adherence to aseptic principles. Statistical analysis also revealed no significant difference in the total complication rates between NOSES and control patients, indicating that NOSES does not increase the risk of postoperative complications and demonstrates a certain level of safety for rectal cancer procedures.

In summary, compared to conventional laparoscopic surgery, NOSES demonstrates superior outcomes in terms of reduced pain and injury, more stable mood, faster recovery, and overall safety. However, this study has limitations due to its retrospective design. While it effectively addressed the research objectives and managed time and costs, the analysis is subject to various biases and confounding factors inherent in retrospective studies. Additionally, the study was conducted at a single institution with a relatively small sample size, which may limit the generalizability of the findings. Therefore, future research should design larger, multi-center randomized controlled trials to validate these conclusions and enhance the applicability of the results.

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Disclosure of conflict of interest

None.

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References

[1] Siegel RL, Wagle NS, Cercek A, Smith RA and Jemal A. Colorectal cancer statistics, 2023. CA Cancer J Clin 2023; 73: 233-254.

[2] Feng Q, Yuan W, Li T, Tang B, Jia B, Zhou Y, Zhang W, Zhao R, Zhang C, Cheng L, Zhang X, Liang F, He G, Wei Y and Xu J; REAL Study Group. Robotic versus laparoscopic surgery for middle and low rectal cancer (REAL): short-term outcomes of a multicentre randomised controlled trial. Lancet Gastroenterol Hepatol 2022; 7: 991-1004.

[3] Yu M, Cai Z, Zhou H, Fingerhut A, He Z, Xue P, Song H, Yang X, Cheng X, Zhang S, Xu X, Zhong H, Abuduaini N, Liu J, Wang X and Feng B. Natural orifice specimen extraction surgery versus small-incision assisted laparoscopic radical right hemicolectomy. Future Oncol 2023; 19: 2641-2650.

[4] Zhou H, Wang A, Lu H, Wu J, Ying J, Hu Z and Ruan C. Three-port with natural orifice specimen extraction versus conventional laparoscopic anterior resection for rectal-sigmoid cancer: a matched pair analysis. J Invest Surg 2022; 35: 788-792.

[5] Muhammad S, Gao Y, Guan X, QingChao T, Fei S, Wang G, Chen Y, Liu Z, Jiang Z, Kaur K, Tatiana K, Ul Ain Q, Wang X and He J. Laparoscopic natural orifice specimen extraction, a minimally invasive surgical technique for mid-rectal cancers: retrospective single-center analysis and single-surgeon experience of selected patients. J Int Med Res 2022; 50: 3000605221134472.

[6] Houqiong J, Ziwen W, Chonghan Z, Penghui H, Hongxin Y, Weijie L, Dongning L and Taiyuan L. Comparison of transabdominal wall specimen retrieval and natural orifice specimen extraction robotic surgery in the outcome of colorectal cancer treatment. Front Surg 2023; 10: 1092128.

[7] Brincat SD, Lauri J and Cini C. Natural orifice versus transabdominal specimen extraction in laparoscopic surgery for colorectal cancer: meta-analysis. BJS Open 2022; 6: zrac074.

[8] Lin J, Lin S, Chen Z, Zheng B, Lin Y, Zheng Y, Liu Y and Chen SQ. Meta-analysis of natural orifice specimen extraction versus conventional laparoscopy for colorectal cancer. Langenbecks Arch Surg 2021; 406: 283-299.

[9] Mirshahvalad SA, Hinzpeter R, Kohan A, Anconina R, Kulanthaivelu R, Ortega C, Metser U and Veit-Haibach P. Diagnostic performance of [18F]-FDG PET/MR in evaluating colorectal cancer: a systematic review and meta-analysis. Eur J Nucl Med Mol Imaging 2022; 49: 4205-4217.

[10] Zhang Y, Xiang C and Liang J. Correlation between pain and anal defecation function in postoperative patients with colorectal cancer and related factors affecting patients' prognosis. Ann Ital Chir 2024; 95: 136-143.

[11] Legg M, Meertens RM, van Roekel E, Breukink SO, Janssen ML, Keulen ETP, Steindorf K, Weijenberg MP and Bours M. The association between sleep quality and fatigue in colorectal cancer survivors up until two years after treatment: a cross-sectional and longitudinal analysis. Cancers (Basel) 2022; 14: 1527.

[12] Avisar A, Cohen M, Aharon A, Katz R and Bar-Sela G. Positive affect and fatigue as predictors of anti-inflammatory IL-10 concentrations among colorectal cancer patients during adjuvant chemotherapy. J Psychosom Res 2023; 167: 111162.

[13] Pilz MJ, Gamper EM, Efficace F, Arraras JI, Nolte S, Liegl G, Rose M and Giesinger JM; EORTC Quality of Life Group. EORTC QLQ-C30 general population normative data for Italy by sex, age and health condition: an analysis of 1,036 individuals. BMC Public Health 2022; 22: 1040.
[14] Hao SZ and Zhang JJ. The application value of concept of enhanced recovery after surgery in patients with colorectal carcinoma after natural orifce specimen extraction surgery. Zhonghua Zhong Liu Za Zhi 2019; 41: 796-800.
[15] Feng Z, Sun Z, Zhang Q and Ren S. Analysis of clinical efficacy and safety of hand-sewn anastomosis for the digestive tract with Da Vinci robot in rectal cancer surgery. World J Surg Oncol 2023; 21: 317.
[16] Dağdelen M, Çatal TK, Demirel ÖF, Ürün E, Kaçar S, Çepni K, Can G, Öksüz DÇ and Duran A. Evaluation of depression, anxiety, and sexual function in rectal cancer patients before and after neoadjuvant chemoradiotherapy. J Gastrointest Cancer 2023; 54: 1347-1352.
[17] Schoormans D, van Es B, Mols F, Wasowicz D, Beijer S and Ezendam NPM. The relation between sleep quality, sleep quantity, and gastrointestinal problems among colorectal cancer survivors: result from the PROFILES registry. Support Care Cancer 2022; 30: 1391-1398.
[18] Yang J, Han X, Liu X, Cao Y, Yu K, Liu L, Miao H and Li T. Exploration of perioperative sleep disturbance in 208 patients undergoing non-cardiac surgery: protocol for a prospective cohort study. Med Sci Monit 2023; 29: e938832.
[19] Tang NKY, Stella MT, Banks PDW, Sandhu HK and Berna C. The effect of opioid therapy on sleep quality in patients with chronic non-malignant pain: a systematic review and exploratory meta-analysis. Sleep Med Rev 2019; 45: 105-126.
[20] Zhao Q, Han D, Yang F, Han S and Xing N. Transvaginal natural orifice specimen extraction surgery (NOSES) in 3D laparoscopic partial or radical nephrectomy: a preliminary study. BMC Urol 2021; 21: 123.
[21] Dobó N, Márki G, Hudelist G, Csibi N, Brubel R, Ács N and Bokor A. Laparoscopic natural orifice specimen extraction colectomy versus conventional laparoscopic colorectal resection in patients with rectal endometriosis: a randomized, controlled trial. Int J Surg 2023; 109: 4018-4026.
[22] Hashemzehi M, Naghibzadeh N, Asgharzadeh F, Mostafapour A, Hassanian SM, Ferns GA, Cho WC, Avan A and Khazaei M. The therapeutic potential of losartan in lung metastasis of colorectal cancer. EXCLI J 2020; 19: 927-935.
[23] Zińczuk J, Maciejczyk M, Zaręba K, Romaniuk W, Markowski A, Kędra B, Zalewska A, Pryczynicz A, Matowicka-Karna J and Guzińska-Ustymowicz K. Antioxidant barrier, redox status, and oxidative damage to biomolecules in patients with colorectal cancer. Can malondialdehyde and catalase be markers of colorectal cancer advancement? Biomolecules 2019; 9: 637.
[24] Skrzydlewska E, Sulkowski S, Koda M, Zalewski B, Kanczuga-Koda L and Sulkowska M. Lipid peroxidation and antioxidant status in colorectal cancer. World J Gastroenterol 2005; 11: 403-6.
[25] Zhao Z, Chen Q, Zheng H, Li J, Zheng S and Zhao E. Analysis of the clinical effect of natural orifice specimen extraction surgery combined with transanal endoscopic operations. J Laparoendosc Adv Surg Tech A 2022; 32: 378-383.
[26] Cancro MP and Tomayko MM. Memory B cells and plasma cells: the differentiative continuum of humoral immunity. Immunol Rev 2021; 303: 72-82.
[27] Yamamoto S, Inomata M, Katayama H, Mizusawa J, Etoh T, Konishi F, Sugihara K, Watanabe M, Moriya Y and Kitano S; Japan Clinical Oncology Group Colorectal Cancer Study Group. Short-term surgical outcomes from a randomized controlled trial to evaluate laparoscopic and open D3 dissection for stage II/III colon cancer: Japan Clinical Oncology Group Study JCOG 0404. Ann Surg 2014; 260: 23-30.
[28] Wang W, Xu F, Gao F, Liang M, Li J, Li Q and Miao H. Short-term clinical effects and inflammatory response of natural orifice specimen extraction surgery versus conventional laparoscopic-assisted surgery for the treatment of sigmoid and rectal cancer. J Gastrointest Oncol 2023; 14: 815-823.
[29] Shapira I, Richman J, Pace TWW, Lim KO, Polusny MA, Hamner MB, Bremner JD, Mumba MN, Jacobs ML, Pilkinton P and Davis LL. Biomarker response to mindfulness intervention in veterans diagnosed with post-traumatic stress disorder. Mindfulness (N Y) 2022; 13: 2448-2460.
[30] Ogura Y, Fukuchi K, Morimoto H, Yuki T, Otsuka M, Shimauchi T, Honda T and Tokura Y. Elevation of circulating neutrophil extracellular traps, interleukin (IL)-8, IL-22, and vascular endothelial growth factor in patients with venomous snake mamushi (Gloydius blomhoffii) bites. J Dermatol 2022; 49: 124-132.
[31] Wu L, Jin Y, Zhao X, Tang K, Zhao Y, Tong L, Yu X, Xiong K, Luo C, Zhu J, Wang F, Zeng Z and Pan D. Tumor aerobic glycolysis confers immune evasion through modulating sensitivity to T cell-mediated bystander killing via TNF-α. Cell Metab 2023; 35: 1580-1596, e9.

[32] Sharma B, Gupta M, Sharma R, Gupta A, Sharma N, Sharma M, Sharma V, Vats S, Gupta M and Seam RK. Four percent formalin application for the management of radiation proctitis in carcinoma cervix patients: an effective, safe, and economical practice. J Cancer Res Ther 2019; 15: 92-95.

[33] Guend H, Widmar M, Patel S, Nash GM, Paty PB, Guillem JG, Temple LK, Garcia-Aguilar J and Weiser MR. Developing a robotic colorectal cancer surgery program: understanding institutional and individual learning curves. Surg Endosc 2017; 31: 2820-2828.