

Role of Robotic Natural Orifice Specimen Extraction Surgery in Colorectal Neoplasms

Hongliang Yao

The Second Xiangya Hospital, Central South University

Tiegang Li

The Second Xiangya Hospital, Central South University

Weidong Chen

The Second Xiangya Hospital, Central South University

Sanlin Lei

The Second Xiangya Hospital, Central South University

Kuijie Liu

The Second Xiangya Hospital, Central South University

Bo Liu

The Second Xiangya Hospital, Central South University

Jiangjiao Zhou (✉ zhoujiangjiao@csu.edu.cn)

The Second Xiangya Hospital, Central South University

Research Article

Keywords: Colorectal neoplasms, Natural orifice specimen extraction surgery, Robotic surgery

Posted Date: December 15th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-125641/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

To explore the safety and feasibility of robotic natural orifice specimen extraction surgery (NOSES) for colorectal neoplasms. All patients underwent robotic NOSES from March 2016 to October 2019 in our hospital were enrolled for retrospective analysis. Clinicopathological data were collected and analyzed. A total of 180 patients were enrolled. The average distance from the lower edge of the tumor to the anus was (8.64 ± 3.64) cm and Maximum circumferential diameter (CDmax) of specimen was (3.5 ± 1.6) cm. In terms of safety, the average operation time, intraoperative blood loss, and postoperative hospital stay were (187.5 ± 78.3) min, (47.4 ± 34) mL, and (11.3 ± 7.5) days, respectively. In terms of feasibility, the average number of lymph node harvested was (14.8 ± 5) . Notably, a close distance from the lower edge of the tumor to the anus with long operation time and postoperative hospital stay indicates high incidence of anastomotic leakage. In addition, either received nRCT has no effect on perioperative safety. Robotic NOSES shows advantages in terms of safety and feasibility compared with laparoscopic NOSES. This procedure could not only be a safe procedure but also could achieve good oncological outcomes.

Introduction

The progress of medical science includes the progress of concept and technology. Total mesorectal resection (TME) and neoadjuvant radiotherapy and chemotherapy (nRCT) are the major concept breakthroughs for colorectal cancer surgery. Benefitting from electronic, optical, and material science and technology advances, laparoscopic surgery emerged in the 1980s and has developed rapidly. Many clinical studies have shown the advantages, including low analgesic use, decreased postoperative pain, good cosmetic effect, and short length of hospital stay, for laparoscopic surgery. However, an incision must still be made at the abdominal wall to remove the specimen. Furthermore, this process could not completely avoid pain, infection, hernia, scarring, and other wound complications and could not meet the esthetic needs of patients, such as actors and gymnasts, engaged in specific occupations. Natural orifice specimen extraction robotic surgery (NOSES) can solve these problems. NOSES is designed to use laparoscopic instruments or soft endoscopy and other equipment to complete intra-abdominal surgery. No auxiliary incision is made at the abdominal wall, and the specimen is removed through the natural lumen (anus or vagina). Compared with traditional laparoscopic surgery, the most evident advantage of NOSES is the avoidance of auxiliary incision. However, several minuscule scars remain on the abdominal wall. To date, NOSES can be used for colorectal, stomach, small intestine, hepatobiliary, and gynecological tumors[1]. Many reports had also verified the effectiveness and safety of NOSES for colorectal neoplasms [2, 3].

In 2000, the Food and Drug Administration (FDA) approved the da Vinci Surgical System; our hospital installed the da Vinci Surgical System in 2015. Although the procedure of NOSES could be performed by laparoscopy, the da Vinci Surgical System still has its unique advantages due to its high-definition field of vision and seven degrees of freedom of the operation arm. Our department is one of the centers which previously carried out robotic NOSES for colorectal cancer in China[4]. This study aimed to summarize

single-center experience in robotic NOSES for sigmoid and rectal neoplasms through a retrospective analysis of the collected cases.

Materials And Methods

1. Inclusion and exclusion criteria of cases

From March 2016 to October 2019, all patients with sigmoid and rectal neoplasm and underwent robotic NOSES in the General Surgery Department of The Second Xiangya Hospital, Central South University were considered for retrospective analysis.

Inclusion criteria: (1) age ≥ 18 years old; (2) diagnosis of sigmoid and rectal neoplasm by biopsy via colonoscopy or benign neoplasm located in rectum that could not be resected locally through the anus; (3) written informed consent of patients; (4) expected removal of the specimen through the anus indicated by preoperative evaluation.

Exclusion criteria: (1) age < 18 years old; (2) emergency operation due to gastrointestinal obstruction, perforation, or bleeding; (3) metastasis of the lung, bone, or liver that cannot be removed simultaneously; (4) contraindications for robotic surgery.

This work is in accordance with the declaration of Helsinki and is approved by the Ethics Committee of the Second Xiangya Hospital, Central South University.

2. Information collection

The statistical information included the following: (1) patient characteristics: gender, age, chief complaint, comorbidity, history of laparotomy, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, distance from the lower edge of the tumor to the anus, and presence or absence of nRCT; (2) perioperative information: operation time, intraoperative blood loss, protective ileostomy, conversion to laparotomy, postoperative hospital stay, postoperative complications, reoperation, and total costs; (3) pathological information: histological type, differentiation, maximum circumferential diameter (CDmax) of specimen, depth of tumor invasion, the number of lymph nodes harvested, and the number of metastatic lymph nodes.

3. Surgical procedure

After successful general anesthesia, the patient assumed the Trendelenburg position. Five trocars were used (Fig. 1): one 12 mm trocar located at 3 cm above the umbilicus for robotic camera and another 12 mm trocar located at the right midclavicular line 1 cm above the umbilicus for assistant; three 8 mm trocar for robotic arms (R1 located at the right anterior superior iliac spine, R2 located at the left midclavicular line 1 cm above the umbilicus, and R3 located at the left anterior superior iliac spine). First,

an ultrasonic scalpel via R1 was used to separate the internal and external peritoneum of sigmoid colon, and the left ureter was properly protected. The inferior mesenteric artery and vein were isolated and clipped by absorbable vascular clamps (Fig. 1A). The descending colon artery was preserved. The rectum was completely isolated until 2–5 cm to the lower edge of the tumor. Then, the colorectum was ligated with self-locking nylon bandage (Figs. 1B and 1C). After the rectum was cut off by an ultrasonic scalpel, the assistant inserted an endoscope-sterile sleeve for the specimen into the pelvic cavity through the anus, and the resected specimen was pulled out through the anus. The assistant sent an orvil through the anus, and the operator sutured the stump of the sigmoid colon and placed the orvil into the sigmoid colon (Fig. 1D). After the operator sutured the stump of the rectum (Fig. 1E), the assistant placed the curved intraluminal stapler through the anus to complete the anastomosis (Fig. 1F). Then, the assistant injected air into the rectum through the anus. If air leakage occurred from the anastomosis or serous membrane eversion, suture can be performed. Perioperative management followed the international guidelines[5].

4. Statistical analysis

Data processing and statistical analysis were performed using SPSS (version 22.0, SPSS Inc., Chicago, IL, USA). Measurement data were expressed as the mean \pm standard deviation, and an independent sample t-test or variance analysis was used to compare the mean values. Qualitative data were expressed as frequency and percentage, and Pearson's χ^2 test or Fisher's exact probability method was used. $P < 0.05$ was considered statistically significant (two-tailed test).

Results

1. Patient characteristics

This study included 180 patients who underwent robotic NOSES from March 2016 to October 2019 in our hospital. In terms of gender, men accounted for 60% (108/180) and women for 40% (72/180). The mean age was (57.3 \pm 13.1) years old, and the mean BMI was (23.6 \pm 3.3) kg/m². The chief complaints included hematochezia in 81.1% of patients (146/180), increased frequency of defecation in 13.9% (25/180), abdominal discomfort in 1.1% (2/180), anal distention in 1.1% (2/180), and routine examination in 2.8% (5/180). In this study, 165 patients were tested for carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 242 before operation, of which 17.6% of patients (29/165) showed abnormal increase of CEA, and 4.8% (8/165) presented abnormal increase of CA242 level. A total of 133 patients were tested for CA19-9 before operation, wherein 6.8% (9/133) exhibited abnormal increase. The distance from the lower edge of the tumor to the anus was based on the colonoscopy report, with an average of (8.64 \pm 3.64) cm; those measuring less than 5, 5–10, and greater than or equal to 10 cm accounted for 7.2% (13/180), 54.4% (98/180), and 38.3% (69/180), respectively. The proportion of patients with nRCT was 15% (27/180). Twenty-six patients had abdominal or pelvic surgery history (14.4%). In terms of systemic disease, 41 patients presented with hypertension, 16 with diabetes, 10 with heart disease, 6 with lung disease, 7 with cerebrovascular disease, 5 with cirrhosis, and 9 with other

systemic diseases, such as hyperthyroidism and gout. ASA classification levels 1, 2, 3, and 4 reached 3.3% (6/180), 50.5% (91/180), 44.4% (80/180), and 1.7% (3/180) of patients, respectively (Table 1).

Table 1
Patient Characteristics

	Cases(n)	Ratio (%)
Gender		
Male	108	60
Female	72	40
Age		
20–39	16	8.9
40–59	79	43.9
60–79	75	41.7
≥ 80	10	5.6
Chief complaint		
Hematochezia	146	81.1
increased times in defecation	25	13.9
Abdominal discomfortable	2	1.1
Anal distention	2	1.1
Routine examination	5	2.8
Systemic disease		
Hypertension	41	22.8
Diabetes	16	8.9
Cardiovascular diseases	10	5.6
Respiratory diseases	6	3.3
Cerebrovascular disease	7	3.9
Cirrhosis	5	2.8
Other	9	5
ASA score		
1	6	3.3
2	91	50.5
3	80	44.4

	Cases(n)	Ratio (%)
4	3	1.7
History of abdominal surgery		
Yes	26	14.4
No	154	85.6
nCRT		
Yes	27	15
No	153	85
Distance from the lower edge of the tumor to the anus		
<5 cm	13	7.2
5-10cm	98	54.4
≥ 10 cm	69	38.3
CEA(ng/mL)		
Normal	136	82.4
Higher	29	17.6
CA19-9(ng/mL)		
Normal	124	93.2
Higher	9	6.8
CA242(ng/mL)		
Normal	157	95.2
Higher	8	4.8

2. Postoperative pathological information

In this study, 170/180 (94.4%) of histological types were tubular adenocarcinoma, 5 were adenomas, 3 were mucinous adenocarcinoma or signet ring cell carcinoma, 1 was endometriosis, and 1 was a neuroendocrine tumor. In terms of the degree of differentiation of tubular adenocarcinoma, the most common was moderately differentiated adenocarcinoma, accounting for 80.6% (137/170), followed by 1.8% (3/170) high differentiation and 17.6% (30/170) low differentiation. The average CDmax of specimen was (3.5 ± 1.6) cm, and the highest CDmax value was 12 cm. The number of lymph nodes harvested in all cases ≥ 12 accounted for 73.9% (133/180), and the average number of lymph nodes harvested for each case was (14.8 ± 5). Based on the depth of tumor invasion, Tis stage was 1.2% (2/173), T1 stage was 8.1% (14/173), T2 stage was 26.6% (46/173), T3 stage was 37.6% (65/173), and

T4 stage was 26.6% (46/173). In all patients with colorectal cancer, lymph node metastasis accounted for 33.5% (58/173), and simultaneous liver metastasis was observed in one case. The circumferential resection margins (CRMs), including the upper and lower resection margins, were negative in all patients (Table 2).

Table 2
Pathological information

	Cases(n)	Ratio (%)
Histology type		
Tubular adenocarcinoma	170	94.4
Mucinous adenocarcinoma	3	1.7
Adenoma	5	2.8
Endometriosis	1	0.6
Neuroendocrine tumor	1	0.6
Differentiation		
Highly	3	1.8
Moderately	137	80.6
Poorly	30	17.6
CDmax		
<3 cm	59	32.8
3-5cm	84	46.7
≥ 5 cm	37	20.6
T staging		
Tis	2	1.2
T1	14	8.1
T2	46	26.6
T3	65	37.6
T4	46	26.6
Lymph node harvested		
<12	47	26.1
≥ 12	133	73.9
Lymph node metastasis		
Yes	58	33.5
No	115	66.5

	Cases(n)	Ratio (%)
Liver metastasis of adenocarcinoma		
Yes	1	0.6
No	172	99.4
Resection margins		
Positive	0	0
Negative	180	100

3. Perioperative outcomes

All 180 cases completed robotic NOSES successfully, and no conversion to laparotomy was observed. The average medical cost was 110046 ± 35003 CNY. The mean operative time was (187.5 ± 78.3) min, and the mean intraoperative blood loss was (47.4 ± 34) ml. According to the surgical procedures, 171 patients underwent robotic TME for the rectum or complete mesocolic excision (CME) for the sigmoid. One patient underwent robotic TME plus subtotal colectomy, one underwent robotic TME plus resection of liver metastasis; one underwent robotic TME plus partial transverse colectomy. Two patients underwent robotic TME plus ovariectomy; another two underwent robotic TME plus hysterectomy. One patient underwent robotic TME plus left partial nephrectomy due to renal angioliomyoma, and another one underwent robotic TME plus ureteral repair due to intraoperative injury of the left ureter. All specimens were removed through the anus. Cases for protective ileostomy accounted for 6.7% (12/180). The average postoperative fasting time was (4.2 ± 3.9) days, and the average postoperative hospital stay was (11.3 ± 7.5) days. The incidence of postoperative complications was 11.7% (21/180). The incidence of anastomotic leakage was 4.4% (8/180), and the other complications included abdominal infection, lung infection, anastomotic bleeding, and abdominal hemorrhage. The reoperation rate was 2.2% (4/180), which was achieved with ileostomy in all cases after anastomotic leakage. The other 17 patients with complications were managed with anti-infective therapy, ultrasound-guided percutaneous drainage, colonoscopy, and endoscopic treatment. No postoperative anal dysfunction nor 90-day death was observed (Table 3).

Table 3
 Perioperative outcomes

	Cases(n)	Ratio(%)
Surgical procedure		
TME or CME	171	95
TME + Subtotal colectomy	1	0.6
TME + Resection of liver metastasis	1	0.6
TME + Resection of partial transverse colon	1	0.6
TME + Ovariectomy	2	1.1
TME + Hysterectomy	2	1.1
TME + Left partial nephrectomy	1	0.6
TME + Ureteral repair	1	0.6
Protective ileostomy		
Yes	12	6.7
No	168	93.3
Clavien-Dindo Classification		
I	1	0.6
II	10	5.6
IIIa	6	3.3
IIIb	3	1.7
4b	1	0.6
Anastomotic leakage		
Yes	8	4.4
No	172	95.6
Reoperation		
Yes	4	2.2
No	176	97.8
Postoperative anal function		
Abnormal	0	0

	Cases(n)	Ratio(%)
Normal	180	100
90-day mortality		
Yes	0	0
No	180	100

4. Influence on robotic NOSES by the distance between tumor and anus or nRCT

According to the *International consensus on natural orifice specimen extraction surgery (NOSES) for colorectal cancer*[6], the tumor was divided into three groups based on the distance from the lower edge of the tumor to the anus: lower group (distance of less than 5 cm), middle group (distance of greater than or equal to 5 and less than 10 cm), and upper group (distance of greater than or equal to 10 cm). The safety indexes included operation time, intraoperative blood loss, conversion to laparotomy, postoperative hospital stay, anastomotic leakage, reoperation, and 90-day mortality. The feasibility indexes comprised the numbers of lymph node harvested and positive resection margins. Table 4 shows the results. Close distance from the lower edge of the tumor to the anus means long operation time, high intraoperative blood loss, and high incidence of anastomotic leakage. The difference was statistically significant ($P < 0.05$). nRCT had no effect on the safety and feasibility for robotic NOSES. The results are shown in Table 5.

Table 4
Influence on robotic NOSES by the distance between the lower edge of the tumor to the dentate line

	<5 cm	5-10cm	≥ 10 cm	P
Safety				
Operative time (min)	263.9 ± 178.6	184 ± 61.9	178 ± 61.7	0.001
Blood loss (ml)	54.6 ± 48.4	45.2 ± 29.8	49.3 ± 36.8	0.546
Conversion to laparotomy (%)	0	0	0	N/A
Postoperative hospital stay (d)	16.5 ± 12.4	12 ± 8.3	9.4 ± 3.3	0.002
Anastomotic leakage (n, %)	1/13,7.7%	7/98,7.1%	0/69,0%	0.048
Reoperation (n, %)	0,0%	4/98,4.1%	0,0%	0.266
90-day mortality (%)	0	0	0	N/A
Feasibility				
Lymph node harvested	13 ± 3.1	14.5 ± 5.3	15.5 ± 4.7	0.192
Positive resection margins (%)	0	0	0	N/A

Table 5
Influence on robotic NOSES by nRCT

	With nRCT	No nRCT	P
Safety			
Operative time (min)	184.8 ± 76.1	187.9 ± 78.9	0.846
Blood loss (ml)	57.4 ± 39	45.7 ± 32.9	0.098
Conversion to laparotomy (%)	0	0	N/A
Postoperative hospital stay (d)	11.7 ± 5.8	11.3 ± 7.7	0.774
Anastomotic leakage (n, %)	6/158,3.8%	2/27,7.4%	0.076
Reoperation (n, %)	0,0%	4/153,2.6%	>0.999
90-day mortality (%)	0	0	N/A
Feasibility			
Lymph node harvested	14 ± 5.6	14.9 ± 4.9	0.423
Positive resection margins (%)	0	0	N/A

Discussion

Surgical incision is not only related to esthetics but also associated with postoperative pain and increased wound complications, including infection, hernia formation, and scarring. Surgical incision also causes panic, anxiety, irritability, and other adverse psychological emotions, which could have a negative impact on recovery, among patients. Until the end of the 20th century, the traditional understanding was performing surgery and scar binding together. In 1985, the first laparoscopic cholecystectomy in the world shortened the surgical scar but failed to completely eradicate it. In 2007, French doctor Marescaux completed the first truly scar free operation in the world, and transvaginal cholecystectomy, which minimally invasive surgery requirements, has entered a new era[1]. NOSES is a kind of operation that can realize the concept of “no scar” surgery to a certain limit. NOSES is a kind of operation that uses soft endoscope or laparoscope to enter the abdominal or chest cavity through the mouth, gastrointestinal tract, vagina, bladder, and other natural orifices to conduct medical procedures, including exploration, biopsy, appendectomy, hysterectomy, and cystectomy, without any auxiliary incision on the body surface[7, 8].

NOSES is especially suitable for colorectal surgery. Incisions in the oral cavity, rectum, vagina, and other natural orifices for appendectomy, cholecystectomy, and nephrotomy are often necessary to remove specimens from the natural lumen. The rectum has to be disconnected during colorectal surgery. The rectum and anus could be natural orifices for specimen extraction and could be used to avoid performing any artificial incision, rendering them with evident natural advantage. Based on the orifice for specimen extraction, NOSES could be divided into transanal and transvaginal NOSES. However, all cases presented in these reports were transanal NOSES. We excluded the specimen removal from the vagina for the following reasons. First, transvaginal NOSES could only be applicable for female patients. Second, incision on the vaginal wall may increase the risk of postoperative complications and sexual dysfunction. Third, transvaginal NOSES is also limited by ethics. In June 2017, China NOSES Alliance was established and released *Expert consensus of natural orifice specimen extraction surgery in colorectal neoplasm (2017 edition)*[9] to promote the application of NOSES. The International Alliance of NOSES also issued *International consensus on natural orifice specimen extraction surgery (NOSES) for colorectal cancer* in 2019[6].

Many reports are available on laparoscopic NOSES for colorectal cancer[2, 10, 11]; compared with conventional laparoscopic surgery, laparoscopic NOSES is a safe procedure and can achieve similar oncological outcomes. Wolthuis et al. conducted a clinical trial comparing the short-term effects of conventional laparoscopic surgery and laparoscopic NOSES; their results showed that the postoperative pain of patients in the NOSES group was alleviated significantly[12]. According to the report of an international multicenter study including 412 cases of conventional laparoscopic radical resection of rectal cancer and 356 cases of laparoscopic NOSES, no difference was observed in the operation time, the number of lymph nodes harvested, incidence of anastomotic leakage, and length of postoperative hospital stay. Incision infection and incisional hernia were also observed in the conventional laparoscopic radical resection group[11]. A retrospective study of 718 cases of colorectal cancer in 79 hospitals in

China showed the following results: incidence of anastomotic leakage of 3.5%, reoperation rate of 3.6%, and average intraoperative blood loss less than 100 mL; these findings fully demonstrated the safety of laparoscopic NOSES for rectal cancer[13]. Two meta-analysis involving 1,435 and 837 patients also showed that compared with conventional laparoscopic surgery, NOSES may be a safe procedure and can significantly reduce the duration of hospital stay, accelerate the postoperative recovery with good cosmetic results, result in less postoperative pain and limited complications, and achieve similar oncological outcomes[14, 15].

Da Vinci Robot System was approved by FDA in 2000. The first robot-assisted radical resection of rectal cancer was reported in 2002[16]. Since then, numerous studies have reported robot-assisted radical resection of colorectal cancer [11, 17–20]. However, in most reports, the specimens were extracted through a small abdominal incision; meanwhile, the reports on robotic NOSES are rare. Three retrospective analysis reports exist, and the rest are case reports[21–24]. Compared with the previous reports on laparoscopic NOSES, robotic NOSES in our hospital revealed advantages in terms of safety and feasibility[3, 13]. In terms of the safety of robotic NOSES, our results showed that the average operation time was (187.5 ± 78.3) min, intraoperative blood loss was (47.4 ± 34) mL, no conversion to laparotomy occurred, postoperative hospital stay was (11.3 ± 7.5) days, the incidence of anastomotic leakage was 4.4%, the reoperation rate was 2.2%, and no 90-day death was observed. In terms of the feasibility, the average number of lymph nodes harvested was (14.8 ± 5), and no case with positive margin was observed (Table 6).

Table 6
Comparison between robotic NOSES and Laparoscopic NOSES

	Robotic NOSES	Wang ³	Xu ¹²
Safety			
Operative time (min)	187.5 ± 78.3	198.9 ± 55.2	210.5 ± 39.4
Blood loss (ml)	47.4 ± 34	73.7 ± 54.2	61.8 ± 23.1
Conversion to laparotomy (%)	0	0	0
Postoperative hospital stay (d)	11.3 ± 7.5	12.3 ± 4.1	12.1 ± 4.0
Anastomotic leakage (n, %)	8,4.4%	9,4.43%	25,3.5%
Reoperation (n, %)	4,2.2%	2,1%	23,3.2%
90-day mortality (%)	0	0	0
Feasibility			
Lymph node harvested	14.8 ± 5	12.9 ± 5.1	13.4 ± 3.5
Positive resection margins (%)	0	0	0

Either laparoscopic or robotic NOSES could be performed in our department[25]. As per our experience, especially in ultra-low rectal cancer, robotic NOSES has several advantages compared with laparoscopic NOSES. First, the da Vinci Surgery System has a high-definition 3D vision and requires no cooperation from the assistant holding the camera. This procedure can display the pelvic autonomic nerve and the loose connective tissue space between the rectum and pelvic cavity. Therefore, complete TME and the protection of bladder and sexual function are conducive. Second, for ultra-low rectal tumor, if the rectum is cut off directly by an ultrasonic scalpel during laparoscopic surgery, suturing of the pouch is difficult. However, if the rectum is to be amputated with an endoscopic linear cutter, the procedure may not be completed due to the narrow pelvic cavity. However, the problems mentioned above could be resolved by robotic NOSES. The ultra-low rectum can be sutured directly after the rectum is amputated by an ultrasonic scalpel. If the anastomosis is unsatisfactory, we can use the da Vinci Robot System to sew and strengthen the anastomosis directly to reduce the incidence of anastomotic leakage.

This study showed that T4 stage cases accounted for 26.6%, and the proportion of patients whose maximum diameter of tumor is greater than or equal to 5 cm was 20.6%, which is inconsistent with the recommendations of the *International consensus on natural orifice specimen extraction surgery (NOSES) for colorectal cancer*[6]. Based on the recommendations, cases of T2 and T3 stage tumors should be appropriate for NOSES, whereas T4 stage cases are not recommended given the difficulty of guaranteeing a negative CRM. However, we believe that for experienced teams in colorectal minimally invasive surgery, robotic NOSES for T4 stage cases is safe while strictly observing the principle of tumor-free technique. In terms of the CDmax of specimen, the consensus suggested that if the specimen is to be removed through the anus, then the CDmax should be less than 3 cm. However, our data show that the proportion of CDmax of specimen exceeding 3 cm accounted for 67.3%, that exceeding 5 cm accounted for 20.6%, and the largest reached 12 cm. We believe that if CDmax is limited to specimens not exceeding 3 cm, more than a half of patients will lose the opportunity for NOSES. Based on our experience, indications for NOSES could be appropriately relaxed. On the premise of full anal dilation, most specimens with CDmax of less than 5 cm can be removed through the anus. This procedure will not lead to laceration of the rectum and anus. In addition, the specific situation should be analyzed in detail. When the specimens are extracted from the anus during NOSES, one end of the rectum is clamped by surgical forceps, and the specimens are extracted from the anus along the longitudinal axis of the rectum. Therefore, if the CDmax is along the longitudinal axis of the rectum, specimens can still be easily extracted from the anus despite a CDmax exceeding 5 cm. On the contrary, a CDmax vertical to the longitudinal axis of the rectum will increase the difficulty of pulling out the specimen from the anus. In this study, the largest CDmax of specimen extracted from the anus was 12 cm. However, this length was measured along the longitudinal axis of the rectum, and its short axis was less than 2 cm. Thus, the specimen was a long strip that can be naturally removed through the anus. Whether the specimen can be extracted from the anus is also affected by other factors. For example, if the distance between the lower edge of the tumor and the anus is relatively close, dilation of the rectum, which needs to be protected during specimen extraction, is unnecessary. Thus, the CDmax of specimens could be large. Otherwise, if the distance is relatively long, the free rectum in the pelvic cavity must be dilated during specimen

extraction, which will lead to laceration of the rectum and anus if the CDmax of specimen is notably large. As a promising minimally invasive technique, we appeal to all surgical colleagues working on robotic NOSES to promote the development of robotic NOSES in the world for the benefit of colorectal patients.

Our analysis has several limitations. First, progression-free survival and overall survival of all selected cases need to be verified through a long follow-up. Second, this research is a retrospective study. Thus, the integrity and homogeneity of research data cannot be guaranteed.

Declarations

ACKNOWLEDGEMENTS

We are grateful for the help of colleagues in the operating room and anesthesiology department during robotic NOSES.

Institutional review board statement:

This study was reviewed and approved by the Ethics Committee of the Second Xiangya Hospital, Central South University.

Supported by:

No funding was received for writing this study.

Author contributions:

Jiangjiao Zhou conceived and designed the article; Hongliang Yao, Tiegang Li, Kuijie Liu, Bo Liu, and Sanlin Lei performed the operation; Weidong Chen and Sanlin Lei analyzed the data; Jiangjiao Zhou wrote the study; Tiegang Li, Weidong Chen, and Hongliang Yao proofread and revised the manuscript.

Conflict-of-interest statement:

We have no financial relationships to disclose.

Data sharing statement:

No additional data are available.

References

1. Zorron R, Filgueiras M, Maggioni LC, et al (2007) NOTES. Transvaginal cholecystectomy: report of the first case. Surg Innov 14:279–283

2. Park JS, Kang H, Park SY, et al (2018) Long-term outcomes after Natural Orifice Specimen Extraction versus conventional laparoscopy-assisted surgery for rectal cancer: a matched case-control study. *Ann Surg Treat Res* 94:26–35
3. Yuliuming W, Qian Z, Lei Y, et al (2019) Retrospective study of 203 cases of colorectal neoplasms treated by natural orifice specimen extraction surgery. *Chin J Colorec Dis (Electronic Edition)* 29:32–37
4. Yao H, Li T, Chen W, et al (2020) Safety and Feasibility of Robotic Natural Orifice Specimen Extraction Surgery in Colorectal Neoplasms During the Initial Learning Curve. *Frontiers in Oncology* 10
5. Gustafsson UO, Scott MJ, Hubner M, et al (2019) Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS((R))) Society Recommendations: 2018. *World J Surg* 43:659–695
6. Guan X, Liu Z, Longo A, et al (2019) International consensus on natural orifice specimen extraction surgery (NOSES) for colorectal cancer. *Gastroenterol Rep (Oxf)* 7:24–31
7. China Natural Orifice Specimen Extraction Surgery A (2019) [Consensus of natural orifice specimen extraction surgery in gastric cancer (2019)]. *Zhonghua Wei Chang Wai Ke Za Zhi* 22:711–714
8. Su H, Li B, Ren W, et al (2018) Successful treatment of recurrent rectal implantation metastasis of ovarian cancer by natural orifice specimen extraction surgery: a case report. *Onco Targets Ther* 11:5925–5931
9. Alliance CN (2017) Expert consensus of natural orifice specimen extraction surgery in colorectal neoplasm (2017 edition). *Chin J Colorec Dis (Electronic Edition)* 6:266–273
10. Zhou JJ, Tian YT, Liu H, et al (2013) [Analysis of the relationship between clinicopathological factors and lymph node metastasis of pancreatic adenocarcinoma]. *Zhonghua zhong liu za zhi [Chinese journal of oncology]* 35:132–134
11. Liu Z, Efetov S, Guan X, et al (2019) A Multicenter Study Evaluating Natural Orifice Specimen Extraction Surgery for Rectal Cancer. *J Surg Res* 243:236–241
12. Wolthuis AM, Fieuws S, Van Den Bosch A, et al (2015) Randomized clinical trial of laparoscopic colectomy with or without natural-orifice specimen extraction. *Br J Surg* 102:630–637
13. Xu G, Qingchao T, Guiyu W, et al (2017) Retrospective study of 718 colorectal neoplasms treated by natural orifice specimen extraction surgery in 79 hospitals. *Chin J Colorec Dis (Electronic Edition)* 6:469–477
14. Liu RJ, Zhang CD, Fan YC, et al (2019) Safety and Oncological Outcomes of Laparoscopic NOSE Surgery Compared With Conventional Laparoscopic Surgery for Colorectal Diseases: A Meta-Analysis. *Frontiers in oncology* 9:597
15. Ma B, Huang XZ, Gao P, et al (2015) Laparoscopic resection with natural orifice specimen extraction versus conventional laparoscopy for colorectal disease: a meta-analysis. *Int J Colorectal Dis* 30:1479–1488
16. PA W, S M, A W, et al (2002) Telerobotic-assisted laparoscopic right and sigmoid colectomies for benign disease. *Dis Colon Rectum* 45:1689–1694

17. Cao C-L, Li T-Y, Liu D-N, et al (2016) Comparison of short-term outcomes between roboticassisted and laparoscopic surgery for rectal cancer. *World Chinese Journal of Digestology* 24:2264–2269
18. ZOU Zhen, Bo T, Dongning L, et al (2018) Short-term outcomes of robotic versus laparoscopic radical resection for middle and low rectal cancer: a single-center randomized, controlled study. *Chinese Journal of General Surgery* 27:408–413
19. Megevand JL, Lillo E, Amboldi M, et al (2019) TME for rectal cancer: consecutive 70 patients treated with laparoscopic and robotic technique-cumulative experience in a single centre. *Updates Surg* 71:331–338
20. Liu WH, Yan PJ, Hu DP, et al (2019) Short-Term Outcomes of Robotic versus Laparoscopic Total Mesorectal Excision for Rectal Cancer: A Cohort Study. *Am Surg* 85:294–302
21. Xuefeng Z, Chi L, Cheng Z, et al (2013) Totally robotic surgery for rectal cancer with transanal specimen extraction. *Chinese Journal of Practical Surgery* 33:871–873
22. Hu R, Jiang L, Kun Z, et al (2014) Trans-natural orifice transuminal specimen extraction in robotic rectal cancer surgery: An analysis of 21 patients. *Chinese Journal of Practical Surgery* 34:252–254
23. Efetov SK, Tulina IA, Kim VD, et al (2019) Natural orifice specimen extraction (NOSE) surgery with rectal eversion and total extra-abdominal resection. *Techniques in coloproctology* 23:899–902
24. Minjares-Granillo RO, Dimas BA, LeFave JJ, et al (2019) Robotic left-sided colorectal resection with natural orifice IntraCorporeal anastomosis with extraction of specimen: The NICE procedure. A pilot study of consecutive cases. *American journal of surgery* 217:670–676
25. Zhou J, Xiong L, Miao X, et al (2020) Outcome of robot-assisted pancreaticoduodenectomy during initial learning curve versus laparotomy. *Scientific reports* 10:9621

Figures

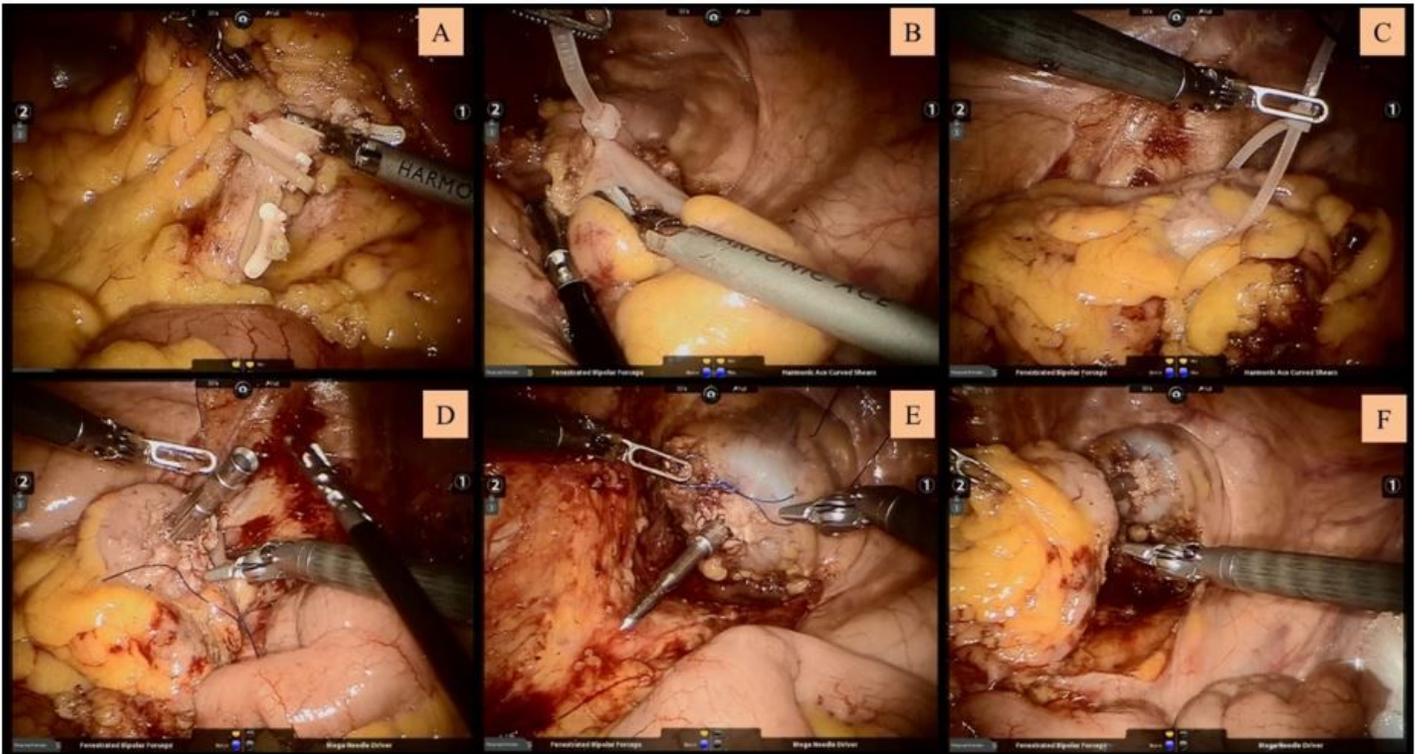


Figure 1

Surgical procedure. A: The inferior mesenteric artery and vein were isolated and clipped by absorbable vascular clamps; B: Rectum was ligated with self-locking nylon bandage; C: Sigmoid colon was ligated with self-locking nylon bandage; D: Suture the stump of sigmoid colon and put the orvil into the sigmoid colon; E: Suture the stump of rectum; F: Complete the anastomosis.

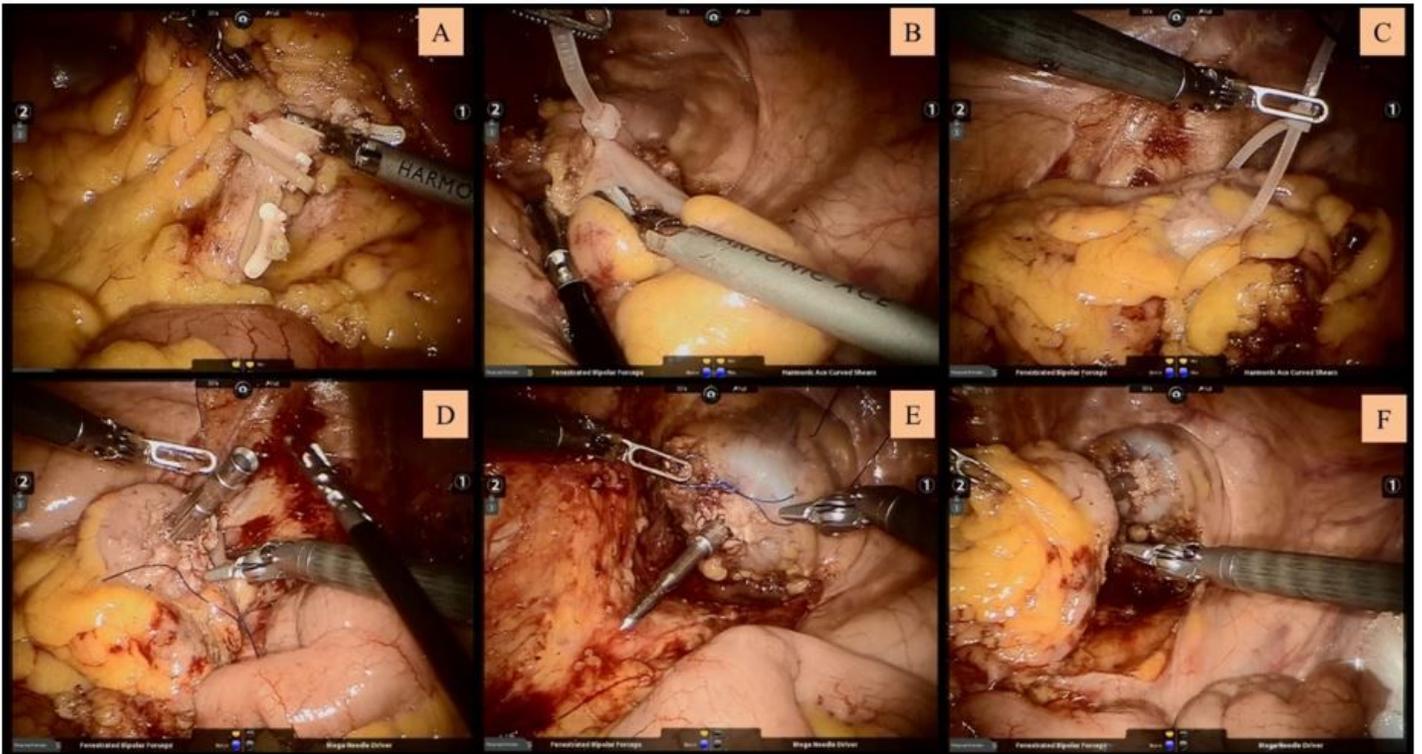


Figure 1

Surgical procedure. A: The inferior mesenteric artery and vein were isolated and clipped by absorbable vascular clamps; B: Rectum was ligated with self-locking nylon bandage; C: Sigmoid colon was ligated with self-locking nylon bandage; D: Suture the stump of sigmoid colon and put the orvil into the sigmoid colon; E: Suture the stump of rectum; F: Complete the anastomosis.