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Comparison of side-to-side anastomosis vs. end-to-end anastomosis in NOSES operation for left colon cancer: a retrospective study

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Abstract

Objective To analyze and compare the application and efficacy of side-to-side anastomosis and end-to-end anastomosis in natural orifice specimen extraction surgery (NOSES) NOSES operation for left colon cancer.

Methods A retrospective analysis of 69 patients in our hospital from February 2018 to February 2022 who underwent NOSES for left colon tumors. The observation group was performed with side-to-side anastomosis (Overlap). For digestive tract reconstruction, the control group was anastomosed by end-to-end anastomosis; the intraoperative and postoperative conditions and complications were compared between the two groups.

Results There was no significant difference in operation time and intraoperative blood loss between the two groups ($P > 0.05$). However, the intraoperative anastomosis time in the observation group was significantly shorter than that in the control group ($P < 0.001$). Additionally, there was no significant difference in the time of first exhaustion, defecation time, degree of patency of defecation, frequency of defecation, postoperative hospital stays and postoperative pain between the two groups ($P > 0.05$). Furthermore, the overall incidence of postoperative complications did not show a significant difference ($P > 0.05$).

Conclusions In the NOSES surgery of left colon cancer, both side-to-side anastomosis (Overlap) and end-to-end anastomosis yielded comparable intraoperative and postoperative conditions and complications, but the side-to-side anastomosis (Overlap) method was simpler operation-wise and had a shorter intraoperative anastomosis time. As such, this method is the preferred anastomosis method when NOSES for colorectal cancer is carried out in primary hospitals.

Trial registration number ChiCTR1900026104 (2019-09-21).

Keywords NOSES, Colon cancer, Laparoscopic surgery, Side-to-side anastomosis, End-to-end anastomosis

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Introduction

Colon cancer is one of the common malignancies of the digestive tract. According to the 2020 Global Cancer Statistics Report [1], the total incidence and death of colorectal cancer accounted for 10% and 9.4% of the total cancer incidence respectively, ranking third in terms of incidence and second in mortality. With the improvement of the living standards of our people and the change of dietary structure, the overall incidence of colorectal cancer is increasing annually. It is estimated that the number of CRC cases will reach approximately 3.2 million by 2040 [2]. At present, the treatment of colon cancer is still mainly surgery, supplemented by medical adjuvant chemotherapy or other comprehensive treatment. In recent years, laparoscopic techniques have emerged as the primary approach for colon cancer treatment. The COLOR clinical trial [3] demonstrated that laparoscopic surgery for colorectal cancer is as effective as open surgery, with benefits in patient prognosis and length of hospital stay. NOSES surgery is a novel concept and technique that involves opening a hollow viscus that already communicates with the outer environment, such as the vagina or distal gastrointestinal tract, in order to retrieve specimen [4].

Ongoing research focuses on the continuous exploration of its safety, feasibility, and significant advantages in radical colon cancer resection. In NOSES surgery, intraoperative gastrointestinal reconstruction is one of the crucial steps. Studies have shown [5] that total laparoscopic radical resection of left colon cancer and the use of "Overlap" anastomosis for gastrointestinal reconstruction are simple and satisfactory compared with traditional anastomosis methods. In this study, in order to further explore the therapeutic effects of side-to-side anastomosis and end-to-end anastomosis in NOSES for left colon cancer under complete laparoscopy, clarify the advantages of the two anastomosis methods in colonic anastomosis, and further advocate for the adoption of NOSES technique in primary healthcare settings.

Information and methods

Clinical data

A retrospective cohort study was performed on 69 patients with left colon cancer who underwent laparoscopic colon cancer resection through natural orifice specimen extraction (NOSES) from the Department of Gastrointestinal Surgery, Huizhou Third People's Hospital, from February 2018 to February 2022. According to the different anastomosis of the colon, it was divided into side-to-side anastomosis group ($n=30$) and end-to-end anastomosis group ($n=39$). Inclusion criteria includes: (1) preoperative colonoscopy, pathological results diagnosed as left colon cancer; Preoperative CT to evaluate tumors as T1-T3; (2) The tumors were all single primary colon tumors, with no metastasis and no preoperative chemoradiotherapy; (3) Laparoscopic radical resection of colon cancer (NOSES surgery) was performed. Exclusion criteria includes: (1) atients with large tumor lesions (>3 cm) or metastasis, mesenteric hypertrophy and severe obesity (BMI > 30 kg/m^2); (2) Patients converted to open surgery; (3) Patients with joint resection of other organs during surgery; (4) Previous history of laparoscopic surgery resulted in extensive abdominal adhesions. The age, gender, BMI, tumor location and stage of the two groups were not statistically significant ($P>0.05$) and were comparable.

Surgical methods

(1) Routine preoperative management involved improving examinations and applying standardize treatment and strictly following the diagnosis and treatment guidelines. To perform the NOSES, strict bowel preparation was required. Oral administration of polyethylene glycol one day before operation until defecation was clear and no fecal residue in the intestine, with preoperative enema performed if necessary.

(2) After general anesthesia, patients took the modified lithotomy, flat supine position. The five-hole method is used for trocar arrangement (as shown in Fig. 1a).

(3) Explore the abdominal cavity and pelvis and detect tumor location, tumor metastases, ascites, and enlarged lymph nodes; mark the distance between the proximal and distal ends of the tumor (as shown in Fig. 1b).

(4) Ultrasonic scalpel was employed for mobilization, lymphadenectomy and dissection. Selectively dissects the left colonic artery or sigmoid artery and free descending colon, splenic flexure or sigmoid colon.

According to the CME principle, the mesentery is freed 10 cm from both the distal and proximal end of the tumor. And then the affected bowel segment is excised with a 10 cm distance preserved from the tumor, followed with an incision protective sleeve placed in the main operation hole. The anal canal is exteriorized into the abdominal cavity to create an isolated channel (as shown in Fig. 1c), while the tumor specimen was excised.

(5) For side-to-side anastomosis group, an opening is made 7–8 cm near the colon and 1–2 cm at the distal colon cutoff on the contralateral intestinal wall (as shown in Fig. 1d). A disposable linear cutting sutra (60–35 mm) is placed to perform colonic side-to-side anastomosis (Overlap; as shown in Fig. 1e); For end-to-end anastomosis group, 2 cm incision was cut 10 cm above the proximal end of the left colon tumor for excision, the head of tubular stapler was inserted into the abdominal cavity through the channel after disinfection (as shown in Fig. 1f). The excised tumor specimen was pulled out from the channel. Thereafter, the distal colonic incision is sutured with a straight stapler, and a tubular stapler

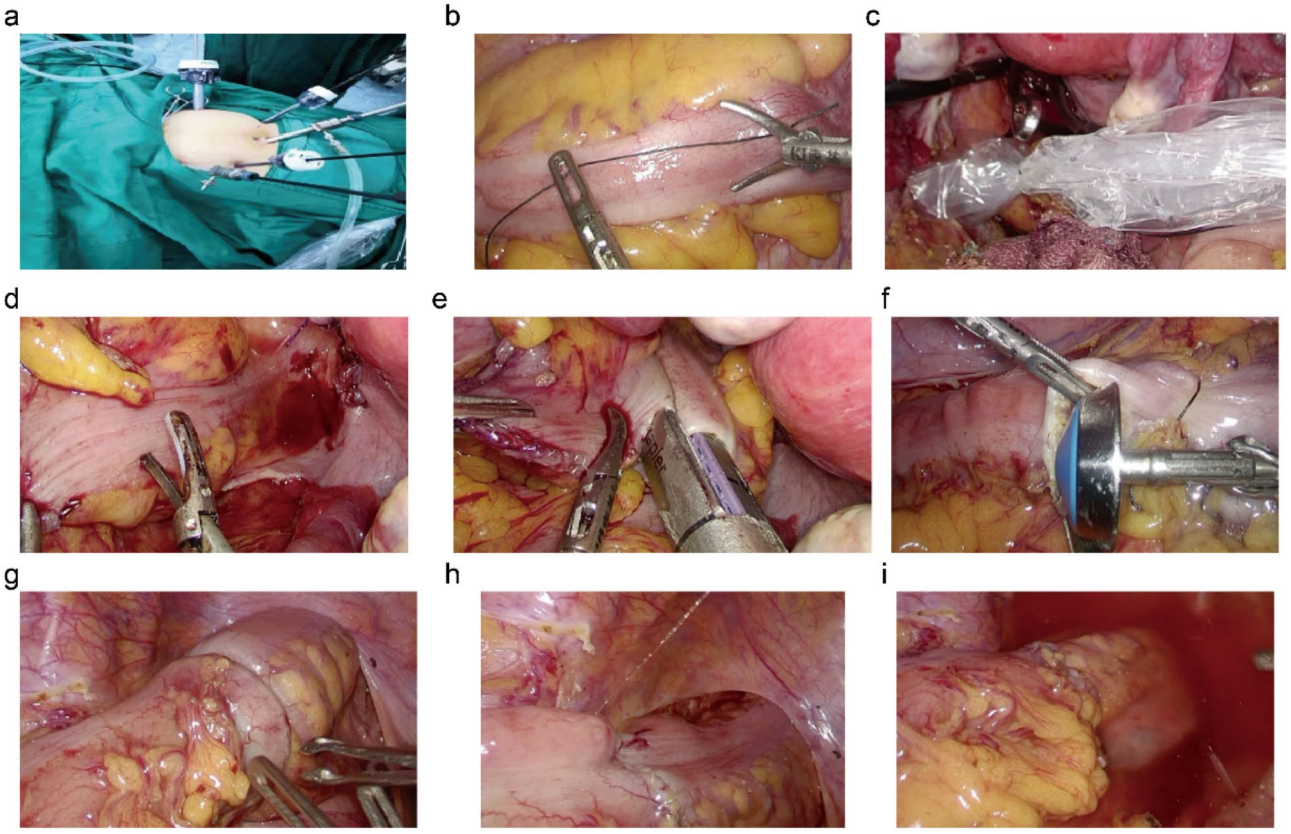

Fig. 1 Key surgical steps of NOSES. **(a)** Five-hole method trocar arrangement; **(b)** explored the tumor location and marked the distance between the anterior and proximal bowel of the tumor; **(c)** inserts an incision protector to pull out the anus to make an isolation cavity; **(d)** Ultherapy opening at the distal and proximal end of the colon; **(e)** Straight cutting stapler for side anastomosis of the broken end; **(f)** Proximal colon with nail base; **(g)** Tubular stapler for end-to-end anastomosis; **(h)** Absorbable stitches (3 – 0) reinforcement anastomosis opening; **(i)** Pelvic floor water injection to test anastomotic leakage

was inserted through the anus to connect and anastomosis with the its head at end of the proximal (as shown in Fig. 1g). To confirm intact blood flow and exclude the possibility of bleeding of the intestine stump, pulsation of the mesenteric arteries and the color of the anastomosis was checked.

(6) After anastomosis, 3 – 0 absorbable barbed suture line was use to full-thickness continuous suture of the common opening of the colonic cut (as shown in Fig. 1h), pelvic perfusion with saline was used to check for any signs of anastomotic leakage (as shown in Fig. 1i).

Observation index and outcome measures

The primary outcome was complication rate within 6 months after operation. Other outcomes included operation time, estimated intraoperative blood loss, intraoperative anastomosis time, postoperative stay and postoperative pain score. Pain score was assessed 24 h after operation using a 0-to-5-point verbal rating scale (VRS-5, 0 for no pain; 1, mild discomfort; 2, discomforting pain; 3, distressing pain; 4, intense pain; 5, excruciating pain). Patients were followed up with outpatient visits or telephone interviews at 1-week and 6-months after discharge. Patients were required to subjectively record the frequency of defecation and defecation patency (rated in 4 categories: patency, impatency, strenuousness, need for intervention to defecate - including oral medication, glycerine enema and other methods to assist defecation) during the two-week period after surgery. Colonoscopy examination was performed on all patients 6 months (180.7 ± 9.2 days) after surgery.

Statistics

SPSS 25.0 software was used for data analysis. Data were presented as mean ± standard deviation (SD), and independent t-test were used for comparison. Data that did not conform normal distribution were adjusted with Mann-Whitney U test. P value < 0.05 was considered statistically significant.

Results

Clinical baseline characteristics

Table 1 shows that the age, gender, BMI, tumor location and tumor stage of the two groups were compared in the study, and there was no significant difference in clinical

Table 1 Comparison of clinical data of two groups of patients

	Observation group	Control group	t/χ2	*P* value
Age(	62.53 ± 11.02	63.79 ± 9.26	-0.516	0.607
Sex				
Male (%)	17(56.7%)	23(58.9%)	0.037	0.847
Female (%)	13(43.3%)	16(41.1%)		
BMI (kg/m^3)	23.96 ± 1.684	23.11 ± 2.243	1.727	0.089
Tumor location*				
Splenic flexion	2(6.7%)	0(0.0%)	2.810	0.209
Descending colon	11(36.7%)	12(30.8%)		
Sigmoid colon	17(56.7%)	27(69.2%)		
Tumor stage				
I	8(26.7%)	8(20.5)	0.480	0.787
II	11(36.7%)	17(43.6%)		
III	11(36.7%)	14(35.9%)		
Underlying disease				
Hypertension (%)	6(20.0%)	9(23.1%)	0.094	0.759
Diabetes (%)	5(16.7%)	7(17.9%)	0.019	0.889

* Using Fisher's exact probability method

Table 2 Comparison of the intraoperative and postoperative conditions between the two groups

	Observation group	Control group	t/X^2	*P* value
Intraoperative blood loss (ml)	50.00(30.00,60.00)	50.00(30.00,50.00)	-0.495	0.620
Surgery time (min)	184.76 ± 17.78	190.26 ± 18.84	-1.241	0.219
Anastomosis time (min)	17.2 ± 1.6	27.8 ± 2.7	-20.56	<0.001
First exhaust time (d)	2.50 ± 0.23	2.61 ± 0.25	-1.769	0.081
First bowel movement time (d)	6.15 ± 0.77	6.07 ± 0.82	0.408	0.685
Frequency of bowel movements (/2 weeks)	16.50 ± 2.71	16.13 ± 3.15	0.516	0.608
Degree of defecation patency *				
Smooth	5(16.7%)	7(17.9%)	0.758	0.735
Less smooth	23(76.7%)	27(69.2%)		
Laborious	2(6.7%)	7(12.8%)		
Requires intervention	0(0.0%)	0(0.0%)		
Postoperative hospital stays (day)	9.00(7.00,10.00)	8.00(7.00,11.00)	-0.759	0.448
Pain score	3.00(2.00,5.00)	4.00(3.00,5.00)	-1.395	0.163

* Using Fisher's exact probability method

Table 3 Comparison of surgical complications between the two groups

	Observation group	Control group	t/χ2	*P* value
Anastomotic leakage	1	2		
Anastomotic bleeding	1	1		
Anastomotic stenosis	0	1		
Intestinal obstruction	0	1		
Total(%)	2(6.67%)	5(12.82%)	0.191	0.662

baseline characteristics between groups ($P > 0.05$), indicating the two groups were comparable.

Comparison of perioperative indexes between side-to-side anastomosis group and end-to-end anastomosis group

There was no significant difference in intraoperative blood loss and operation time during the operation ($P > 0.05$), and the difference in intraoperative anastomosis time was statistically significant (< 0.001). There were no significant differences in the first exhaust time, defecation time, 14-day defecation patency, number of defecations within 2 weeks, postoperative hospitalization time and postoperative pain between the two groups ($P > 0.05$, Table 2). The probability of postoperative complications was 6.67% and 12.82%, respectively, and the difference was not statistically significant ($P > 0.05$, Table 3). For patients with anastomotic leakage, moderate fever appeared on the 1–2 days after surgery, WBC and CRP increased, abdominal drainage was turbid, and after timely examination and upgrade of antibiotics,

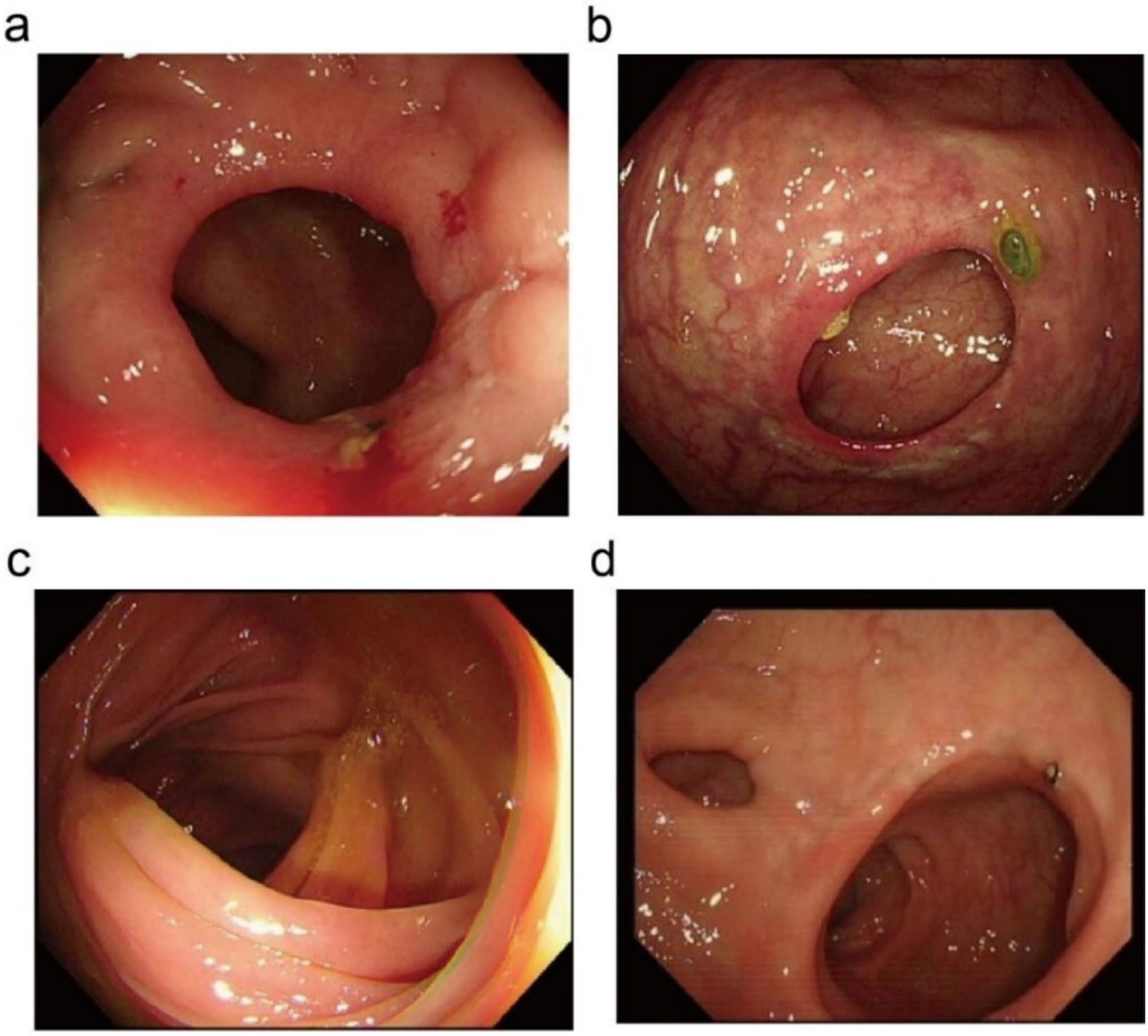

Fig. 2 Colonoscopy of anastomosis 6 months after operation. **(a)** end-to-end anastomosis anastomosis, scarring around the anastomotic port, and mild stenosis. **(b)** anastomosis healed well, and the surrounding mucosa is rosy. **(c)** lateral anastomotic port healed well, the mucosa and the anastomosis are smooth. **(d)** lateral anastomotic orifice healed well, with smooth surrounding mucosa, and there is a stump diverticulum around the anastomotic port

adequate drainage and other treatment, fever decreased on the 4th to 5th day after surgery, and the blood test for infection went down to normal. For patients with anastomotic bleeding, 200 ml of dark red fluid was extracted from the drainage tube 2–3 days after surgery. These patients were improved to discharge after instructed to stay in bed, administered with hemostatic medicine and symptomatic treatment and fluid replenishment. As for patients with intestinal obstruction, bowel function did not recover 3 days after surgery, and intestinal dilation was found after CT review. After fasting, early ambulation and glycerine enema to, patients exhaust gas on 6 days after surgery, and these patients were improved to discharge. As for anastomotic stenosis, patient showed increased frequency of defecation and occasional impotency, and after applying conservative treatment to soften stool and anal exercise, these symptoms became mild and acceptable.

In the 6-month postoperative colonoscopy in both groups, one patient in the end-to-end anastomosis group had mild stenosis of bleeding (as shown in Fig. 2), and the colonoscopy of the rest showed that the anastomotic healed and recovered well.

Discussion

The NOSES procedure involves specimen extraction by means of a natural orifice and digestive tract reconstruction under complete laparoscopy. During the 30-year development of laparoscopic surgery, at the end of the twentieth century, Stewer et al. first published surgery to vaginally retrieve colon specimens [6], after which Franklin et al. successfully solved the problem and published reports [7]. In 1982, after the concept of total mesenterectomy was proposed, Jacobs et al. performed the first laparoscopic TME surgery in 1991 [8]. With the in-depth research of domestic and foreign scholars, from 2002 to 2006, the concept of natural orifice transluminal endoscopic surgery (NOTES) was proposed and put into clinical practice, and Marescaux et al. adopted transvaginal cholecystectomy in 2007, laying the foundation for subsequent NOSES surgery [9]. In 2010, Professor Wang Xishan of China guided the smooth progress of NOSES surgery and opened the development of NOSES surgery. Until 2017, Professor Wang Xishan led the establishment of the China NOSES Alliance, and the "Expert Consensus on Colorectal Tumor Specimen Taking Through Natural Cavity (2017)" was established, which is a new milestone for domestic colorectal surgeons. Various studies on NOSES have also flooded into academia research.

In the last two decades, laparoscopic surgery has developed rapidly, and it offers significant benefits in exposing blood vessels and nerve tissue, and excels at hemorrhage control and reducing clinical complications. A study reported 137 cases of colorectal tumor NOSES surgery [10], which concluded that it met the requirements of radical tumor resection and obtained favorable treatment results; Compared with traditional laparoscopic surgery, NOSES surgery demonstrates superiority in terms of incisional herniation, infection rates, and postoperative pain management which not only avoids incision-related complications, but also provides faster postoperative recovery and less psychological trauma. According to the "International consensus on NOSES for colorectal cancer" [11], NOSES can be divided into ten different anastomosis methods according to tumor location and different ways of removing specimens. Compared to traditional laparoscopic-assisted radical resection of colorectal cancer, laparoscopic radical resection NOSES via an anal approach does not increase the difficulty of surgery and intraoperative risk [12, 13]. Additionally, the reduced bleeding endorses the safety of this type of surgery. A large amount of researches and clinical practice has confirmed that the anus is the most practical and ideal natural channel for NOSES to remove colorectal specimens without impairing its function [14–17].

According to the research report of Kiran et al. [18], the use of side-to-side anastomosis after partial colonectomy has obvious advantages in prevention of anastomotic leakage and related complications. In this study, we compared the peristaltic side-to-side and overlap anastomosis, and yielded comparable intraoperative and postoperative conditions and complications. Before anastomosis, it is essential to closely monitor the intact blood flow of the severed end of the colon and the tension of the anastomotic port, detect whether there is anastomotic bleeding, prevent anastomotic leakage and ensure anastomotic mouth pass smoothly, and the drainage tube was placed at the anastomosis to further ensure smooth drainage. Meanwhile, freeing long enough bowel tube should be a recommended prerequisite when applying this anastomosis method, especially in cases of sigmoid colon tumors, which are prone to the situation that the intestinal tube is insufficient for side-to-side anastomosis after tumor resection. It is also recommended to ensure the length of the free splenic flexure to reduce the anastomosis tension.

The results of this study showed that there was no significant difference in operation time and intraoperative blood loss between the two groups ($P>0.05$), but the intraoperative anastomosis time in the side-to-side anastomosis group was significantly shorter than that in the end-to-end anastomosis group ($P<0.001$), and there were no significant differences in postoperative first exhaust time, defecation time, defecation patency, frequency of defecation, postoperative hospital stays and postoperative pain ($P>0.05$). In terms of the difference in operation time and anastomosis time, we reckoned that the operation steps of observation group were simpler in freeing less mesentery, using a straight cut stapler and did not require extra instrument in the abdominal cavity to assist anastomosis. On the contrary, control group took more time to insert and pull out the nail base of stapler. Although the side-to-side anastomosis came with larger anastomosis area and more reinforcement sutures, both groups of surgeries were performed by surgeons with rich experience in laparoscopic surgery, and there was no significant impact on suture duration. It is worth noting that because side-to-side anastomosis required a sufficiently longer intestine stump, the time to free intestinal tube and mesentery increased in some cases, there was no obvious difference in the overall operation time between the two groups. Both groups performed radical colon cancer resection based on complete laparoscopy, which minimized injury and there was no significant difference in postoperative recovery between the two groups ($P>0.05$). According to Mattei et al. [19], after colon peristaltic function was restored, the stimulation of intestinal contents did not cause edema and had obvious advantages on the recovery of anastomosis, so early restoration of enteral nutrition could further promote postoperative recovery [20]. The postoperative exhaust and defecation time and functional recuperation are consistent with the

report of Smith et al. on intestinal peristalsis function [21].

Common postoperative complications of NOSES surgery include anastomotic bleeding, anastomotic leakage, and abdominal infection [11]. In this study, there were 2 complications in the side-to-side anastomosis group and 5 complications in the end-to-end anastomosis group. One case of anastomotic leakage occurred in the side-to-side anastomosis group and two cases of anastomotic leakage occurred in the end-to-end anastomosis group, both of which recovered after conservative treatment. The management of anastomotic leakage focuses on prevention, and is strictly controlled in terms of intestinal preparation, ensuring anastomotic blood supply, and aseptic operation [22]. There was one case of anastomotic bleeding in each group, both of which improved after conservative treatment, and some studies believed that side-to-side anastomosis led to the risk of anastomosis bleeding due to long anastomosis sutures [23], while we supposed that in this case, the colonic cutting was insufficient, the anastomosis closure was not strict, and the risk of bleeding was increased after anastomosis with a stapler; In addition, there was also a certain connection with improper selection of stapler nail height. In the postoperative follow-up of the end-to-end anastomosis group, there was one case of anastomotic stenosis, manifested as increased frequency of stool, occasional poor bowel movements. After conservative treatment, condition was acceptable and the anastomotic intestinal wall was thickened and scarred in re-examination of colonoscopy. According to reports [24, 25], the causes of anastomotic stenosis are related to a variety of factors, including preoperative chemoradiotherapy, improper use of intraoperative tubular anastomoses, poor blood supply at the severed end of the intestine, anastomotic leakage, and abdominal infection. The treatment of anastomotic stenosis includes interventional expansion, comprehensive endoscopic and surgical treatment. Studies have reported that endoscopic balloon dilatation (EBD) success rate was 80–90%, which was safe and effective [26, 27].

Abdominal infection is a significant complication that warrants attention in rectal NOSES. The occurrence of abdominal infection in rectal NOSES predominantly stems from inadequate preoperative bowel preparation, failure to comply with aseptic protocols during surgery, postoperative anastomotic leaks, suboptimal abdominal drainage, and other underlying factors [28]. Statistically significant association was found between prolonged operative time and infectious complications [29]. Miller and Moritz discovered a statistically significant increase in peritoneal bacterial contamination in patients with intraperitoneal enterotomy during bowel anastomosis compared to those without [30]. Standard procedures such as colonic preparation, prophylactic antibiotics, intraoperative transanal povidone-iodine lavage, temporary closure of the proximal colon, protection of extraction site, and intraoperative peritoneal irrigation can reduce contamination. In an additional randomized controlled trial, a pelvic bacterial contamination rate of 56.5% was documented following left colectomy with NOSES. The study revealed that employing rectal washout with povidone-iodine led to reduced contamination levels [31]. While the patients referenced above did not encounter postoperative infections due to the limitations on data volume and surgery of standardized protocols, it is imperative to still acknowledge postoperative infection as a crucial consideration.

While no significant difference was found in postoperative complications between two groups, conclusion of this study must be applied with discretion because the sample size was limited, and as a retrospective study, there were many confounding factors, and the analysis and comparison of postoperative tumor recurrence and postoperative survival have not been carried out.

Conclusions

In summary, in the left colon cancer NOSES surgery, there is no significant difference between the two different anastomosis methods in the operation time, blood loss, postoperative recovery and complication rate. The radical efficacy of NOSES surgery remains consistent across the methods. However, the side-to-side anastomosis approach stands out for its operational simplicity, shorter intraoperative anastomosis duration, suggesting its suitability for broader adoption in primary hospitals conducting colorectal cancer NOSES procedures.

Abbreviations

SD	Standard deviation
BMI	Body mass index
NOSES	Natural orifice specimen extraction surgery
EBD	Endoscopic balloon dilatation

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None.

Author contributions

JTH and ZMS designed the study; JTH and JCW performed surgical operations; SFF and JMH collected data; JCW, SFF and JMH analyzed the data; JTH and ZMS wrote the manuscript. All authors read and approved the final manuscript.

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Data availability

Access to the data can be obtained from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the institutional review board of Huizhou Third People's Hospital of Department of Gastrointestinal Surgery. The study compliance with the Helsinki Declaration. Written informed consents were obtained from all of the patients.

Consent for publication
Not applicable.

Conflict of interest
The authors declare that they have no competing interests.

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