Chan et al. World Journal of Surgical Oncology (2024) 22:237
https://doi.org/10.1186/s12957-024-03513-3

World Journal of Surgical Oncology

RESEARCH Open Access

Short-term outcomes of Transrectal Natural Orifice Specimen extraction compared with conventional minimally invasive surgery for selected patients with colorectal cancer: a propensity score matching analysis and literature review

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Abstract

Purpose Conventional minimally invasive surgery requires mini-laparotomy to extract the pathological specimen. However, by using a natural orifice as the delivery route, natural orifice specimen extraction (NOSE) surgery avoids the need for a large incision. This study analyzed the short-term outcome of NOSE compared with conventional mini-laparotomy (CL) for colorectal cancer surgery.

Methods We conducted a retrospective analysis of 1,189 patients who underwent surgery for primary colorectal cancer between the cecum and upper rectum. Propensity score analyses were applied to the NOSE and CL groups in a 1:1 matched cohort.

Results After propensity score matching, each group included 201 patients. The NOSE group and CL group did not differ significantly in terms of baseline characteristics. Postoperative morbidity and mortality rates were comparable. Compared with the CL group, the NOSE group experienced a shorter time to first flatus (1.6 ± 0.8 vs. 2.0 ± 1.2 days, $p < 0.001$), first stool (2.7 ± 1.5 vs. 4.1 ± 1.9, $p < 0.001$), liquid diet (2.3 ± 1.3 vs. 3.6 ± 1.8 days, $p < 0.001$), soft diet (3.9 ± 2.0 vs. 5.2 ± 1.9 days, $p < 0.001$) and a shorter hospital stay (5.1 ± 3.5 vs. 7.4 ± 4.8 days, $p < 0.001$). The NOSE group exhibited lower mean pain intensity and lower highest pain intensity on postoperative days 1, 2, and 3.

Conclusion NOSE has several advantages over conventional mini-laparotomy following minimally invasive surgery for colon cancer. These advantages include reduced time to oral intake, shorter hospital stays, and less postoperative pain. NOSE can be adopted and applied to highly selective patients without additional risk of short-term complications.

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Introduction

Colorectal cancer is currently one of the most frequently diagnosed cancers in the world [1]. Minimally invasive surgical approaches for treating colorectal cancer have become increasingly common as more data have demonstrated the safety, feasibility, and oncologic equivalency of such procedures compared with open surgery [2–5]. However, in laparoscopic colorectal surgery, a mini-laparotomy is still necessary to extract pathological specimens. Thus, morbidities associated with larger abdominal incisions, such as wound pain, incisional hernia, and poor cosmetic results, remain a risk. To advance traditional laparoscopy techniques, natural orifice specimen extraction (NOSE) surgery was first introduced by Franklin in 1993 [6]. This new method improves on "conventional" laparoscopy surgery, which entails extraction of specimens through an additional abdominal wound [7], by avoiding the need for a mini-laparotomy and maximizing the advantages of total laparoscopy surgery. Studies have reported transvaginal and transrectal routes for specimen extraction, but these raise concerns regarding increased risk of bacterial contamination [8, 9]. Moreover, oncological safety must be evaluated because of the difficulty of delivering a sizable, bulky specimen through NOSE, resulting in reduced specimen quality.

Several studies have reported NOSE offers promising early postoperative outcomes, including reduced postoperative pain, faster bowel recovery time, and a shorter hospital stay compared to conventional mini-laparotomy (CL) surgery [10–16]. Meta-analyses have demonstrated that NOSE provides oncological outcomes that are non-inferior to those achieved with conventional mini-laparotomy surgery, indicating that NOSE is equally effective in terms of cancer control and patient survival. [14, 17] This finding supports the promising application of NOSE as a viable surgical option. However, these studies predominantly involved sigmoid and rectal lesions. Research focusing on mid and low rectal cancer has added heterogeneity of the results due to different techniques and tumor characteristics in these low-lying tumors [16, 18, 19]. Additionally, studies regarding tumors located in the ascending colon and near the splenic flexure are limited [8, 13, 20–26]. An earlier consensus suggests that NOSE is suitable for non-locally advanced cancer, with patient BMI between 30 and 35 kg/m^2, and tumor size less than 5 cm. [27] Furthermore, factors such as anal stenosis, anal dysfunction, and nulliparity need to be considered when evaluating the suitability for NOSE.

NOSE has been increasingly adopted in colorectal surgery, with various techniques being explored to optimize clinical outcomes. Initially, the transvaginal route was primarily utilized for specimen extraction, particularly following right hemicolectomy, which limited the application of NOSE to female patients. [8, 20] However, recent advancements have broadened the applicability of NOSE, making it accessible to a wider patient population. [7] We conducted a propensity score matching (PSM) analysis to compare the short-term outcomes of transrectal NOSE with CL in patients undergoing minimally invasive surgery for colorectal cancer. This study incorporates a literature review and examines the use of different NOSE techniques, with a particular focus on right-sided and left-sided colorectal tumors, and evaluates the outcomes associated with these varied approaches.

Materials and methods

Patient selection and matched variables

We retrieved detailed information on clinicopathological variables from the Colorectal Section Tumor Registry of Chang Gung Memorial Hospital. The institutional review board approved this study (IRB No.202200141B0). All patients who received minimally invasive surgery for primary colorectal cancer, including between the cecum and upper rectum, between January 2015 and December 2019 were recruited for this study. Figure 1 presents the study flowchart as well as the inclusion and exclusion criteria. A total of 1,189 patients, with 985 in the CL group and 204 in the NOSE group, were enrolled for further evaluation. To reduce the possibility of bias or imbalance arising from the apparent difference in sample sizes and outcomes between the CL and NOSE groups, propensity score matching was used to equate the two groups. A caliper width of 0.045 was employed to ensure precise matching. The matching covariates were age, sex, BMI (categorized as greater than or less than 24), tumor stage, and operation method (categorized as right hemicolectomy, left hemicolectomy, and anterior resection). A 1:1 matching ratio was employed to maintain a balanced comparison between the two groups.

Surgical procedures

Right hemicolectomy and left hemicolectomy

For tumors located in the ascending colon, hepatic flexure, and proximal transverse colon, right hemicolectomy was performed with D2 lymph node dissection using techniques detailed in a previous study [21]. For tumors located in the distal transverse colon, splenic flexure, or proximal descending colon, standard left hemicolectomy was performed using techniques described previously [23, 28]. For NOSE, a transanal endoscopic microsurgery (TEM) scope (Richard Wolf, Tubingen, Germany) was inserted through the anus and then gently pushed until it reached the upper rectum. An incision was made at the upper rectum, and a suction device was used to clean any fecal spillage. The TEM scope was forwarded beyond the rectal incision, and then the specimen was pulled out through the TEM scope. The rectal incision was closed using a barbed suture (Fig. 2).

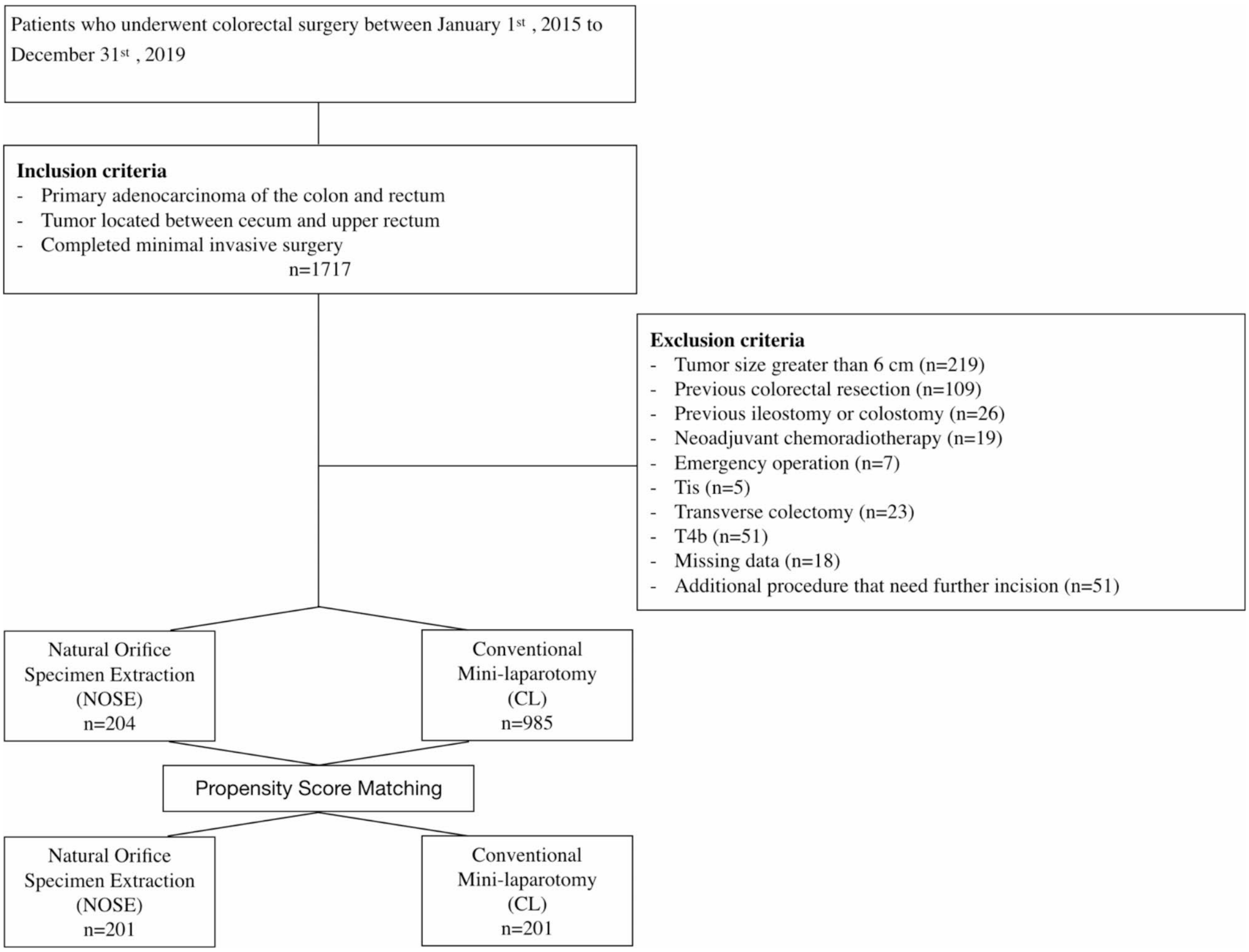

Fig. 1 Flowchart of the study design. This flowchart illustrates the inclusion and exclusion criteria for the study, along with the final number of patients in the NOSE and CL groups

Anterior resection

For tumors located in the distal descending colon, sigmoid colon, and upper rectum, anterior resection was performed. The rectum was transected by a linear stapler. In the NOSE group, the rectal stump was opened. A TEM scope was introduced through the anus as a working channel to deliver the anvil and specimen. Anvil fixation was performed by purse-string suture. Linear staples were then used to seal the rectal stump, and colorectal anastomosis was performed using a circular stapler (Fig. 2). All patients under went curative surgery with radical resection in accordance with the principle of total mesocolic excision.

Clinical outcomes

Measurement outcomes included short-term postoperative complications, recovery, readmission, and pain intensity. Postoperative complications were defined as morbidity occurring within 30 days and wound-related complications (wound infection or wound dehiscence); pulmonary (atelectasis or pneumonia), urinary (urinary tract infection or neurogenic bladder), cardiovascular (myocardial infarction, stroke, or embolism), ileus, or intra-abdominal (abscess or hemorrhage) complications; chylous ascites; anastomosis leakage; and other rare complications. Anastomosis leakage was defined as the clinical or radiological detection of a defect of the intestinal wall at the anastomotic site. Dehiscence of the rectal incision in patients who underwent NOSE after right or left hemicolectomy was classified as an intra-abdominal complication. The severity of morbidity was rated using the Clavien–Dindo classification [29].

Postoperative mortality was defined as death occurring within 30 days of surgery. The postoperative recovery evaluation was based on blood test reports, time to first flatus and stool, time to oral intake, pain intensity, and length of postoperative hospital stay. Postoperative 30-day hospital readmission data were also collected. For the postoperative pain assessment, pain intensity was assessed using a numeric rating scale with scores from

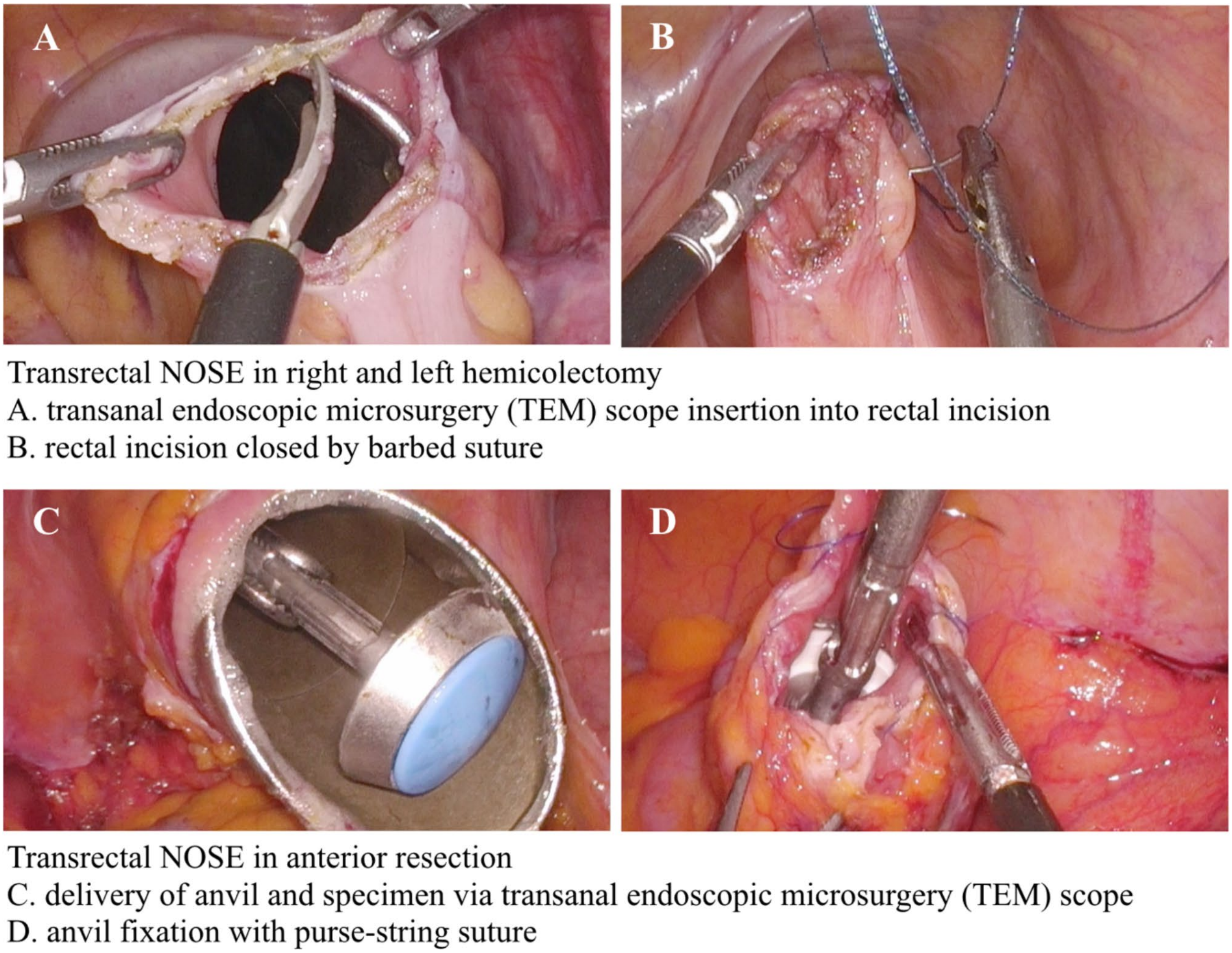

Fig. 2 Critical steps of NOSE

0 to 10 (10 representing the worst pain). The mean and highest pain scores on each day for three consecutive days postoperatively were used for further evaluation. Both groups received the same pain management strategies. Parenteral analgesics were initially administered in the postoperative period and switched to enteral ones once the patient could tolerate a liquid diet. Parenteral analgesics could be administered to patients in case of acute severe pain. Enteral and parenteral administration of analgesia were also collected for further analysis.

Statistical analysis

All analyses were conducted using SPSS software, version 25.0 (IBM, Armonk, NY, USA). Clinicopathological characteristics with categorical variables are presented as frequencies and proportions and were compared using the Chi-square test. Continuous variables are expressed as means with standard deviations and were analyzed using Student's t-test. Statistical significance was set at $p<0.05$. The love plot for propensity score matching was created using R (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria) and RStudio (version 2024.04.2; RStudio, Inc., Boston, MA, USA).

Results

After exclusion, we included 985 patients who had received CL surgery and 204 patients who had undergone NOSE. After PSM, we enrolled 402 in total, 201 in each group, to perform the final analysis. The demographic data before and after matching are presented in Table 1. Before matching, the NOSE group was younger, had more T1 lesions, was diagnosed with an earlier TNM stage, and had predominantly received anterior resections. After matching, confounding factors exhibited no significant difference between the groups. Figure 3 displays the love plot, which demonstrates the patient characteristics before and after propensity score matching. The standardized mean difference being near zero indicates that a good balance was achieved post-matching.

Table 1 Demographic data of before matching and after matching cohorts

	Before matching			After matching		
	NOSE	CL	*p*-value	NOSE	CL	*p*-value
	(*n*=204)	(*n*=985)		(*n*=201)	(*n*=201)	
Age (year)	62.1±12.5	64.5±12.2	0.011	62.4±12.4	63.6±11.9	0.319
Sex			0.29			0.762
Male	117 (57.4)	525 (53.3)		115 (57.2)	118 (58.7)	
Female	87 (42.6)	460 (46.7)		96 (42.8)	83 (41.3)	
BMI (kg/m2)			0.286			0.134
<24	103 (50.5)	457 (46.4)		101 (50.2)	86 (42.8)	
≥24	101 (49.5)	528 (53.6)		100 (49.8)	115 (57.2)	
Albumin (g/dL)			0.095			0.503
<3.5	3 (1.5)	39 (4.0)		3 (1.5)	6 (3.0)	
≥3.5	201 (98.5)	943 (96.0)		198 (98.5)	195 (97.0)	
Hemoglobin (g/dL)			0.076			0.563
<10	16 (7.8)	120 (12.2)		16 (8.0)	13 (6.5)	
≥10	188 (92.2)	865 (87.8)		185 (92.0)	188 (93.5)	
ASA Score			0.671			0.293
1	1 (0.5)	1 (0.1)		1 (0.5)	0 (0.0)	
2	70 (34.3)	339 (34.5)		67 (33.3)	80 (40.0)	
3	132 (64.7)	640 (65.0)		132 (65.7)	120 (60.0)	
4	1 (0.5)	4 (0.4)		1 (0.5)	0 (0.0)	
Operative method			<0.001			0.308
Right hemicolectomy	40 (19.6)	336 (34.1)		40 (19.9)	40 (19.9)	
Left hemicolectomy	19 (9.3)	108 (11.0)		19 (9.5)	11 (5.5)	
Anterior resection	145 (71.1)	541 (54.9)		142 (70.6)	150 (74.6)	
Tumor Stage (TNM)			0.017			0.943
I	88 (43.1)	321 (32.6)		85 (42.3)	87 (43.3)	
II	43 (21.1)	239 (24.3)		43 (21.4)	45 (22.4)	
III	65 (31.9)	350 (35.5)		65 (32.3)	63 (31.3)	
IV	8 (3.9)	75 (7.6)		8 (4.0)	6 (3.0)	
T stage			0.001			0.650
T1	69(33.8)	213(21.6)		67(33.3)	59(29.4)	
T2	34(16.7)	170(17.3)		33(16.4)	42(20.9)	
T3	84(41.2)	466(47.3)		84(41.8)	82(40.8)	
T4	17(8.3)	136(13.8)		17(8.5)	18(9)	

Postoperative outcomes

The intraoperative characteristics and postoperative outcomes are summarized in Table 2. The NOSE group experienced a shorter operative time (203.1±57.3 vs. 216.6±56.1 min, $p=0.018$) and lower estimated blood loss (33.2±22.3 vs. 43.9±33.3 ml, $p<0.001$) than the CL group. A robotic-assisted procedure was performed on nine patients in the NOSE group and two in the CL group. No patients in the two study groups received an elective diverting stoma. The quality of surgical specimens, including the specimen length, the number of lymph nodes retrieved, the percentage of cases with fewer than 12 lymph nodes retrieved, the number of positive lymph nodes examined, and the resection margin, were similar in both groups. The NOSE group exhibited a statistically significantly smaller tumor size (2.44±1.12 vs. 2.67±1.14).

Indicators of gastrointestinal recovery were statistically significant between the two groups. The NOSE group experienced a shorter mean time to first flatus (1.6±0.8 vs. 2.0±1.2 days, $p<0.001$), first stool (2.7±1.5 vs. 4.1±1.9 days, $p<0.001$), liquid diet (2.3±1.3 vs. 3.6±1.8 days, $p<0.001$), and soft diet (3.9±2.6 vs. 5.2±1.9 days, $p<0.001$). The postoperative hospitalization period was shorter in the NOSE group (5.1±3.5 vs. 7.4±4.8 days), which was statistically significant ($p<0.001$).

Postoperative pain and analgesics

The mean pain intensity and highest pain intensity are presented in Fig. 4. The NOSE group had lower mean pain intensity on postoperative day (POD) 1 (2.67±0.79 vs. 3.07±0.77, $p<0.001$), POD 2 (2.37±0.71 vs. 2.53±0.82, $p=0.037$), and POD 3 (2.07±0.75 vs. 2.44±0.92, $p=0.045$); the NOSE group also had lower highest pain intensity on POD 1 (3.29±1.57 vs. 4.29±1.82, $p<0.001$),

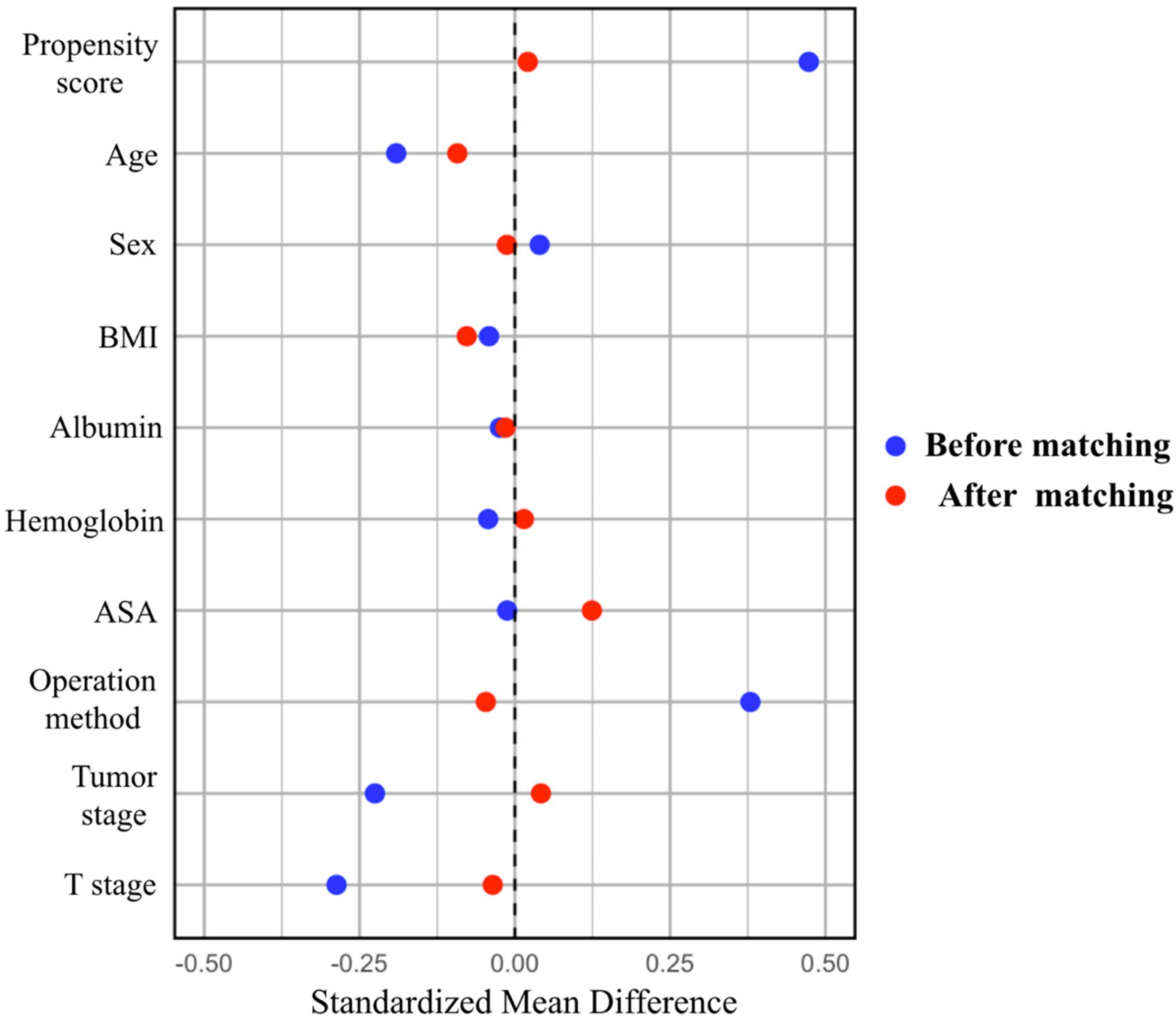

Fig. 3 Love plot illustrating patient characteristics before and after propensity score matching

POD 2 (2.59±1.15 vs. 3.06±1.45, $p<0.001$), and POD 3 (2.14±0.87 vs. 2.50±1.28, $p=0.001$). The percentage of patients who received only enteral analgesics on POD 1–3 is presented in Fig. 5. A higher percentage of patients in the NOSE group received only enteral analgesics on POD 1 (71.6% vs. 40.3%, $p<0.001$), POD 2 (89.6% vs. 72.1%, $p<0.001$), and POD 3 (97.0% vs. 84.6%, $p<0.001$). These patients tolerated postoperative pain without additional intravenous analgesics.

Postoperative complications

The overall morbidity rate within 30 days of surgery was lower in the NOSE group with borderline significance (4.5% vs. 9.0%, $p=0.073$), as presented in Table 3. No statistical differences were evident between the NOSE and CL groups with regard to intra-abdominal infection (2.0% vs. 0.5%, $p=0.372$) or anastomotic leakage (1.0% vs. 0.5%, $p=1.000$). The results for severity of morbidity were also not statistically significant. Mild complications (Clavien–Dindo grade I and II) occurred in 5 patients (2.5%) in the NOSE group and 14 (7.0%) in the CL group, and severe complications (Clavien–Dindo grade III and IV) occurred in 4 (2.0%) patients in the NOSE group and 4 (2.0%) in the CL group. Within 30 days of discharge, the overall readmission rate was 1.7%, exhibiting no statistical significance between the two groups (2% vs. 1.5%, $p=1.000$).

Discussion

Our study collected consecutive five-year data from a tertiary referral hospital, concluding with a case-matched analysis comparing NOSE and CL surgery. Our results demonstrated that the NOSE technique was a feasible procedure associated with less postoperative pain,

Table 2 Intraoperative characteristics and postoperative outcomes

	NOSE (*n* = 201)	CL (*n* = 201)	*p*-value
Operative time (min)	203.1 ± 57.3	216.6 ± 56.1	0.018
Estimated blood loss (ml)	33.2 ± 22.3	43.9 ± 33.3	< 0.001
Intracorporeal anastomosis	201 (100%)	9 (4.5%)	< 0.001
Robotic-assisted	9 (4.5%)	2 (1.0%)	0.026
Tumor size (cm)	2.44 ± 1.12	2.67 ± 1.14	0.040
Specimen length (cm)	15.7 ± 6.1	16.0 ± 5.9	0.584
Lymph node retrieved (n)	28.2 ± 14.0	29.7 ± 13.8	0.272
Less than 12 lymph nodes retrieved (n)	6 (3.0%)	6 (3.0%)	1.000
Positive lymph node (n)	1.0 ± 2.5	1.7 ± 5.6	0.137
Resection margin (cm)	4.7 ± 2.9	4.6 ± 2.5	0.780
First flatus passage (day)	1.6 ± 0.8	2.0 ± 1.2	< 0.001
First stool passage (day)	2.7 ± 1.5	4.1 ± 1.9	< 0.001
Tolerate liquid diet (day)	2.3 ± 1.3	3.6 ± 1.8	< 0.001
Tolerate soft diet (day)	3.9 ± 2.6	5.2 ± 1.9	< 0.001
Postoperative hospital stay (day)	5.1 ± 3.5	7.4 ± 4.8	< 0.001

shorter hospital stays, and no differences in postoperative complications.

Previous studies have determined that postoperative pain is not adequately managed in a significant portion of patients [30]. This is associated with various adverse outcomes, including increased morbidity, the development of chronic postoperative pain, impaired function, delayed recovery from surgery, impaired quality of life, prolonged opioid use, and increased medical costs. Poor controlled acute postoperative pain has also been associated with poorer long-term physical functioning and global perceived recovery [31]. Therefore, we aimed to achieve improved management of or even reduced postoperative pain. In addition to younger age, female sex, level of preoperative pain, and type of surgery, incision size is an independent predictor of severe postoperative pain [32]. The NOSE procedure reduces the incision size by abandoning the 5–8-cm mini-laparotomy incision required in CL. Studies have acknowledged that patients who undergo NOSE have less postoperative pain [11, 13, 14, 21, 33–35]. In our study, NOSE exhibited superior results in mean pain intensity and highest pain intensity on POD 1–3. Moreover, a higher percentage of patients in the NOSE group needed solely enteral analgesics to control postoperative pain. Compared to the NOSE group, the CL group scored higher in pain intensity and required more parenteral analgesics. Our data demonstrated that NOSE leads to less postoperative pain, easier pain management, earlier recovery, and shorter hospital stays.

Concerns about NOSE include bacterial contamination during intracorporeal anastomosis and specimen extraction. Some studies have obtained intraoperative peritoneal fluid as a measurable means of evaluation. Costantino et al. reported a higher contamination rate of peritoneal fluid during left-sided colorectal resection in the NOSE group [36]. However, another recent study revealed no difference in bacterial outcomes in the peritoneal lavage fluid, attributing this to using a sterile specimen bag to prevent contamination during resected specimen extraction [37]. Nevertheless, studies have described non-inferior results in infection rates regardless of bacterial contamination during NOSE [14, 21, 38]. Moreover, several studies and three meta-analyses have reported that the short-term postoperative complications related to NOSE were significantly less than those of CL [10, 11, 13]. This favorable result was not observed in our study. In our study, patients in the NOSE and CL

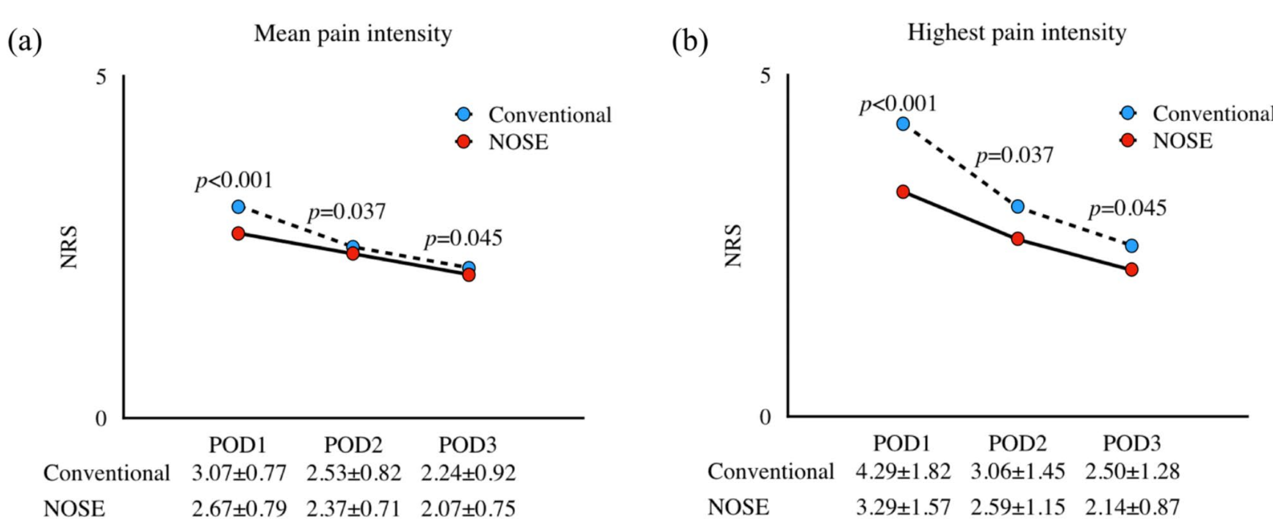

Fig. 4 Development of mean pain intensity (**a**) and highest pain intensity (**b**) on postoperative day. Values are presented as mean ± standard deviation. NRS = numeric rating scale; POD = postoperative day

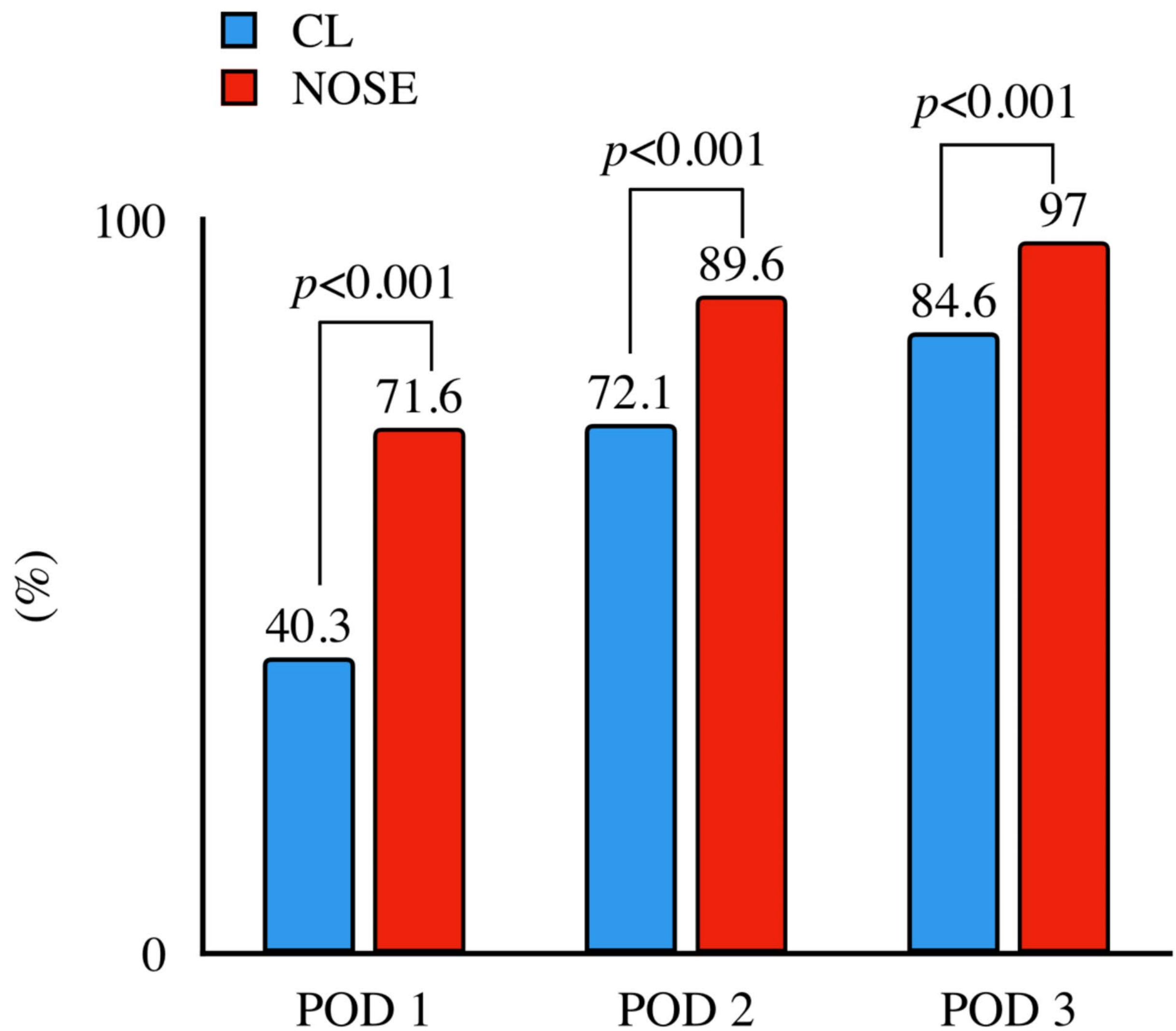

Fig. 5 Percentage of patients who received only enteral analgesics on postoperative day 1–3

groups had similar complication rates, but the complication rates in NOSE were identical to those of previous studies (4–15%). Two patients in the NOSE group developed anastomosis leakage and were treated using diverting colostomy and surgical drainage, respectively. Four patients who underwent NOSE developed an intra-abdominal infection. A CT scan was performed on three of these patients, revealing that the site of intra-abdominal infection was not located in the pelvis; this indicated that the condition did not originate from the specimen extraction site of the NOSE procedure.

Variation in techniques

Numerous studies have been conducted using various techniques on NOSE. We conducted a literature review on different NOSE techniques performed in colorectal cancer surgery, categorizing them into two groups: right-side colon cancer (Table 4) and left-side colon cancer (Table 5). Additionally, we analyzed our data by tumor location and included the results.

In the earlier studies, the transvaginal route was mainly used for specimen extraction after right hemicolectomy, which limits the method's use to female patients [8, 13]. Kong et al. reported the use of colonoscope and endoscopic snare to complete a transcolonic route for specimen extraction in ascending colon cancer, which expand the application of NOSE [25]. In addition, recent study conducted by Zhang et al. reported using a transrectal route after right hemicolectomy employing a technique very similar to that used at our institution, and found no difference in operation time between NOSE and CL [26].

In our study, a total of 40 patients underwent transrectal NOSE after right hemicolectomy. Only one patient developed pancreatitis in the NOSE group and no

Table 3 Postoperative morbidity and mortality

	NOSE ($n = 201$)	CL ($n = 201$)	*p*-value
Morbidity in 30 days	9 (4.5%)	18 (9.0%)	0.073
Wound	1 (0.5%)	5 (2.5%)	0.215
Pulmonary	0 (0.0%)	2 (1.0%)	0.499
Urinary	0 (0.0%)	1 (0.5%)	1.000
Ileus	1 (0.5%)	3 (1.5%)	0.623
Intra-abdominal infection	4 (2.0%)	1 (0.5%)	0.372
Anastomotic leakage	2 (1.0%)	1 (0.5%)	1.000
Chylous ascites	1 (0.5%)	3 (1.5%)	0.623
Other	0	2 (1.0%)	0.499
Death	0	0	1.000
Grade of morbidity			0.107
No morbidity	192 (95.5%)	183 (91.0%)	
Clavien-Dindo I-II	5 (2.5%)	14 (7.0%)	
Clavien-Dindo III-IV	4 (2.0%)	4 (2.0%)	
Readmission in 30 days	4 (2.0%)	3 (1.5%)	1.000

complications were found relating to the rectal incision. The data from Zhang et al. also showed no complication related to the rectal incision, attributing this to the sufficient blood supply and lack of tension in the upper rectum [26]. These findings suggest the feasibility of rectal incision for transrectal specimen extraction. However, the mean operation time was longer in the NOSE group in our study. This may reflect the time required for careful specimen extraction to avoid damaging the specimen, resulting in contamination and tumor dissemination. Moreover, meticulous closure of the rectal incision was also a time-consuming in our experience.

Comparison of studies on NOSE performed on left-sided tumors with a lower margin located above 10 cm from anal verge is included in Table 5. The transanal route of specimen extraction was considered analogous to the transrectal route. Various techniques were used in specimen resection which can be broadly categorized into the pull-through method and the total intracorporeal method.

Table 4 Characteristics of included studies on right-sided colon

Authors	Publication year	Patient number, NOSE vs. CL	Location	Specimen extraction site	Method to close natural orifice	Surgical time (min), NOSE vs. CL (*p*)	All Complications (%) NOSE vs. CL (*p*)
Park et al. [8]	2011	34 vs. 34	Right side colon	Transvaginal	Close colpotomy transvaginally	171 vs. 147 ($p = 0.094$)	11.7 vs. 26.5 ($p = 0.119$)
Li et al. [13]	2019	31 vs. 31	Right side colon	Transvaginal	Endoscopic suture	186 vs. 182 ($p = 0.578$)	6.4 vs. 29.0 ($p = 0.006$)
Kong et al. [25]	2021	45 vs. 45	Ascending colon	Transcolonic	Linear stapler	125 vs. 118 ($p = 0.963$)	20 vs. 22.2 ($p = 0.960$)
Zhang et al. [26]	2023	40 vs. 80	Right side colon	Transrectal	Endoscopic suture	170 vs. 165 ($p = 0.894$)	17.5 vs. 25.0 ($p = 0.505$)
This study	2023	40 vs. 40	Right side colon	Transrectal	Endoscopic suture	241 vs. 206 ($p = 0.017$)	2.5 vs. 7.5 ($p = 0.615$)

Table 5 Characteristics of included studies on left-sided colon

Authors	Publication year	Patient number, NOSE vs. CL	Location of tumor	Specimen extraction site	Specimen resection	Surgical time (min), NOSE vs. CL (*p* value)	All complications (%), NOSE vs. CL (*p* value)
Kim et al. [39]	2014	58 vs. 58	Sigmoid colon or rectum	Transvaginal	Total intracorporeal and pull-through method	149 vs. 132 ($p = 0.023$)	3.4 vs. 12.1 ($p = 0.162$)
Hisada et al. [34]	2014	20 vs. 50	Distal sigmoid to upper rectum	Transanal	Pull-through method	278 vs. 240 ($p > 0.05$)	20.0 vs. 24.0 ($p > 0.05$)
Ding et al. [12]	2019	43 vs. 43	Sigmoid colon or upper rectum	Transrectal	Total intracorporeal	132 vs. 123 ($p = 0.130$)	9.3 vs. 9.3 ($p > 0.05$)
Zhou et al. [10]	2020	100 vs. 119	Sigmoid colon or upper rectum	Transrectal	Total intracorporeal	167 vs. 146 ($p = 0.014$)	9.0 vs. 15.9 ($p = 0.016$)
Chang et al. [15]	2020	94 vs. 94	Sigmoid colon or upper rectum	Transrectal	Total intracorporeal and pull-through method	248 vs. 208 ($p < 0.001$)	7.4 vs. 11.7 ($p > 0.05$)
This study	2023	142 vs. 150	Distal descending colon to upper rectum	Transrectal	Total intracorporeal	191 vs. 218 ($p < 0.001$)	9.3 vs. 4.2 ($p = 0.084$)

In the pull-through method, after resection of the distal margin, the proximal colon along with the tumor was pulled out from the rectal stump or through the vaginal opening. This method requires the proximal colon to be mobilized as much as possible. Fixation of the anvil was also performed extracorporeally in the usual manner as in conventional laparoscopy. In the total intracorporeal method, the specimen resection was first performed intracorporeally. The specimen was then extracted through the rectal stump and the anvil was delivered. Anvil fixation to the proximal colon may be done with a snare or a purse-string suture. The rectal stump may be closed by purse-string suture or linear stapler. In our study, we used a purse-string suture for anvil fixation and closed the rectum with linear stapler to conducted a double-stapling end-to-end anastomosis. The shorter operative time and comparable complication rate in the NOSE group suggest that this technique is an efficient method for transrectal NOSE for left-side colon cancer.

Notably, most studies conducted on left-side colon cancer did not include tumors near the splenic flexure. Performing left hemicolectomy for splenic flexure tumors may leave a long colon stump, making it more technically challenging to use the same transrectal NOSE technique as in anterior resection. This is due to the lengthy route the specimen must travel within the colon, and anastomosis using a circular stapler may not be feasible because of the limited shaft insertion length. In our study, for tumors near the splenic flexure, we performed a standard left hemicolectomy and intracorporeal side-to-side anastomosis. An additional rectal incision was made for specimen extraction and closed with barded suture using the same techniques as for right-sided colon cancer. We conducted this technique on a total of 59 patients, all without complication related to the rectal incision. According to the guidelines on NOSE for colorectal cancer, it is recommended that the rectal incision be made on the anterior wall of the middle rectum above the peritoneal reflection, with a length of about 3 cm, and the incision direction should be parallel to the direction of the rectum. In our institute, the rectal incision was made at the upper rectum, and its fair elasticity allows the TEM scope to advance through the rectal opening.

Natural orifice specimen extraction (NOSE) has gradually gained attention, including in surgeries beyond colorectal surgery such as hepatectomy, pancreaticoduodenectomy, and gastrectomy [40–42]. However, the transvaginal route was mainly used for NOSE, limiting its application to female patients. Moreover, young women who have not completed their families should not be recommended for transvaginal NOSE. [27] We hope that our study has contributed to the positive short-term outcomes and feasibility of transrectal NOSE and that it will expand its use for other types of specimen extraction, regardless of patient sex. However, the specimen size should also be taken into account. We recommend the use of transrectal NOSE for tumors smaller than 5 cm. Larger tumors may still require the transvaginal route for NOSE [27, 43].

This study is limited due to its retrospective nature and lack of randomization. We used propensity score matching (PSM) to balance the sampling bias of patients likely to undergo NOSE. However, additional confounding variables may influence the results.

One significant issue is that previous studies have shown that intracorporeal anastomosis has a positive impact on bowel recovery and wound-related outcomes compared to extracorporeal anastomosis [44, 45]. In this study, the majority of patients in the CL group received extracorporeal anastomosis, similar to previous conducted studies on NOSE. In contrast, all patients in the NOSE group received intracorporeal anastomosis, which may account for the better postoperative recovery results observed in the NOSE group. A small number of studies that conducted intracorporeal anastomosis in both the NOSE and CL groups showed better bowel function recovery and wound pain outcomes in the NOSE group.

Another limitation is that in our study, the mini-laparotomy incision in the CL group was performed with a Pfannenstiel incision or by extending the midline umbilical port wound or right lower quadrant port wound. Due to the heterogeneity of incision sites, patients were expected to have higher pain scores in the CL group. If all CL patients had used the Pfannenstiel incision, the difference in pain scores might have been less pronounced.

Additionally, intraoperative findings such as a bulky mesocolon, narrow pelvis, or extensive adhesions may affect the surgeon's decision to perform NOSE. This study did not present data on the NOSE failure rate, specimen damage during extraction, or postoperative anorectal function. Randomized controlled trials could provide more reliable data.

Finally, one of the primary limitations of our study is the lack of long-term follow-up data. Without extended follow-up, it is challenging to assess the durability of the postoperative recovery benefits observed with NOSE and compare the long-term outcomes between NOSE and conventional minimally invasive surgery. Furthermore, our study lacks comprehensive oncological data, which limits our ability to evaluate long-term cancer survival outcomes.

Conclusions

The transrectal NOSE may offer potential advantages over conventional mini-laparotomy following minimally invasive surgery for colorectal cancer such as reduced time to oral intake, shorter hospital stays, and less postoperative pain. However, these findings must be interpreted with caution due to limitations, including the heterogeneity of intra- and extracorporeal anastomosis techniques and incision sites across the study groups, as well as the lack of data on NOSE failure rates and specimen damage. NOSE may be suitable for highly selective patient populations, but more comprehensive prospective studies and randomized controlled trials are required to fully assess its short-term and long-term outcomes.

Acknowledgements
This manuscript was edited by Wallace Academic Editing.

Author contributions
All authors contributed to the study conception and design. Material preparation and data collection were performed by I.L.L., P.S.H., and C.K.L. The analysis was performed by L.Y.C., Y.J.H., and J.F.Y . The first draft of the manuscript was written by L.Y.C., Y.J.C., and B.K.J. All authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

Funding
This study was supported by the Chang Gung Medical Research Fund (CMRPG3J1531 and CPRPG3N0031). The funder had no role in study design and analysis.

Data availability
The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Research involving human participants and/or animals
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional review board.

Informed consent
Informed consent was obtained from all individual participants involved in the study.

Conflicts of interest
The authors declare that they have no conflict of interest.

Competing interests
The authors declare no competing interests.

Received: 2 June 2024 / Accepted: 27 August 2024
Published online: 06 September 2024

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