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Natural orifice versus conventional mini-laparotomy for specimen extraction after reduced-port laparoscopic surgery for colorectal cancer: propensity score-matched comparative study

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Abstract

Background Although reduced port laparoscopic surgery (RPLS), defined as laparoscopic surgery performed with the minimum possible number of ports and/or small-sized ports, is less invasive than conventional laparoscopic surgery by reducing the number of surgical wounds, an extension of the incision is still needed for specimen extraction, which can undermine the merits of RPLS.

Objective To determine the impact of natural orifice specimen extraction (NOSE) in patients undergoing RPLS for colorectal cancer. The endpoints were perioperative outcome and oncologic safety at 3 years.

Setting Single-center experience (2013–2019).

Patients We retrospectively analyzed our prospectively collected patient records (American Joint Committee on Cancer (AJCC) stage I–III sigmoid or upper rectal cancer (tumor diameter ≤ 5 cm) who underwent curative anterior resection via RPLS. We excluded patients who did not undergo intestinal anastomosis.

Interventions Perioperative and oncologic outcomes were compared between patients undergoing natural orifice (RPLS-NOSE) or conventional (mini-laparotomy) specimen extraction (RPLS-CSE). Patients were matched by propensity scores 1:1 for tumor diameter, AJCC stage, American Society of Anesthesiologists score and tumor location.

Results Of 119 eligible patients, 104 were matched (52 RPLS-NOSE; 52 RPLS-CSE) by propensity scores. Compared with RPLS-CSE, RPLS-NOSE was associated with longer operative time (223.9 vs. 188.7 min; $p = 0.003$), decreased use of analgesics (morphine dose 33.9 vs. 43.4 mg; $p = 0.011$) and duration of hospital stay (4.2 vs. 5.1 days; $p = 0.001$). No statistically significant difference was found in morbidity or wound-related complication rates between the two groups. After a median follow-up of 34.3 months, no local recurrence was observed in RPLS-NOSE. The 3-year disease-free survival did not differ statistically significantly between groups (90.9 vs. 90.5%; $p = 0.610$).

Conclusion NOSE enhances the advantages of RPLS by avoiding the need for abdominal wall specimen extraction in patients with tumor diameter ≤ 5 cm. Surgical and oncologic safety are comparable to RPLS with CSE.

Keywords Natural orifice specimen extraction · Reduced-port laparoscopic surgery · Colorectal cancer · Perioperative outcome · Surgical safety · Oncologic survival

Several multicenter, prospective randomized clinical trials have validated the short-term benefits of laparoscopic (vs. open) colorectal surgery including less pain, better cosmetics, and faster recovery, without compromising oncological outcomes [1, 2]. However, conventional laparoscopic surgery (CLS) for colorectal cancer still requires several abdominal incisions for trocars and a mini-laparotomy for specimen extraction. Even though smaller than traditional laparotomy, these incisions can give rise to surgical site pain

Podium presentation Partial results of this study were presented at the SAGES 2018 Annual Meeting and 16th World Congress of Endoscopic Surgery, Seattle 2018 (11–14 April 2018). Partial results of this study were presented at the 26th international Congress of the EAES, London 2018 (30 May–1 June 2018).

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or infection, vessel or nerve injury as well as ventral hernia [3].

Single incision laparoscopic surgery reduces the number of abdominal incisions. Although lauded to produce less pain and shorter hospital stay than CLS [4, 5], technical challenges, such as clashing of instruments, lack of triangulation, and inadequate exposure, limited its development [6]. To overcome these limitations, reduced port laparoscopic surgery (RPLS), defined as laparoscopic surgery performed with the minimum possible number of ports and/or small-sized ports, was reported to have shorter operative duration, fewer conversion rates and less morbidity compared to single incision laparoscopic surgery [7]. However, a mini-laparotomy is still needed to extract the specimen. One alternative might be to use natural orifice specimen extraction (NOSE) via the rectum, anus or vagina [8–10].

However, the literature on RPLS with NOSE for colorectal cancer is sparse. Therefore, the objective of this study was to investigate the impact of NOSE compared to conventional specimen extraction in patients who underwent RPLS for colorectal cancer.

Materials and methods

We identified 140 consecutive patients from our institution's prospective database who underwent elective sigmoid or upper rectal cancer resection via RPLS between April 2013 and July 2019 (Fig. 1) treated by the same surgical team. We excluded 21 patients for the following reasons: metastatic CRC ($n=10$), bulky tumor with diameter > 5 cm ($n=8$) and Hartmann's procedure ($n=3$). Ultimately, 119 patients were enrolled for analysis and divided into two groups, RPLS with NOSE (RPLS-NOSE) and RPLS with conventional specimen extraction by mini-laparotomy (RPLS-CSE). Patients were matched 1:1 according to propensity scores calculated by logistic regression analysis with the following covariates: tumor diameter, American Joint Committee on Cancer

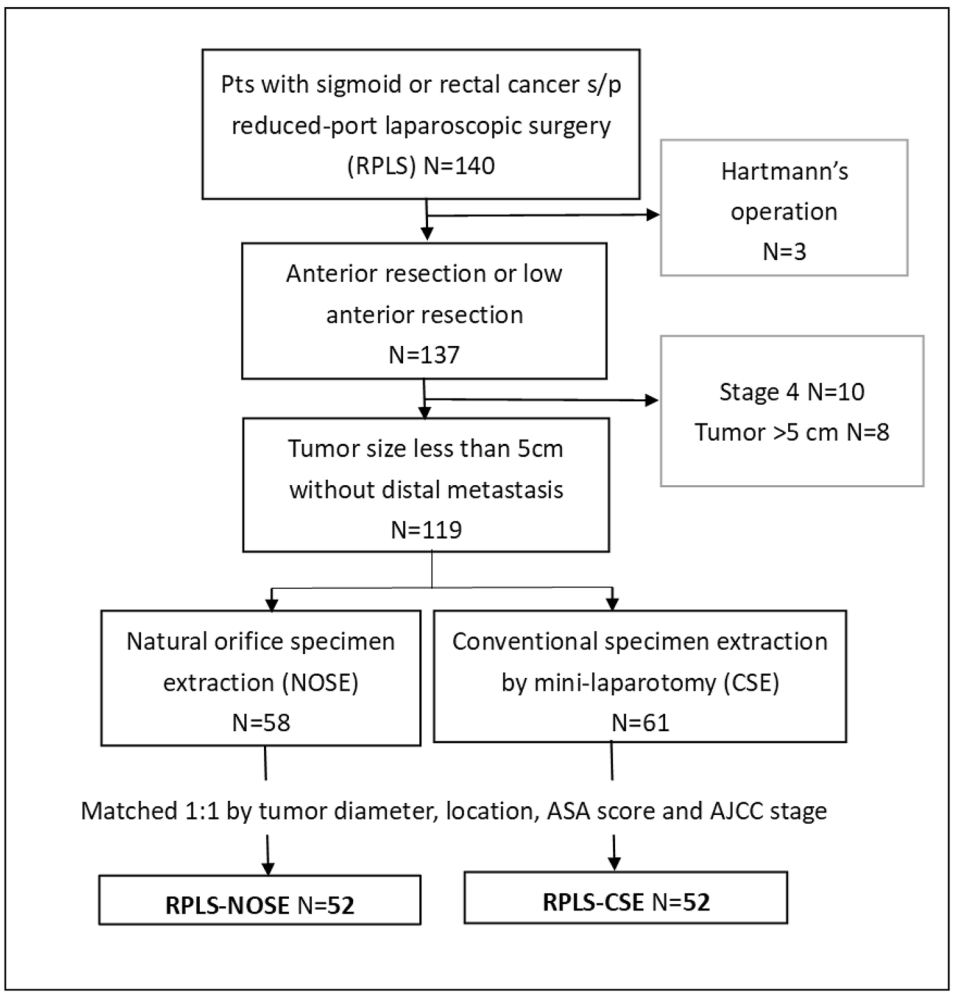


Fig. 1 Patient allocation

Pts: Patients; ASA, American Society of Anesthesiologists; AJCC, American Joint Committee on Cancer

(AJCC) stage, tumor location and American Society of Anesthesiologists (ASA) classification. None of the patients with upper rectal cancer received neoadjuvant chemoradiotherapy. This study was approved by the Institutional Review Board of the China Medical University Hospital (CMUH-REC-02). All procedures were performed by board certified colorectal surgeons at a single tertiary referral center, all well acquainted with both techniques.

Our primary endpoint was peri-operative surgical outcomes, including morbidity, pain evaluation and length of stay. Secondary endpoints were the mid-term oncologic safety, including local recurrence, disease-free survival (DFS) and overall survival (OS).

Post-operative morbidity is defined as the occurrence of any adverse event within 30 days after operation according to the Clavien-Dindo classification [11]. Postoperative use of opioid analgesics was recorded from the end of operation to discharge and converted to morphine equivalents according to the US Department of Health and Human Services Clinical Practice Guidelines [12]. Prolonged postoperative ileus was defined as a temporary impairment in gastrointestinal motility lasting more than 6 days after surgery (nausea, vomiting, abdominal pain, abdominal distention, or a delay in the passage of flatus) [13].

Surgical technique

A vertical trans-umbilical incision was made for a commercially available single port system (Lagiport kit, TLR-0220P LAGIS enterprise Co ltd, Brussels, Belgium) that houses two 5-mm trocars and two 12-mm trocars (Fig. 2A). An additional 5 mm port was inserted at the right iliac fossa, which subsequently served as the drainage site. A 10 mm flexible laparoscope 3-D camera (Endoflex, Olympus, Japan) was used. Both the operating surgeon and camera assistant were positioned to the right of the patient.

After a standard laparoscopic resection technique, and isolation of the specimen, the distal rectal lumen was closed with a nonabsorbable suture (Ethibond EXCEL™ Polyester suture, Ethicon, USA); the distal stump was irrigated transanally with povidone-iodine solution.

The following steps were different according to the method of specimen extraction (RPLS-NOSE or RPLS-CSE).

RPLS-NOSE

The proximal end of the tumor-bearing segment was divided with an articulating linear stapler (EC60A, Blue cartilage) through the Lagiport® kit. Then the distal end was transected by laparoscopic monopolar scissors (Fig. 2B). An Alexis wound protector (extra-small size, Applied Medical, California, North America) was inserted via the Lagiport wound and secured to the rectal stump by pulling out the white ring via the anus (Fig. 2C). We extracted the specimen through the trans-rectal wound protector and then introduced the anvil of the circular stapler into the peritoneum transanally (Fig. 2D, F).

Subsequently, the proximal colon end was delivered extracorporeally through the umbilical wound to create the purse-string suture (Fig. 2E), and then repositioned back into the abdomen, followed by securing the anvil intracorporeally (Fig. 2F). After removing the intraluminal wound protector, the rectal end was closed by either a laparoscopic purse-string suture or an articulating linear stapler through the Lagiport kit (Fig. 2G). Finally, an end-to-end colorectal anastomosis was performed (Fig. 2H).

RPLS-CSE

The distal end of the tumor-bearing segment was divided with an articulating linear stapler (ECHELON Flex 60 Endopath Stapler [EC60A] Green cartilage; Ethicon, USA). Next, the umbilical incision was lengthened enough to pull out the tumor-bearing colon. Extracorporeally, we transected the proximal end and then secured the anvil by purse-string suture ligation. After returning the bowel into the peritoneum, an end-to-end colorectal anastomosis was created with a circular stapler (CDH29A or CDH33A; Ethicon, USA).

Postoperative care

Oral intake was initiated and the urinary catheter was removed on postoperative day 1. Early physical exercise was encouraged. Postoperative antibiotics were administrated if there was any intraperitoneal fecal contamination during surgery. Standard postoperative pain control included intravenous Fentanyl 0.2 mg, injected in the post-operative recovery room and per-oral non-steroid anti-inflammatory drugs or acetaminophen given in the ward. Additional intravenous or intramuscular analgesics were prescribed as needed. Patients were discharged after they tolerated a solid diet without any discomfort or complications [14].

Oncologic treatment

Adjuvant chemotherapy (FOLFOX or XELOX or Capecitabine) was given for 24 weeks according to pathologic reports, including regional lymph nodes metastasis, poor histologic differentiation or T4 tumor invasion [15]. Regular oncologic follow-up visits were prescribed every 3 months for 5 years.

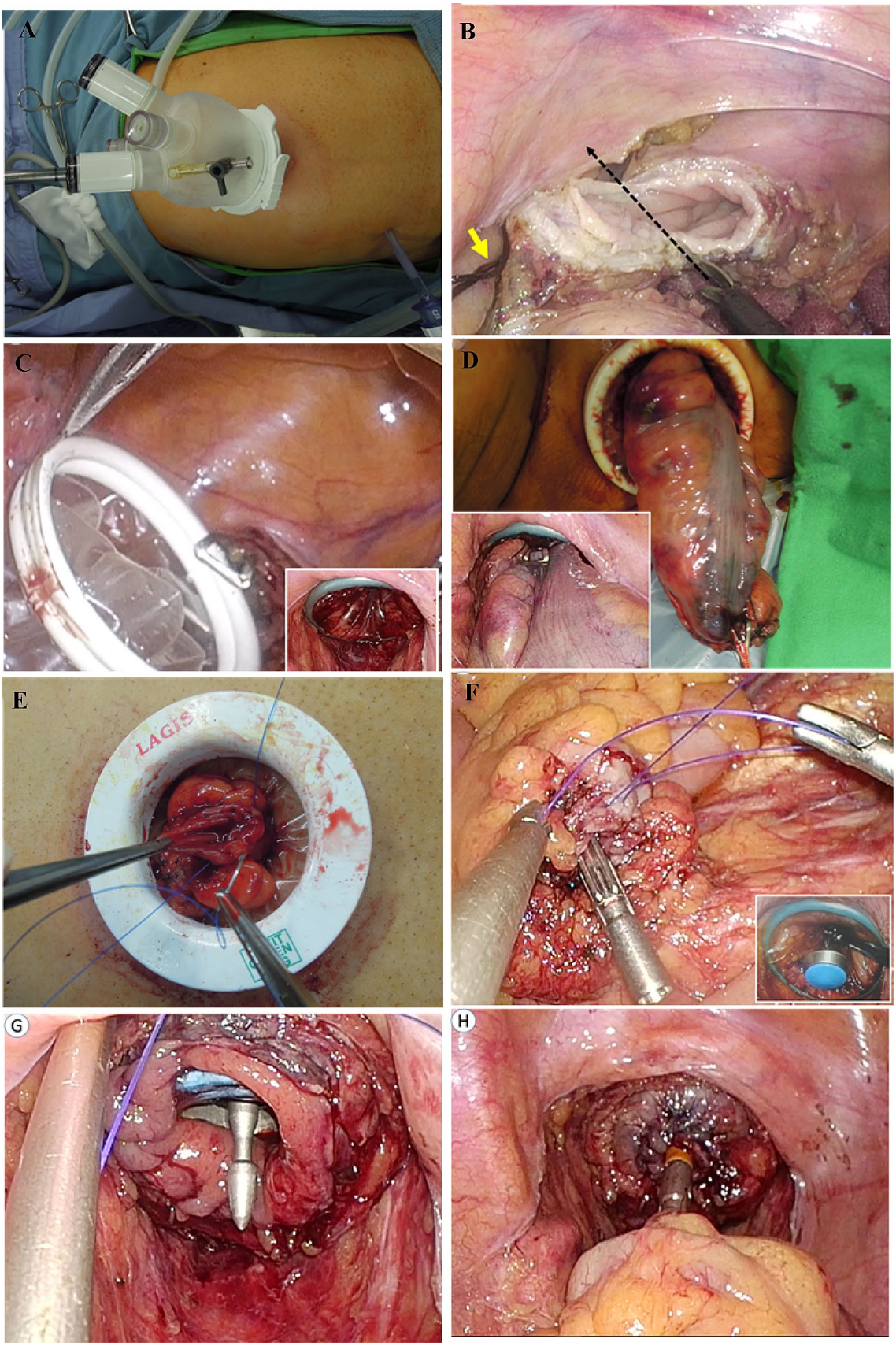


Fig. 2 Operative illustrations showing reduced-port laparoscopic surgery with nature orifice specimen extraction (RPLS-NOSE)

Statistical analysis

Continuous variables were reported as mean ± standard deviation and compared with the independent *t*-test. Categorical variables were presented as percentages and compared with the Chi-square (χ^2) test. The probabilities of overall survival (OS) and of disease-free survival (DFS) were estimated using the Kaplan–Meier method and the log-rank test was used to compare survival between groups.

Logistic regression analysis of clinically relevant variables was performed to compute a propensity score for each patient. The propensity score was then used to obtain one-to-one matching according to the "greedy matching algorithm". All matching was performed with a Statistical Analysis Systems software package (Release 9.1.3; SAS Institute, Cary, NC, USA). Statistical calculations were done using SPSS for Windows® software (version 21.0, SPSS Inc., Chicago, IL, USA). A p-value < 0.05 was considered statistically significant.

Results

After exclusion of patients with tumors > 5 cm in diameter, metastatic stage or absence of bowel anastomosis (Fig. 1), 58 and 61 patients undergoing RPLS-NOSE and RPLS-CSE, respectively, met the inclusion criteria: 104 patients were matched (52 in each group). The two groups were balanced in terms of baseline characteristics, such as age, gender, obesity (body mass index > 25 kg/m^2), ASA score, and previous abdominal surgery and AJCC stage. After propensity score matching, the proportion of tumor location distribution (sigmoid/rectum: 73.1%/26.9%) and average tumor size (2.5 ± 1.4 cm) were the same in both groups (Table 1).

Surgical outcomes and safety

Both are summarized in Table 2. Operative time was longer for RPLS-NOSE compared to RPLS-CSE (223.9 ± 51.0 vs. 188.7 ± 64.8 min, $p = 0.003$) while there was no statistically significant difference found in blood loss or colorectal anastomosis site. One patient with RPLS-NOSE required conversion to RPLS-CSE because of failed specimen extraction due to narrow rectal lumen. Although the incidence of intraoperative complications was not statistically significantly

Table 1 Demographic data of patients undergoing reduced-port surgery

Variable	Overall cohort			Matching cohort		
	RPLS-NOSE (n = 58)	RPLS-CSE (n = 61)	*p* value	RPLS-NOSE (n = 52)	RPLS-CSE (n = 52)	*p* value
Age (years)	63.2 ± 11.9	65.1 ± 12.2	0.385	63.2 ± 12.5	65.4 ± 12.2	0.362
Male gender	33 (56.9)	25 (41.0)	0.083	29 (55.8)	22 (42.3)	0.17
BMI ≥ 25 (kg/m^2)	21 (36.2)	16 (26.2)	0.24	17 (32.7)	14 (26.9)	0.52
ASA score[a]			0.917			0.906
I	2 (3.4)	3 (4.9)		2 (3.8)	2 (3.8)	
II	40 (68.9)	42 (68.9)		35 (67.3)	37 (71.2)	
III	16 (27.6)	16 (26.2)		15 (28.8)	13 (25.0)	
Previous abdominal surgery	5 (8.6)	7 (11.5)	0.605	5 (9.6)	6 (11.5)	0.75
Tumor location[a]			0.567			1
Sigmoid	40 (69.0)	44 (72.1)		38 (73.1)	38 (73.1)	
Upper rectum	18 (31.0)	17 (27.9)		14 (26.9)	14 (26.9)	
Tumor diameter (cm)[a]	2.6 ± 1.4	2.5 ± 1.3	0.619	2.5 ± 1.4	2.5 ± 1.4	0.939
AJCC TNM stage[a]			0.778			0.849
CIS	3 (5.2)	3 (4.9)		2 (3.8)	1 (1.9)	
I	22 (37.9)	25 (41.0)		22 (42.3)	22 (42.3)	
II	13 (22.4)	17 (27.9)		12 (23.1)	15 (28.6)	
III	20 (34.5)	16 (26.2)		16 (30.8)	14 (26.9)	

Values are presented as mean ± standard deviation (SD) or numbers (%)

RPLS reduced-port laparoscopic surgery, *NOSE* Natural Orifice Specimen Extraction, *CSE* Conventional Specimen Extraction, *BMI* Body Mass Index, *ASA* American Society of Anesthesiologists, *CIS* carcinoma in situ, *AJCC* American Joint Committee on Cancer, *TNM* tumor-node-metastasis

[a]Matched factors

Table 2 Perioperative and post-operative outcomes

	RPLS-NOSE ($n=52$)	RPLS-CSE ($n=52$)	p value
Total operative time (min)[a]	223.9 ± 51.0	188.7 ± 64.8	0.003
Blood loss (ml)	24.1 ± 9.8	21.2 ± 5.8	0.063
Distance of anastomosis to anal verge (cm)	11.6 ± 3.0	11.8 ± 5.8	0.784
Intraoperative complications[c]	4 (7.7)	1 (1.9)	0.169
Fecal contamination	3	0	
Iatrogenic bladder injury	0	1	
Anastomotic site bleeding	1	0	
Umbilical incision length (cm)[d]	1.9 ± 0.2	4.7 ± 1.1	< 0.001
Morphine required after surgery (mg)[e]	33.9 ± 12.0	43.4 ± 23.4	0.011
Additional analgesics[f]	29 (55.8)	41 (78.8)	0.012
Return to intestinal activity (days)	1.3 ± 0.7	1.6 ± 0.9	0.049
Hospital stay after surgery (days)	4.1 ± 1.3	5.1 ± 1.6	0.001
Overall morbidity	4 (7.7)	8 (15.4)	0.22
Anastomotic leakage	0	1	
Intraabdominal abscess	0	1	
Intraabdominal infection[g]	2	0	
Prolong ileus	0	2	
Wound complications	1	4	
Pneumonia	1	0	
Clavien–Dindo classification			
I/II	4 (7.7)	6 (11.5)	0.506
III/IV/V	0	2 (3.8)	0.153
Wound complications	1 (1.9)	4 (7.7)	0.169
Infection	0	2	
Umbilical hernia	1	2	
Readmission within 30 days of surgery	0	2 (3.8)	0.153
Mortality within 30 days of surgery	0	0	–

Values are presented as mean ± standard deviation (SD) or numbers (%)

RPLS reduced-port laparoscopic surgery, *NOSE* natural orifice specimen extraction, *CSE* conventional specimen extraction

[a]Total operation time was measured from skin incision to skin closure

[b]Convert to trans-umbilical specimen extraction

[c]Intraoperative complication was the complications occurred during surgery

[d]Umbilical wound length was measured to the incision cross the umbilicus

[e]Different analgesics were converted to morphine equivalence [15] and recorded from end of surgery to discharge

[f]The patients need additional opioid agents after standard postoperative pain control, which was presented in paragraph of post-operative care

[g]Intraabdominal infection was diagnosed by positive ascites culture with clinical symptoms

different between RPLS-NOSE and RPLS-CSE (7.7% vs; 1.9%; $p=0.169$), intraperitoneal fecal contamination during surgery was dominant in RPLS-NOSE group.

Return to intestinal activity and duration of hospital stay after surgery were statistically significantly shorter in RPLS-NOSE than in RPLS-CSE. Overall morbidity was 11.5% without any statistically significant difference between groups. Major complications (Clavien-Dindo classification grades III/IV) were noted in two patients (anastomotic leakage and intraabdominal abscess) in the RPLS-CSE group while there were none in the RPLS-NOSE group; this difference was not statistically significant. No mortality was recorded within 30 days after operation; however, two patients in RPLS-CSE required readmission, one for wound infection and the other for ileus.

Wound-related results

Postoperative wounds are illustrated in Fig. 3 with related data provided in Table 2. Statistically significant differences were found in the length of the umbilical wound (1.9 ± 0.2 vs. 4.7 ± 1.1 cm, $p < 0.001$) and in-hospital total morphine requirements (33.9 vs. 43.4 mg, $p = 0.011$) in the RPLS-NOSE group compared to the RPLS-CSE group, respectively. The daily dosage of morphine requirement had statistically significant difference after post-operative day 2 (Fig. 4). More patients needed additional postoperative analgesic treatment in RPLS-CSE (55.8% vs. 78.8%, $p = 0.012$). Postoperative wound complications included infection ($n = 2$) and umbilical hernia ($n = 2$) in RPLS-CSE, whereas one patient in RPLS-NOSE sustained an umbilical hernia ($n = 1$).

Oncologic outcomes

As shown in Table 3, the pathological results (extent of primary tumor, regional lymph node metastasis and histologic differentiation) were similar in both groups. The mean length of surgical margins and number of lymph nodes harvested were also comparable. Adjuvant chemotherapy was administrated in 32 patients, 18 in RPLS-NOSE and 14 in RPLS-CSE group (36.4% vs. 26.9%, $p = 0.215$).

Our median follow-up was 34.3 (range 7.6–82.0) months. None of the patients undergoing RPLS-NOSE had local recurrence, while three patients developed distant metastasis (two in liver, one in lung) and underwent curative metastectomy. Five patients in RPLS-CSE sustained tumor recurrence. Of these, two patients developed local recurrence combined with multiple liver metastasis or peritoneal carcinomatosis. Both received systemic chemotherapy. The three other patients had isolated distal metastasis and underwent metastectomy.

3-year DFS was 90.9% and 90.5% in RPLS-NOSE and RPLS-CSE ($p = 0.610$), respectively (Fig. 4). There was also no statistically significant difference found in 3-year OS rates (97.8% vs. 95.8%, $p = 0.274$). No transrectal access-site or port-site recurrence occurred in either group (Fig. 5).

Discussion

Our data suggest that hybrid RPLS-NOSE is superior to RPLS-CSE for anterior resection with regard to lower analgesic requirement, earlier bowel function recovery and shorter hospital stay, while short-term safety and 3-year oncologic outcomes were comparable. No complications or local tumor recurrence occurred at the NOSE site. To the best of our knowledge, this is the first matched comparative study showing short-term advantages for RPLS-NOSE.

The major difference between RPLS-NOSE and RPLS-CSE is the length of umbilical incision. The mean length of umbilical incision extension for specimen extraction was

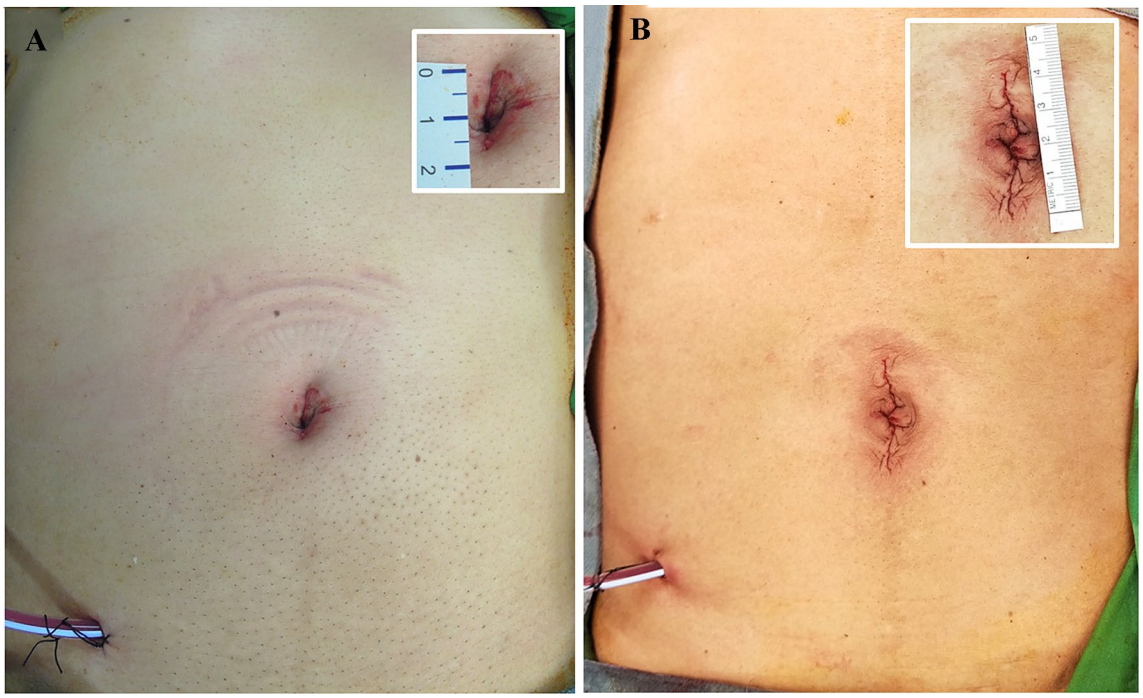
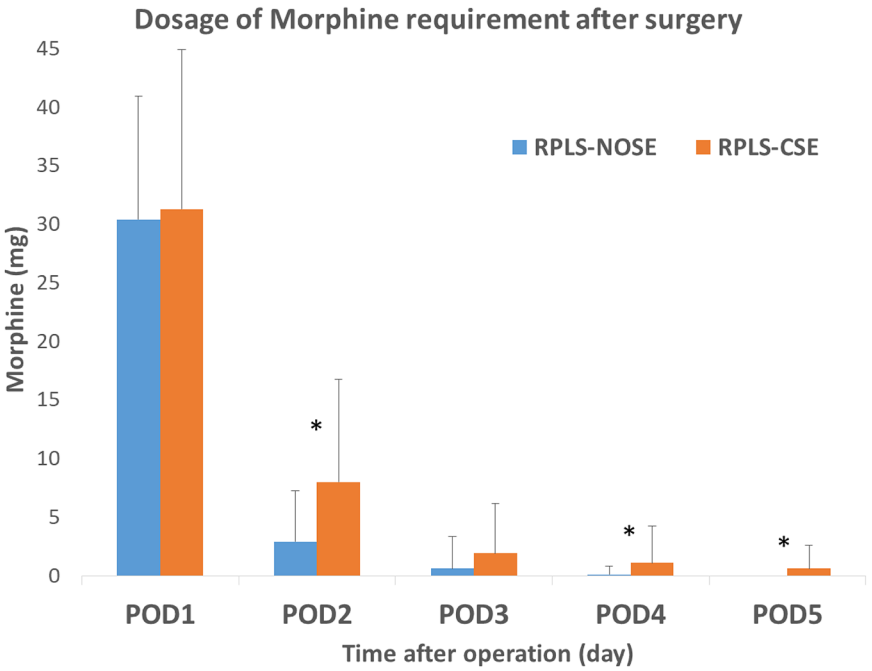


Fig. 3 Appearances of abdominal incision after **A** reduced-port laparoscopic surgery with nature-orifice specimen extraction (RPLS-NOSE) and **B** reduced-port laparoscopic surgery with conventional specimen extraction by mini-laparotomy (RPLS-CSE)



	POD1	POD2	POD3	POD4	POD5
RPLS-NOSE	30.4	2.9	0.6	0.1	0
RPLS-CSE	31.3	8.0	1.9	1.1	0.6
p-value	0.729	0.000	0.066	0.027	0.035

Fig. 4 Dosage of morphine requirement by post-operative day 1 to day 5 were compared between reduced port laparoscopic surgery with natural orifice specimen extraction (RPLS-NOSE) and reduced port laparoscopic surgery with conventional specimen extraction by mini-laparotomy (RPLS-CSE). Values are presented as mean with standard deviation and statistically significant difference ($p < 0.05$) was labeled as star (*)

4.2–5.5 cm for tumor size between 2.75 and 3.9 cm in several studies [16–19], similar to results in our RPLS-CSE group. However, as the specimen was extracted via a natural orifice in patients undergoing RPLS-NOSE, there was no need to extend the umbilical wound, explaining the statistically significantly smaller umbilical incision length (1.9 vs. 4.7 cm, $p < 0.001$) compared to RPLS-CSE. Likewise, as the anvil of the circular stapler is introduced transanally, neither the 2.9 cm diameter in CHD29A nor the 3.3 cm diameter in CDH33A anvils required any extension. The 1.9 cm incision is compatible with extraction of a normally collapsed sigmoid colon 12–16 mm [20], allowing adequate extracorporeal colonic lumen clearance and purse-string suture insertion.

Although reducing the number and total length of incisions in RPLS should logically give rise to less pain and improved perioperative outcome [6], three recent randomized controlled trials (RCT) did not show these expected benefits in RPLS compared to CLS [16–18]. The absence of any statistically significant difference in postoperative pain may be related to specimen extraction stretching of the wound, not from the additional, smaller trocar sites. In the current study, avoidance of extraction-site mini-laparotomy by RPLS-NOSE reduced the impact on incisional pain, as attested by less morphine requirements after RPLS-NOSE (33.9 vs. 43.4 mg, $p = 0.011$). Less consumption of analgesia and lower visual analogue scale in patients undergoing NOSE were also reported in a RCT comparing laparoscopic colectomy with or without NOSE [21].

Quicker gastrointestinal recovery and shorter hospital stay in patients undergoing NOSE is consistent with the results of previous studies [8, 21, 22]. Aside from reduced postoperative pain and less morphine use because of the absence of mini-laparotomy, another potential advantage is that nearly the entire operation is conducted intraperitoneally, therefore, avoiding the need of exteriorization of colon and mesentery, potential source of mesenteric traction, laceration and bleeding [23]. The 2018 Guidelines of Enhanced Recovery After Surgery (ERAS®) suggested that opioid avoiding or sparing techniques, such as RPLS-NOSE, is associated with early mobilization, quicker bowel function recovery, fewer complications and shorter length of stay [24].

Of note, operation time was longer in RPLS-NOSE than in RPLS-CSE. The reasons might be (a) performance of the anastomosis entirely intraperitoneally with laparoscopic purse-string suturing, (b) the difficulty of NOSE procedure in obese patients (c) lack of ports for the assistant. Previous studies reported a steady reduction of operation time for NOSE, indicating the existence of a learning curve [10, 25]. While we believe that operation time can be shortened with increasing experience in RPLS-NOSE, this also emphasizes the need for formation and training with the technique.

Table 3 Pathologic and oncologic outcomes

	RPLS-NOSE ($n=52$)	RPLS-CSE ($n=52$)	p value
Extent of primary tumor			0.764
Tis	2 (3.8)	1 (1.9)	
T1	14 (26.9)	12 (23.1)	
T2	13 (25.0)	11 (21.2)	
T3	22 (42.3)	25 (48.1)	
T4a	1 (1.9)	3 (5.8)	
Lymph node metastasis			0.247
N0	36 (69.2)	39 (73.1)	
N1	8 (15.4)	11 (21.2)	
N2	8 (15.4)	3 (5.8)	
Numbers of lymph nodes harvested	21.4 ± 6.6	20.6 ± 8.6	0.594
Proximal resection margin (cm)	7.2 ± 2.9	7.1 ± 2.6	0.873
Distal resection margin (cm)	4.3 ± 1.6	4.3 ± 1.5	0.844
Histologic differentiation			0.196
Well	7 (13.5)	6 (11.5)	
Moderate	42 (80.8)	46 (88.5)	
Poor/others	3 (5.8)	0	
Adjuvant chemotherapy	18 (34.6)	14 (26.9)	0.215
FOLFOX	12	11	
XELOX	4	0	
Xeloda	2	3	
Recurrence	3 (5.8)	5 (9.6)	0.462
Local regional recurrence	0	2 (3.8)	0.153
Distal metastasis	3 (5.8)	5 (9.6)	0.462
Liver	2	2	
Lung	1	1	
Peritoneal seeding	0	2	

Values are presented as mean ± standard deviation (SD) or numbers (%)

RPLS reduced-port laparoscopic surgery, *NOSE* natural orifice specimen extraction, *CSE* conventional specimen extraction, *FOLFOX* 5-fluorouracil, leucovorin, oxaliplatin, *XELOX* capecitabine/oxaliplatin

Only a few studies have evaluated the combination of reduced port laparoscopic principle and NOSE. Nishimura et al. [26] reported the feasibility, safety, and oncological acceptability in a series of five patients who underwent reduced port laparoscopic anterior resection with transvaginal assistance and transvaginal specimen extraction. Meillate et al. [27] reported acceptable short and mid-term outcomes in a case-series (combined endoscopic transanal TME and single laparoscopic ileostomy-site proctectomy with transanal specimen extraction (TASE) for rectal cancer). A comparative study between transanal or trans-umbilical specimen extractions after single incisional laparoscopic surgery for colorectal cancer [25] found reduced wound-related complications in patients with TASE.

In our study, we observed a higher rate of peritoneal fecal contamination during operation in RPLS-NOSE (5.7% vs. 0%). Possible causes include intraperitoneal enterotomy for NOSE and specimen rupture during extraction. Notwithstanding, the consequences were minimal as there was no statistically significant difference in the incidence of postoperative intraperitoneal infection (3.8% vs.3.8%) or overall morbidity (7.7% vs. 15.4%, $p=0.220$) compared to RPLS-CSE; this is consistent with the results of Costantino et al. [28]. Similar to a retrospective study in patients who underwent single incision laparoscopic surgery with NOSE for CRC [25], our wound related complications were lower in RPLS-NOSE than in RPLS-CSE, although the difference did not reach statistical significance (1.9% vs. 7.7%, $p=0.169$).

A meta-analysis reported that single-port laparoscopic surgery through the umbilicus was associated with a 2.4-fold increase in the odds of incisional hernia compared to traditional laparoscopic surgery [29]. In our study, umbilical incisional hernias rates were 2/52 = 3.8% and 1/52 = 1.9% in the RPLS-CSE and RPLS-NOSE groups, respectively at a median follow-up of 34.3 months (even though the specimen was not extracted via the umbilical port-site in RPLS-NOSE). The suprapubic or Pfannenstiel incision technique has been reported to lower the risk of incisional hernia, compared with the midline incision, and has been recommended for specimen extraction in single-port site laparoscopic colorectal surgery [30, 31].

Oncological safety is an important issue for a new surgical technique in terms of radical cancer resection and in particular, local or extraction site recurrence. With proper protection of the specimen extraction site, NOSE has the same survival outcomes and oncological safety as conventional laparoscopic anterior resection [14]. In our study, only two patients sustained local recurrence, both in the RPLS-CSE group. Of note, these two patients had T4 tumors and also developed distal metastasis, similar to previous studies [9].

We have to acknowledge several limitations in our series. This was a single center, retrospective analysis. To minimize selection bias, propensity score matching was used according to known confounding factors, but other unknown factors may have influenced our outcomes. We lacked data to evaluate physiologic anorectal function after NOSE. The numbers were small and therefore this limits our power to come to any formal conclusions or assess long-term oncological outcomes.

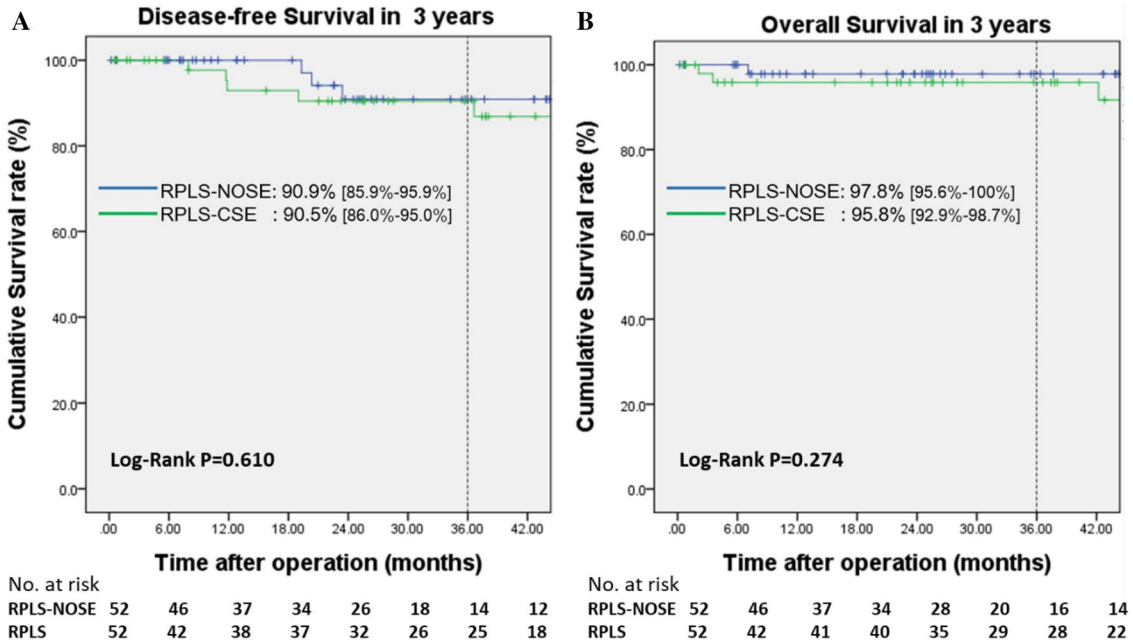


Fig. 5 **A** Disease-free survival rates at 3 years postoperatively were 90.9 versus 90.5% ($p=0.610$) in the reduced-port laparoscopic surgery with nature-orifice specimen extraction (RPLS-NOSE) and reduced port laparoscopic surgery with conventional specimen extraction by mini-laparotomy (RPLS-CSE), respectively. **B** Overall survival rates at 3 years postoperatively were 97.8 versus 95.8% ($p=0.274$) in RPLS-NOSE and RPLS-CSE

Conclusion

This retrospective case matched study suggests that NOSE is associated with reduced analgesic requirements, enhanced bowel recovery and shortened hospital stay in patients undergoing RPLS for sigmoid and upper rectal cancer. As the peri-operative and oncologic safety are comparable to conventional RPLS, NOSE in RPLS can be expected to provide superior surgical outcomes by reducing abdominal wall insult in selected patients with a tumor diameter of ≤ 5 cm. NOSE appears to be safe and effective- and may even be superior, though larger studies should be performed comparing these modalities.

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Compliance with ethical standards

Disclosures Sheng-Chi Chang, Tsung-Han Lee, Yi-Chang Chen, Mei-Tsz Chen, Hung-Chang Chen, Tao-Wei Ke, Yuan-Yao Tsai, Abe Fingerhut, William Tzu-Liang Chen have no conflicts of interest or financial ties to disclose.

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