



Comparison of natural orifice and conventional transabdominal specimen extraction: literature review

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Background and Objective: Conventional laparoscopic (CL) surgery is widely used in colorectal surgery. However, specimen extraction in CL requires an abdominal incision, which leads to increased rates of incision-related complications, such as postoperative pain, hernia, and surgical site infection (SSI). To reduce these complications, a novel and minimally invasive surgical approach known as natural orifice sample extraction (NOSE) has gained increasingly widespread use. The aim of this review is, intended to compare NOSE and CL in terms of postoperative complications and oncological outcomes in colorectal surgery.

Methods: Various medical databases were searched up to May 2021. We included retrospective, cohort study, randomized controlled trials and meta-analysis on the treatment of colorectal cancer (CRC) with NOSES.

Key Content and Findings: The results of this review showed that; compared with CL, NOSE showed less intraoperative bleeding, less postoperative pain and less analgesic requirement, fewer postoperative complications, better cosmetic recovery, less hospital stay, and better quality of life (QoL). While the operation time was found to be longer in NOSE, oncological results were similar in the two groups.

Conclusions: NOSE can be applied in colorectal surgery with better clinical outcomes and similar oncologic outcomes. Large-scale multicenter studies are required to confirm its clinical benefits.

Keywords: Conventional laparoscopy (CL); natural orifice sample extraction (NOSE); specimen extraction; colon; rectum; colorectal

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Introduction

Colorectal cancer (CRC) is the third most common malignancy worldwide with high rates of morbidity and mortality (1). Surgical resection is the most appropriate treatment for CRC (2). Since Jacobs (3) reported the first laparoscopic CRC resection, compared with traditional open surgery, conventional laparoscopy (CL) has offered significant advantages, such as less trauma and pain, less

intraoperative blood loss, fewer postoperative complications, faster recovery, and comparable oncological outcomes (4-8). However, specimen extraction in CL requires an abdominal incision (approximately 4-8 cm), which leads to increased rates of incision-related complications, such as postoperative pain, hernia, and surgical site infection (SSI) (9-11). To reduce these complications, a novel and minimally invasive surgical approach known as natural orifice sample extraction

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Table 1 The search strategy summary

Items	Specification
Date of search	To 01 May 2022
Databases and other sources searched	PubMed/MEDLINE, Scopus and Google Scholar
Search terms used	Laparoscopy or NOSE or natural orifice or specimen extraction or rectum or rectal or colorectal
Time frame	2011–2022
Inclusion and exclusion criteria	All studies were accepted for analysis, including congressional presentations and abstracts presenting the clinical course of the patients. Articles that did not meet the inclusion criteria, letters to the editor without patient data, experimental studies, and articles for which full versions could not be reached were excluded from study. References of selected related articles were also checked for additional studies. Articles written in English were considered for the study
Selection process	All studies in PubMed/MEDLINE were evaluated by two reviewers (AA, EC)

NOSE, natural orifice sample extraction.

(NOSE) has gained increasingly widespread use (12). The main feature of NOSE in colorectal surgery is complete intraperitoneal anastomosis and natural orifice specimen extraction, which means that an additional abdominal incision is not required to achieve complete intraperitoneal anastomosis (13). Therefore, NOSE reduces postoperative complications and improves patients' quality of life (QoL) by reducing incision-related trauma in the abdomen and postoperative pain (14,15). Franklin was the first to report NOSE for laparoscopic rectal and sigmoid resections in 1993 (16). Recently, several studies have confirmed the safety and feasibility of laparoscopic resection with NOSE for the treatment of colorectal disease (12,17-19). However, owing to some concerns, such as intra-abdominal infection, risk of tumor implantation, and oncologic safety, its use has remained limited (20-23).

The present review is, therefore, intended to compare NOSE and CL in terms of postoperative complications and oncological outcomes in colorectal surgery. We present the following article in accordance with the Narrative Review reporting checklist (available at <https://ales.amegroups.com/article/view/10.21037/ales-22-27/rc>).

Methods

To 01 May 2022, an electronic search was performed using (laparoscopy or NOSE or natural orifice or specimen extraction or rectum or rectal or colorectal) keywords in PubMed/MEDLINE, Scopus and Google Scholar databases. All studies were accepted for analysis, including

congressional presentations and abstracts presenting the clinical course of the patients. All studies in PubMed/MEDLINE were evaluated by two reviewers (AA and EC). Articles that did not meet the inclusion criteria, letters to the editor without patient data, experimental studies, and articles for which full versions could not be reached were excluded from study. References of selected related articles were also checked for additional studies. Articles written in English were considered for the study (*Table 1*).

Discussion

Postoperative results

Operative time

In CL, the specimen is removed via an abdominal incision, and the incision is then closed with a primary suture. In NOSE, no abdominal incision is made for extracting the specimen, but sutures may be required to close the posterior colpotomy only in transvaginal NOSE (5,11,13-15,17). It is not a routine practice for gynecologists to close posterior colpotomy wounds, and if they experience difficulty in using the technique, the posterior colpotomy incision may be left open (24). Studies show that the operative time in NOSE is longer than that in CL (5,11,13-15,17). Karagul *et al.* reported that male sex, presence of colon disease, and large-sized tumors posed difficulties in applying the technique and that they prolonged the operative times (25). Except for the meta-analysis by Chin *et al.* (11), all meta-analyses that met the study criteria and included in the systematic review show that the operative time was longer in NOSE (*Table 2*).

Table 2 Results of meta-analysis in comparison of natural orifice and conventional transabdominal specimen extraction

Authors	Study design	Number of patients NOSE/CL	Shorter operation duration	Less blood loss	Less postoperative pain/few analgesics	Earlier time to first flatus/the resumption of diet	Less duration of hospital stay	Less postoperative complications (overall/anastomotic/incision-related/intra-abdominal infection)	Better cosmetic result	More harvested lymph node	Better proximal resection margin/better distal resection margin/better CRM	Better disease recurrence/better survival
Zhou Z (15)	21 RCT	1,058/1,054	CL	NOSE	NOSE/-	NOSE/-	NOSE	NOSE/Similar/ NOSE/NOSE	NOSE	-	-/-/-	Similar/Similar (3-48 months)
Lin J (5)	10 RS; 1 RCT; 1 cohort	665/772	CL	Similar	NOSE/-	NOSE/-	NOSE	NOSE/Similar/ NOSE/Similar	NOSE	Similar	Similar/Similar/ Similar	-/-
Wang S (14)	10 RS; 4 RCT	1,116/1,150	CL	NOSE	NOSE/ NOSE	NOSE/-	NOSE	NOSE/Similar/ NOSE/Similar	NOSE	Similar	-/-/-	-/Similar (3 years)
Chin YH (11)	17 RS; 3 RCT; 1 cohort	1,079/1,299	Similar	NOSE	NOSE/ NOSE	NOSE/NOSE	NOSE	NOSE/Similar/ NOSE/Similar	NOSE	Similar	-/-/-	Similar/Similar (5 years)
He J (26)	10 RS	804/983	CL	Similar	NOSE/ NOSE	NOSE/-	NOSE	NOSE/Similar/ NOSE/-	-	Similar	Similar/NOSE-	-/Similar (5 years)
He J (13)	7 RS; 1 RCT	293/393	CL	Similar	NOSE/ NOSE	NOSE/NOSE	NOSE	NOSE/-/-/-	NOSE	Similar	Similar/-/-	-/-
Ma B (17)	1 RCT; 8 cohort	381/456	CL	-	NOSE/-	NOSE/-	NOSE	NOSE/-/NOSE/-	NOSE	-	-/-/-	Similar-
Liu RJ (27)	2 RCT; 7 RS; 5 cohort	660/775	CL	Similar	NOSE/-	NOSE	NOSE	NOSE/Similar/ NOSE/Similar	-	Similar	Similar/ Similar/-	-/Similar (5 years)

“-”, none. NOSE, natural orifice specimen extraction; CL, conventional laparoscopy; CRM, circumferential resection margin; RCT, randomized controlled trial; RS, retrospective study.

There are some possible reasons for the long operative time: (I) Intracorporeal suture and anastomosis performed completely intraperitoneally; (II) difficulties in performing the procedure in obese patients; (III) lack of port for use of resident physicians; and (IV) learning curve and low familiarity of surgeons with the laparoscopic techniques (5,28-30). Studies show that advances in laparoscopic equipment and increased experience in CL have reduced the operative times in NOSE (5,29-34). Compared with CL, different results have been reported for the operative times in transrectal and transvaginal NOSE. While Wolthuis *et al.* reported shorter operative time in transrectal NOSE than in CL, the meta-analysis of Lin *et al.* stated that the operative times were similar for transanal NOSE and CL and that the operative time was longer in transvaginal NOSE than in CL (5,35).

Intraoperative bleeding

One of the indicators for assessing the safety of laparoscopic surgery is the amount of intraoperative bleeding, which is lower in the NOSE group than in the CL group (5,11,14). Studies involving at least 100 cases for each of the CL and NOSE groups show that the amount of intraoperative bleeding was significantly lower in the NOSE group (11,14,15,36-38). However, in the study where Liu *et al.* included 100 patients in each of the two groups, the amounts of intraoperative bleeding were found to be comparable in NOSE and CL (39). The reason for the low amount of bleeding in NOSE is that it does not require additional abdominal incisions and that the procedure is performed more rigorously and gently under laparoscopic guidance (40). Additionally, there are meta-analyses reporting that there is no significant difference between the two groups in terms of the amount of intraoperative bleeding (5,13,26,27). The number of patients included in these meta-analyses is usually below 100 for each group.

Postoperative pain and analgesic needs

NOSE prevents additional abdominal wall incision for specimen extraction, thereby reducing abdominal wall trauma and causing less postoperative pain (12). Less postoperative pain also reduces analgesic use, which leads to earlier initiation of gastrointestinal function and postoperative activity, thereby reducing the duration of hospital stay (14). Although Awad *et al.* reported no difference between NOSE and CL in terms of postoperative pain scores and analgesic needs (28), the studies where Park *et al.* performed right colon resection and where Gundogan

et al. performed total colectomy reported that pain scores in the first 3 postoperative days were lower in the NOSE group (29,41). Meta-analyses included in the systematic review also showed that there was a significant reduction in the postoperative pain scores and analgesic needs in the NOSE group (11-14,26). Subgroup analysis based on specimen extraction sites revealed that transvaginal specimen extraction resulted in lower pain scores compared with CL, and a similar finding was observed for transanal specimen extraction (5).

Postoperative complications

Postoperative complications are among the important indicators of the safety of a surgical technique because serious postoperative complications can lead to the failure of the operation process (27). Postoperative complications are usually associated with mini-incision, anastomotic leak, or intra-abdominal infection, which may have an incidence rate of up to 23.3% in CL and 9.9% in NOSE (5,11,14,15,26,27).

One of the biggest advantages of minimally invasive surgery is the reduction of incision-related complications. Although less common than in open surgery, the incidence rates of SSI and incisional hernia in CL are 10.3–22.7% and 6.0–10.8%, respectively (25). The main cause of these wound-related complications in CL is the mini-incision performed on the abdominal wall (25,42). Ma *et al.* reported that 54% of the postoperative complications in CL were incision-related (17). Because there is no additional abdominal wall incision in NOSE, incision-related complications are expected to have lower rates of incidence (37,41,42). Wang *et al.* reported the incidence rate of incision-related complications to be 0.4% in the NOSE group and 6.5% in the CL group, and He *et al.* reported the incidence rate of incision-related complications to be 0.2% in the NOSE group and 5.9% in the CL group (14,26). Therefore, the lower incidence rates of incision-related complications in NOSE leads to a reduction in the incidence of general postoperative complications (5,11,14,15,26,27).

Another concern with NOSE is performing an enterotomy to place the anvil, the risk of spilling of the intestinal contents into the peritoneal cavity, and the risk of disruption of the aseptic environment once the rectal stump or vaginal cuff is opened to extract the specimen (7,20,43). Although peritoneal contamination is reported in up to 100% of the patients undergoing NOSE, the incidence rate of infection is not as high as believed (21). A study in

China that included 718 patients showed that the incidence of intraperitoneal SSI after NOSE was only 0.8% (44). Studies also report that there is no difference between the groups in terms of infectious morbidity (4,12,21). Some measures can be applied to reduce peritoneal contamination while performing the NOSE procedure: rectal irrigation with iodized saline, preoperative bowel preparation, administering prophylactic antibiotics, peritoneal irrigation, using wound retractor, extracting the specimen in endo-bag, and performing abdominal drains (14,30,42,45,46).

Postoperative anastomotic leaks are serious complications in colorectal surgery. Various factors, such as extreme tension at the anastomotic ends, ischemia, and anastomosis technique, increase the incidence rate of anastomotic leaks (30,47). Circular stapler and end-to-end anastomosis are widely used in both groups. However, anastomosis is performed extracorporeally (EA) in CL and intracorporeally (IA) in NOSE. In EA, outward opening of the intestine requires further mobilization of the colonic segments and the mesentery, which can result in mesenteric laceration and bleeding, thus compromising the blood flow to the anastomotic ends. IA requires less mobilization than EA does and, therefore, permits tension-free anastomosis. Hence, NOSE may have a significant advantage in terms of reducing anastomotic leaks, particularly in cases of lower rectal cancers (48). Although Han *et al.* claim that the incidence of anastomotic leak is less common in transanal NOSE (49), meta-analyses show that there is no difference between the groups in terms of the incidence of anastomotic leak (5,11,14,15,26,27). Subgroup analysis was also performed for different methods of specimen extraction. The combined results showed that compared with the CL group, the transanal and transvaginal groups were similar in terms of postoperative anastomotic complications (14).

Cosmetic improvement

Postoperative cosmetic recovery has a positive effect on psychosocial morbidity (50) because, unlike CL, the NOSE procedure does not require an additional abdominal incision to extract the specimen. Hence, scar-free healing and a better cosmetic appearance are ensured in the NOSE group (12,13,41,42,51). In all meta-analyses evaluating cosmetic recovery, cosmetic recovery was shown to be better in the NOSE group (5,11,13-15,17).

Duration of hospital stay

In NOSE, the stimulation of inflammatory pathways is minor because no additional incisions are made on the

abdominal wall. The levels of postoperative stress and pain are, therefore, lower, which result in faster recovery of bowel function, better rehabilitation of the patients, and shorter hospital stays (12,27,42,52). Although a randomized controlled trial by Wolthuis *et al.* reported that the durations of hospital stay were similar in the two groups despite the postoperative pain score being lower and the need for analgesics being less in the NOSE group (12), all published meta-analyses show that the duration of hospital stay after NOSE was shorter than that in CL (5,11,13-15,17,26). Compared with transanal NOSE, transvaginal NOSE may be associated with delayed postoperative recovery and increased duration of hospital stay because of possible injury to the neighboring organs (sigmoid colon and rectum) (53). In the meta-analysis of Lin *et al.*, the durations of hospital stay after transvaginal NOSE and CL were found to be comparable and the duration of hospital stay in transanal NOSE was shorter than that in CL (5).

QoL

Psychological health is critical for the patients' QoL in the postoperative period. NOSE can significantly increase the patients' QoL because it does not require an additional incision on the abdominal wall (54). Increased QoL leads to better rehabilitation of the patients and improved quality of treatment (55,56). Studies have also shown that patients in the NOSE group have better postoperative QoL and, therefore, better role physiological and emotional functions (36,37,40).

Oncologic outcomes

Lymph node metastasis, local recurrence, and positive surgical margin are life-threatening conditions in CRC surgery and are often associated with poorer overall survival (OS) and disease-free survival (DFS) (27). Anatomically, the distribution of lymph nodes is parallel to the colonic mesenteric vessels. To resect the intestines, the associated lymph nodes are also removed and the mesenteric vessels are connected. The number of lymph nodes removed is an important consideration in assessing the surgical quality of laparoscopic colectomy because an insufficient number of removed lymph nodes has a negative impact on the survival outcomes of patients with CRC. In NOSE and CL, the steps of exploration, mobilization, and dissection are almost identical, which signifies similar lymph node removal in both groups (5,11,13,14,26).

A tumor can reach distant invasion via intramural spread; therefore, inadequate surgical resection may

lead to a positive limit, which is an independent factor for DFS (57). Because the surgical technique is the same in NOSE and CL, the proximal and distal and peripheral resection margins generally have similar lengths (4,5,11,13,14,26,29,51). However, a few studies have reported that the distal resection margin is longer in NOSE (26,58). This difference may be attributed to the fact that specimen extraction in the NOSE group is performed transanally and extra-abdominally under direct view or the fact that the robotic procedure is used (59).

One of the biggest concerns in NOSE is the implantation of tumor cells in the natural orifice site during specimen extraction, which affects the results of local recurrence and DFS (60). Winslow *et al.* reported that the likelihood of tumor implantation may increase in NOSE (61), whereas Park *et al.* reported that patients who underwent laparoscopic hemicolectomy with NOSE did not experience transvaginal recurrences during their 23-month follow-up (29). In another study, Park *et al.* reported that locally recurrent disease was present in four patients who underwent NOSE, but none of them had transrectal or transvaginal tumor recurrence (38). Meta-analyses reported that NOSE and CL had similar rates of local recurrence and DFS (11,14,15,17,26,27). These results eliminated the concerns about the implantation of tumor cells and their spread via natural orifices in patients undergoing NOSE. However, because some of the included studies used NOSE in patients with smaller tumors and because 5-year survival rates were not reported in these studies, the results need to be interpreted cautiously (4,11,14,15,58,62). For the prevention of tumor implantation in laparoscopic colorectal surgery, the recommended measures include routine bowel preparation, prophylactic antibiotic use, cutting of the proximal and distal surgical margins of the specimen using a stapler, peritoneal lavage, and use of sterile specimen bags (45,62,63). In a study where rectal irrigation with iodine-containing saline was applied, Hisada *et al.* also reported that no tumor cells were seen in the rectal lavage water (30).

Others results

Epidural anesthesia

Epidural anesthesia is applied only in an extremely small number of cases undergoing colorectal surgery. However, Hisada *et al.* showed that anterior resection can be performed with epidural anesthesia. Although the researchers did not use visual analog scale (VAS) to assess postoperative pain in their study, they did show a significant

reduction in postoperative use of analgesics and duration of pain in the NOSE group (30).

Robotic NOSE

Laparoscopic surgery for cancer of the middle and lower rectum is associated with various difficulties: limited view and difficulty in using laparoscopic instruments in a narrow space. Robotic surgery, on the contrary, can provide better postoperative recovery by reducing surgical trauma and complications, thanks to its three-dimensional high resolution and flexible robotic arms (59). In a study where Feng *et al.* compared CL with robotic NOSE, they reported that the rate of cases switching to open surgery was lower in the group of patients undergoing robotic NOSE. The possible reasons were less intraoperative bleeding, less postoperative pain, smaller number of cases with \geq II Clavien-Dindo complication grade, shorter hospital stays, and longer distal resection margin for lower rectal cancer. The groups of CL and robotic NOSE were similar in terms of long-term survival (59).

Age

Given the prolonged life expectancy, the number of geriatric patients undergoing laparoscopic colorectal surgery is increasing. However, elderly patients have weaker surgical tolerance and higher rates of postoperative morbidity and mortality. Therefore, perioperative evaluation should be performed meticulously in geriatric patients undergoing laparoscopic colorectal surgery (64,65). Zhang *et al.* showed that colorectal NOSE can be performed in patients aged \geq 65 years. They found that CL and NOSE were similar in terms of OS, DFS, local recurrence, and distant metastasis. However, the NOSE group was found to have faster recovery of gastrointestinal function, fewer postoperative complications, lower postoperative pain scores, better anal function, and better cosmetic recovery than the CL group (54).

NOSE type

NOSE is usually performed in two ways, i.e., transanally and transvaginally. The transanal route can be used in both sexes, whereas the transvaginal route is used only in women. The transvaginal route permits greater volumes of tumors to be extracted and can be used in more obese individuals. However, transvaginal NOSE is not appropriate for women with extensive pelvic adhesions, endometriosis, morbid obesity, or a narrow vagina (45). The biggest concerns in transanal and transvaginal NOSE surgery are

anal sphincter injury, sexual dysfunction, and pelvic organ injury. It is important that the anus is dilated completely and the specimen is extracted gently so that anal function is not impaired (54). Studies show that anal dysfunctions are rarely seen in the NOSE group; the symptoms are usually mild and reversible, basal and maximum anal tightening pressures of the postoperative period (6th week–3rd month) are comparable, and there is no significant difference in terms of anal function even in the early postoperative period (6th week) and late postoperative period (24th month) (12,17,28–30,37,38,40,66). In the meta-analysis of He *et al.*, it was shown that there was no difference between the two groups in terms of sexual and urinary functions (26,30). Previous studies report that the incidence of dyspareunia is low and that the symptoms are usually mild and reversible (28,30). Studies have also indicated the safety of transvaginal access, where high satisfaction of sexual function was reported by patients themselves (28,67).

This study has some limitations. First, NOSE is an emerging field, most studies are retrospective or observational, and there are not enough randomized controlled trials. Second, this study compared NOSE and conventional surgery for specimen extraction, mostly in laparoscopic colorectal surgery, due to the small number of robotic NOSE studies. Robotic NOSE findings could change the results of this study.

Summary

This was the review to support that NOSE is superior to CL surgery in terms of postoperative morbidity, postoperative pain and analgesic requirement, hospital stay, intraoperative blood loss, the time to first flatus, cosmetic results, wound infections, and postoperative recovery. However, NOSE was associated with a longer operative time, and similar oncological safety and long-term prognosis in comparison with CL. However, RCTs that focus on long-term outcomes are needed for further validation.

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