

Original Article

Natural Orifice Specimen Extraction Surgery yields superior long-term oncological outcomes compared to traditional laparoscopic surgery in stage II-III rectal cancer

Yanle Fang, Lin Lin, Hongxun Ruan, Xiaoning Qin

Department of General Surgery, The Second Hospital of Hebei Medical University, No. 215, Heping West Road, Shijiazhuang 050000, Hebei, China

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Abstract: Objectives: To compare the long-term oncological and clinical outcomes of natural orifice specimen extraction surgery (NOSES) versus traditional laparoscopic surgery (TLS) in patients with Stage II-III rectal cancer. Methods: This retrospective cohort study analyzed data from 320 patients who underwent curative resection for Stage II-III rectal cancer between January 2020 and January 2025. Of these, 162 received NOSES and 158 underwent TLS. Perioperative outcomes, postoperative recovery, complications, disease-free survival (DFS), overall survival (OS), recurrence and metastasis rates, and quality of life were evaluated. Multivariate analyses were performed to identify independent prognostic factors for long-term outcomes. Results: Compared with TLS, NOSES resulted in shorter operative times and less intraoperative blood loss (both $P < 0.001$). Patients in the NOSES group experienced faster return of bowel function and shorter hospital stays (both $P < 0.001$). At five-year follow-up, NOSES was associated with significantly improved DFS ($P = 0.014$), OS ($P = 0.009$), and higher quality of life scores ($P < 0.001$). The NOSES group also exhibited fewer postoperative complications and a lower incidence of distant metastasis ($P = 0.034$). Multivariate analysis identified NOSES as an independent predictor of improved long-term survival and quality of life. Conclusions: NOSES offers significant advantages over TLS in the management of Stage II-III rectal cancer, including enhanced operative efficiency, accelerated recovery, reduced complications, and superior long-term oncological outcomes and quality of life. These findings support the wider clinical adoption of NOSES as a preferred minimally invasive surgical approach in eligible rectal cancer patients.

Keywords: Rectal cancer, Natural Orifice Specimen Extraction Surgery, laparoscopic surgery, oncological outcomes, postoperative recovery, quality of life

Introduction

Colorectal cancer remains a major global health burden, ranking as the third most commonly diagnosed malignancy and the second leading cause of cancer-related deaths worldwide [1, 2]. Among these, rectal cancer presents unique challenges due to its complex anatomical location and the delicate balance required in surgical management [3]. The primary goal of rectal cancer surgery is curative resection - complete tumor removal while preserving function and minimizing morbidity [4, 5]. With advancements in surgical techniques, reducing invasiveness without compromising oncological efficacy has become a central focus.

Laparoscopic surgery has become the standard approach for rectal cancer, offering several advantages over open surgery, including reduced postoperative pain and faster recovery [6]. However, conventional laparoscopic surgery still requires an abdominal incision for specimen extraction, which can lead to wound-related complications such as infections or incisional hernias, potentially diminishing the benefits of minimally invasive techniques [7].

Natural orifice specimen extraction surgery (NOSES) addresses this limitation by eliminating the need for an abdominal incision. Instead, the resected specimen is removed through natural orifices, such as the anus or vagina [8]. This approach reduces postoperative pain and

lowers the risk of wound complications. While early findings are promising, robust evidence on the long-term oncological safety and efficacy of NOSES remains limited [9, 10].

For patients with stage II-III rectal cancer - often characterized by deeper invasion and lymph node involvement - rigorous evaluation of NOSES is essential. Long-term outcomes, including local recurrence, distant metastasis, and overall survival (OS), are critical in determining its efficacy. Although short-term studies suggest favorable results, uncertainties remain regarding potential risks such as inadequate resection margins or intraoperative tumor cell dissemination.

This study aims to compare the long-term oncological outcomes of NOSES and traditional laparoscopic surgery (TLS) in patients with stage II-III rectal cancer, addressing critical gaps in current evidence and informing clinical decision-making.

Materials and methods

Research design and ethical compliance

This retrospective study reviewed 320 patients with stage II-III rectal cancer treated at the Second Hospital of Hebei Medical University between January 2020 and January 2025. Patients were divided into two groups based on the surgical approach. The NOSES group included 162 patients who underwent NOSES, while the TLS group comprised 158 patients who received TLS. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of the Second Hospital of Hebei Medical University. To protect patient confidentiality, all data were anonymized. As the study posed minimal risk to participants, the requirement for informed consent was waived. All procedures complied with relevant ethical guidelines and regulatory standards.

Patient selection criteria

Inclusion criteria: Patients were required to meet the diagnostic criteria for rectal cancer [11], confirmed through imaging modalities (CT and colonoscopy) and histopathological biopsy. Eligible patients were aged ≥ 18 years, with complete baseline records and clear surgical indications. An expected survival time of more

than six months was required, primarily due to tumor-related factors rather than systemic comorbidities. All patients underwent successful surgery with complete, accessible follow-up data and had not received prior radiotherapy or chemotherapy.

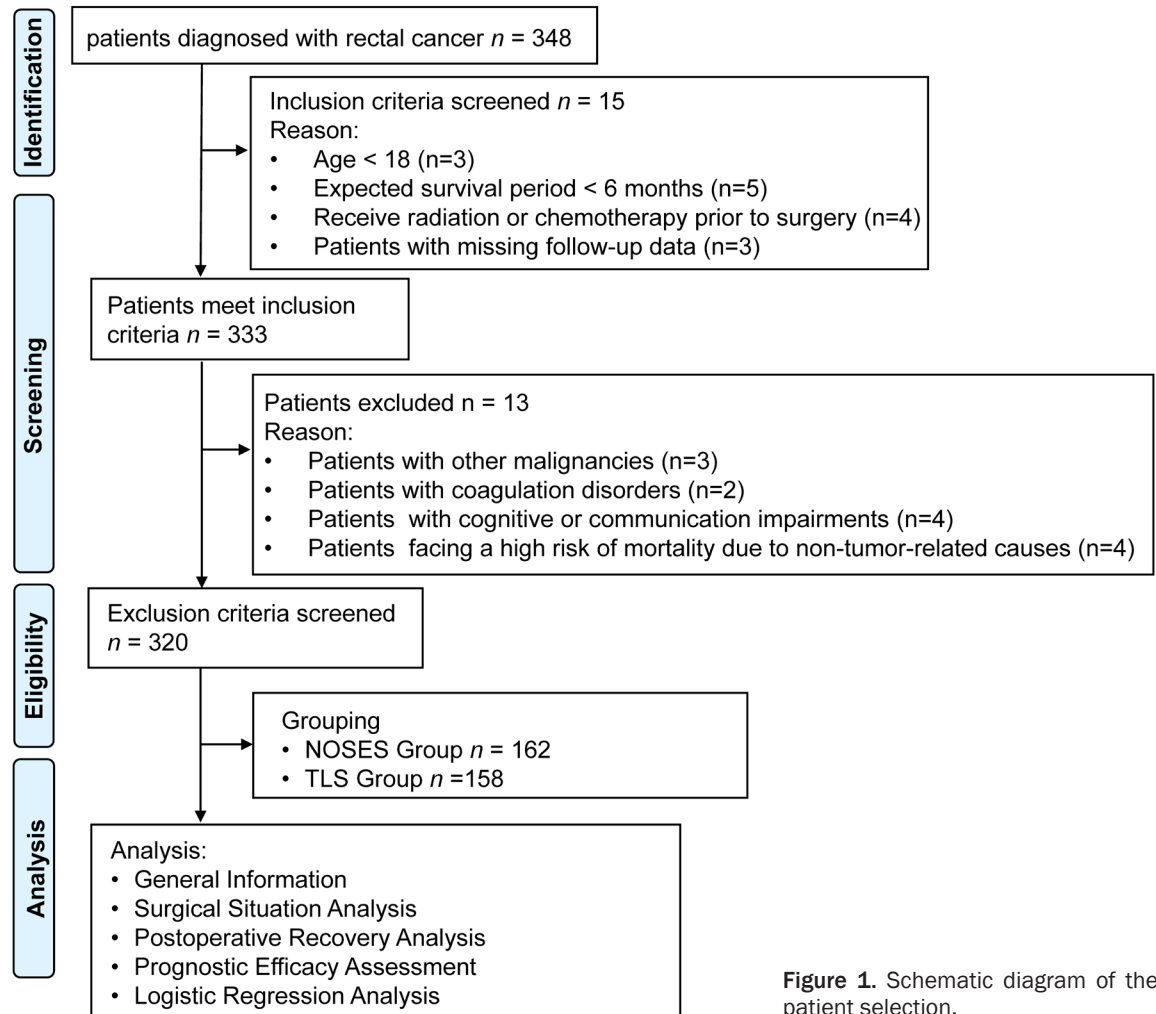
Exclusion criteria: Exclusion criteria included significant organ dysfunction, particularly severe comorbidities affecting life expectancy, coagulation disorders, other malignancies, and cognitive or communication impairments. Patients requiring emergency surgery, such as those with bowel obstruction or perforation, were excluded. Additionally, patients with serious uncontrolled diseases likely to result in early non-cancer-related mortality were not included (**Figure 1**).

Data extraction

Data were obtained from multiple sources, including the hospital's electronic medical records (EMR), surgical reports, pathology results, and structured follow-up protocols involving scheduled clinic visits and telephone interviews. The final follow-up date was January 31, 2025. Collected variables included demographic data (e.g., age, sex), tumor characteristics (e.g., stage), surgical details (e.g., operation time, intraoperative blood loss), and postoperative outcomes (e.g., hospital stay duration, adjuvant therapy). Long-term outcomes such as disease-free survival (DFS), OS, local recurrence, distant metastasis, and quality of life were also documented. All data were cleaned and anonymized before statistical analysis to ensure accuracy and confidentiality.

Surgical methods

NOSES group: Procedures were performed under pneumoperitoneum using four laparoscopic ports. A 30° laparoscope was inserted through a port positioned 10 cm above the umbilicus for abdominal exploration. The operation involved dissection of the inferior mesenteric vessels, clearance of regional lymph nodes, and sharp dissection of the presacral space. For mid- and upper rectal cancers, the bowel was transected above and below the lesion, and the specimen was extracted transanally using a rectoscope with a wound protector. A stapler head was then introduced via the anus and attached to the proximal bowel seg-



ment. The distal rectum was closed, and intra-corporeal anastomosis was completed using a circular stapler. For low rectal tumors, the mesentery was dissected to the pelvic floor. The proximal bowel was transected, and the distal tumor-bearing segment was everted and resected transanally using an oval clamp. The anastomosis was then completed intracorporeally.

TLS group: The procedure employed a five-port technique. After sigmoid colon mobilization and dissection of the inferior mesenteric vessels and adjacent tissues, lymph nodes were cleared to expose both ureters. Depending on tumor location, a 5 cm abdominal incision was made for specimen extraction. Pneumoperitoneum was then re-established, and a stapler was used to complete the anastomosis. The abdominal cavity was thoroughly irrigated with

sterile saline, and drainage tubes were placed to prevent fluid accumulation. All incisions and trocar sites were sutured and closed.

Surgical and postoperative indicators

Surgical parameters were retrospectively extracted from EMRs for both groups. These included operation time, intraoperative blood loss (estimated as the weight difference between blood-soaked and dry gauze, with 1 gram approximating 1 mL), number of lymph nodes harvested, and duration of drainage tube placement.

Postoperative recovery indicators were also collected, including time to first flatus, return of bowel sounds, recovery of gastrointestinal motility, and postoperative hospital stay. These metrics were retrieved from inpatient records and follow-up documentation.

Monitoring of Carcinoembryonic Antigen (CEA) tumor marker

CEA levels were monitored using an automated chemiluminescence immunoassay analyzer (Mindray Medical International Ltd., China) to assess disease progression and potential recurrence. CEA monitoring provided critical prognostic information, particularly in relation to tumor stage (II/III) and the tumor's distance from the anal verge, both of which are important for evaluating outcomes and guiding clinical interventions.

Criteria for gastrointestinal motility recovery

Gastrointestinal motility recovery was assessed using both clinical and objective criteria. Clinical indicators included tolerance of oral intake without nausea or vomiting, the presence of at least one spontaneous, formed bowel movement per day, and absence of abdominal distension or tenderness. Objective indicators included radiographic evidence of normal bowel gas distribution, manometric confirmation of normal motility patterns, and laboratory tests showing normal levels of electrolytes, liver enzymes, and inflammatory markers.

Daily evaluations were conducted during hospitalization. Full recovery of gastrointestinal motility was confirmed once all criteria were met [12].

Postoperative pain assessment

Postoperative pain was evaluated 24 hours after surgery using the Visual Analog Scale (VAS) [13], a 10-cm horizontal line anchored by "no pain" (0) and "worst imaginable pain" (10). Patients marked their pain level on the scale, and the score was determined by measuring the distance in centimeters from the "no pain" end.

Pain scores were categorized as follows: 0: no pain, no sleep disturbance; 1-3: mild pain, does not affect sleep; 4-6: moderate pain, disturbs sleep; 7-10: severe pain, causes insomnia or frequent awakenings.

The VAS demonstrated good internal consistency, with a Cronbach's alpha of 0.796. Additionally, the duration of patient-controlled anal-

gesia usage was recorded to assess postoperative analgesic needs over time.

Monitoring of postoperative complications

Postoperative complications were monitored at 1, 3, and 5 years postoperatively. Clinical evaluations included physical examinations and patient interviews to assess symptoms such as fever, pain, or gastrointestinal discomfort.

Imaging assessments included: (1) CT Scans (Ingenuity CT, Philips Healthcare, Netherlands): Used to detect fluid collections, abscesses, pulmonary complications, and possible metastases. (2) MRI (Ingenia Ambition, Philips Healthcare, Netherlands): Provided detailed pelvic imaging to detect anastomotic leaks, recurrent tumors, inflammation, or fibrosis. (3) Endoscopy (EC38-i10, PENTAX Medical, Japan): Used to directly visualize mucosal healing at the anastomosis site, identify abnormal growths, ulcers, strictures, and evaluate the overall condition of the colon and rectum.

This multimodal approach enabled comprehensive evaluation of recovery and early detection of complications.

Quality of life assessment

Quality of life was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) [14]. The instrument consists of 30 items, structured as follows: 1. Functional Scales (0-100): Physical (5 items), Role (2), Emotional (4), Cognitive (2), Social (2). 2. Symptom Scales (0-100): Fatigue (3), Pain (2), Nausea/Vomiting (2). 3. Global Health Status/Quality of Life Scale (0-100): 2 items. (4) Single Items (0-100): Appetite loss, insomnia, dyspnea, constipation, diarrhea, financial difficulties.

Higher functional scores indicate better functioning, while higher symptom scores reflect greater symptom burden. Quality of life was evaluated at 1, 3, and 5 years postoperatively, and scoring was performed according to the official EORTC QLQ-C30 scoring manual [15].

Long-term oncological prognosis

Long-term outcomes, including, OS, local recurrence, distant metastasis, and quality of life,

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Table 1. Comparison of demographic characteristics between two groups

Parameters	NOSSES Group (n = 162)	TLS Group (n = 158)	t/ χ^2	P
Male/Female [n (%)]	96 (59.26%)/66 (40.74%)	92 (58.23%)/66 (41.77%)	0.035	0.851
Age (years)	58.31±10.42	57.89±11.12	0.355	0.723
Ethnicity (Han/Other) [n (%)]	136 (83.95%)	130 (82.28%)	0.159	0.690
Educational level (high school or below/junior college or above) [n (%)]	106 (65.43%)	111 (70.25%)	0.852	0.356
Occupational Status (Retired/Employed (Manual Labor/Service Industry))	89 (55.63%)	95 (60.13%)	0.881	0.348
Residence (Urban/Rural)	114 (70.37%)	105 (66.46%)	0.567	0.451
Smoking history [n (%)]	46 (28.40%)	40 (22.22%)	0.386	0.535
Drinking history [n (%)]	20 (12.34%)	15 (9.49%)	0.668	0.414
Tumor stage (II/III)	78 (48.15%)/84 (51.85%)	76 (48.10%)/82 (51.90%)	0.000	0.993
Distance from the anal verge (cm)	7.51±2.28	7.61±2.49	0.369	0.713
Tumor location (Middle rectum/Lower rectum) [n (%)]	80 (49.42%)/82 (50.60%)	78 (49.41%)/80 (50.62%)	0.000	0.998
Disease duration (months)	6.31±2.12	6.53±2.29	0.909	0.364
Previous treatment (Yes/No)	90 (55.61%)/72 (44.44%)	85 (53.81%)/73 (46.21%)	0.100	0.752
History of intestinal diseases (Yes/No)	45 (27.81%)/117 (72.21%)	40 (25.29%)/118 (74.73%)	0.248	0.618
Family history of rectal cancer (Yes/No)	15 (9.33%)/147 (90.71%)	10 (6.32%)/148 (93.71%)	0.954	0.329
Dietary habits			0.607	0.738
High fiber	60 (37.02%)	55 (34.83%)	0.509	0.475
Moderate fiber	70 (43.22%)	75 (47.52%)	0.434	0.665
Low fiber	32 (19.81%)	28 (17.71%)	0.051	0.821
Constipation (Yes/No)	25 (15.44%)/137 (84.56%)	20 (12.69%)/138 (87.33%)	0.060	0.807
Preoperative CEA (ng/mL)	4.52±2.11	4.63±2.19	0.556	0.579
Hypertension (Yes/No)	48 (29.63%)/114 (70.37%)	45 (28.48%)/113 (71.52%)	0.035	0.851
Diabetes mellitus (Yes/No)	22 (13.58%)/140 (86.42%)	20 (12.66%)/138 (87.34%)	0.355	0.723
BMI (kg/m ²)	24.22±3.11	24.02±3.31	0.159	0.690

BMI: Body Mass Index; CEA: Carcinoembryonic Antigen.

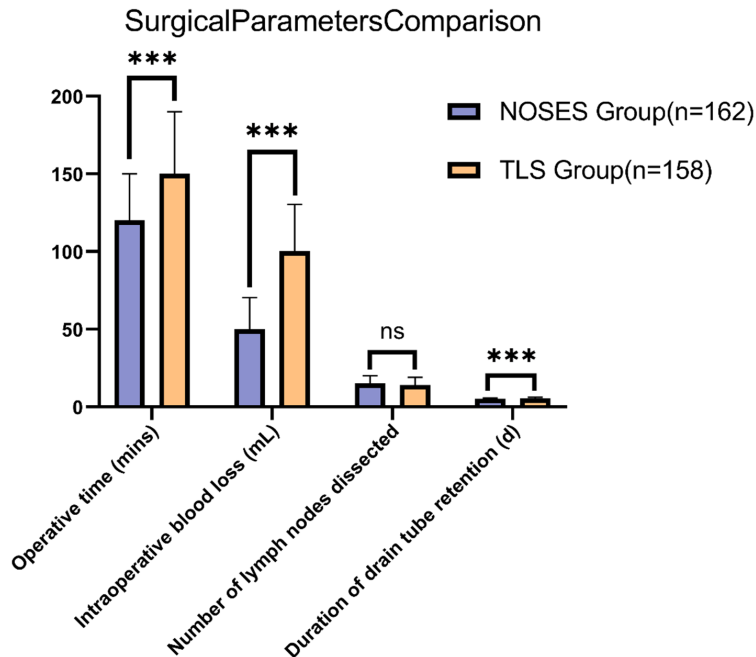


Figure 2. Comparison of surgical outcomes between two groups. ns: no statistically significant difference; ***: $P < 0.001$.

were systematically recorded at 1, 3, and 5 years post-surgery. At each follow-up, survival status and cause of death (tumor-related or unrelated) were documented. This longitudinal follow-up enabled comprehensive evaluation of oncologic control and patient-centered outcomes between the NOSES and TLS groups.

Statistical methods

Data analysis was performed using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean \pm standard deviation ($X \pm sd$) and compared using the independent samples t-test. Categorical variables were presented as frequencies and percentages [n (%)] and analyzed using the chi-square (χ^2) test. Multivariate analysis was conducted using logistic regression to assess the independent impact of surgical approach on key outcomes. A P -value < 0.05 was considered statistically significant.

Results

Comparison of general information

No statistically significant differences were observed between the groups in terms of gen-

der, age, ethnicity, education level, occupation, residence, smoking and alcohol history, tumor stage, tumor distance from the anal verge, tumor location, disease duration, prior treatments, history of intestinal disease, family history of rectal cancer, dietary habits, history of constipation, preoperative CEA levels, hypertension, diabetes mellitus, or body mass index (all $P > 0.05$). Overall, the baseline characteristics between the two groups were well balanced (Table 1).

Comparison of surgical outcomes

The NOSES group had a significantly shorter operative time compared to the TLS group ($P < 0.001$) (Figure 2). Intraoperative blood loss and

drain tube duration were also significantly lower in the NOSES group (both $P < 0.001$). There was no significant difference in the number of dissected lymph nodes between the two groups ($P = 0.075$).

Comparison of postoperative recovery

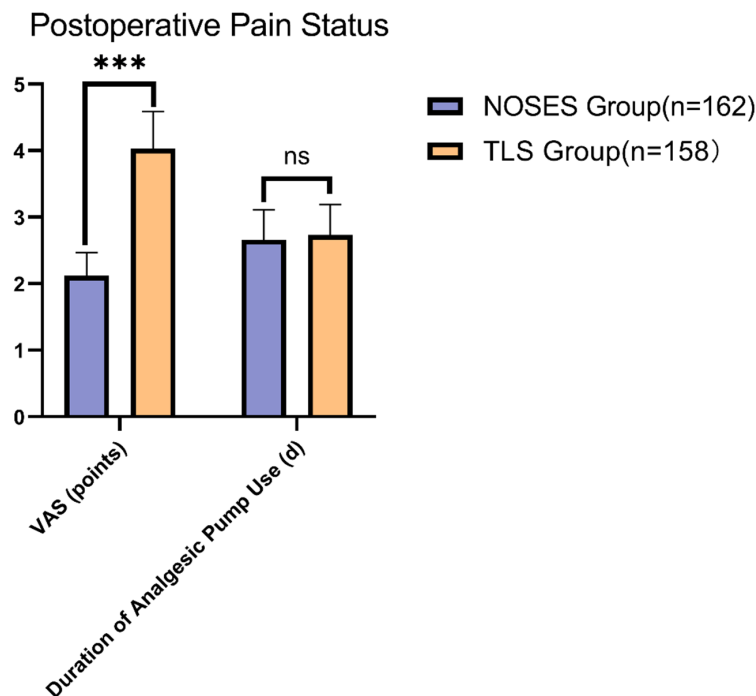
Patients in the NOSES group demonstrated faster postoperative recovery. Time to anal venting, return of bowel sounds, and restoration of gastrointestinal motility were all significantly shorter in the NOSES group (all $P < 0.001$; Table 2). The postoperative complication rate was also significantly lower in the NOSES group ($P = 0.023$), as was the length of hospital stay ($P < 0.001$).

Comparison of postoperative pain

VAS scores 24 hours post-surgery were significantly lower in the NOSES group compared to the TLS group ($P < 0.001$) (Figure 3). However, no significant difference was observed in the duration of analgesic pump use between the two groups ($P = 0.160$). Thus, while analgesic needs were similar, patients undergoing NOSES reported significantly less pain.

Table 2. Comparison of postoperative recovery between two groups

Parameters	NOSES Group (n = 162)	TLS Group (n = 158)	t/ χ^2	P
Time to anal venting (h)	24.14±6.23	36.09±8.15	14.716	< 0.001
Time to bowel sound recovery (h)	17.87±4.79	23.94±5.76	10.229	< 0.001
Time to gastrointestinal motility recovery (h)	36.20±8.15	48.24±10.12	11.709	< 0.001
Complication rate [n (%)]	8 (4.94%)	19 (12.02%)	5.200	0.023
Postoperative hospital stay (d)	7.00±2.00	9.00±3.00	6.965	< 0.001


Figure 3. Comparison of postoperative pain status between two groups. ns: no statistically significant difference; ***: $P < 0.001$.

Comparison of postoperative complications

At 1-year follow-up, the NOSES group had a significantly lower overall complication rate compared to TLS ($P < 0.001$), with specific reductions in intra-abdominal infection ($P = 0.022$) and intestinal obstruction ($P = 0.029$) (Table 3). These differences persisted at 3 years ($P < 0.001$), with continued reductions in intra-abdominal infection ($P = 0.029$) and intestinal obstruction ($P = 0.029$). At 5 years, the NOSES group maintained a significantly lower complication rate ($P < 0.001$), including fewer cases of anastomotic leakage ($P = 0.036$), pulmonary infection ($P = 0.041$), urinary retention ($P = 0.031$), intra-abdominal infection ($P = 0.029$), and intestinal obstruction ($P = 0.041$).

Comparison of oncological outcomes

At 1 year, no significant differences were observed in DFS, OS, local recurrence, or distant metastasis rates between groups. However, the NOSES group reported significantly higher quality of life scores ($P = 0.007$) (Table 4). By 3 years, the NOSES group exhibited significantly improved DFS ($P = 0.027$), OS ($P = 0.021$), and quality of life ($P < 0.001$). These advantages remained evident at 5 years, with better DFS ($P = 0.014$), OS ($P = 0.009$), quality of life ($P < 0.001$), and a lower distant metastasis rate ($P = 0.034$).

Multivariate regression analysis

Multivariate logistic regression revealed that surgical approach significantly influenced long-term outcomes (Table 5). NOSES was independently associated with higher quality of life scores at 1 year (OR = 1.45, $P = 0.008$), 3 years (OR = 1.38, $P = 0.022$), and 5 years (OR = 1.32, $P = 0.045$). It also correlated with improved DFS at 3 years (OR = 1.67, $P < 0.001$) and 5 years (OR = 1.70, $P < 0.001$), and better OS at 3 years (OR = 1.55, $P = 0.009$) and 5 years (OR = 1.60, $P = 0.005$). Moreover, NOSES was associated with a reduced risk of distant metastasis over 5 years (OR = 0.72, $P = 0.024$).

Nomogram development and validation

A prognostic nomogram was developed to visually compare long-term oncological outcomes between NOSES and TLS (Figure 4). The model

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Table 3. Comparison of postoperative complications between two groups

	Parameters	NOSES Group (n = 162)	TLS Group (n = 158)	χ^2	P
One Year	Anastomotic leak [n (%)]	8 (4.94%)	13 (8.23%)	1.412	0.235
	Pulmonary infection [n (%)]	6 (3.70%)	10 (6.33%)	1.161	0.281
	Urinary retention [n (%)]	7 (4.32%)	12 (7.59%)	1.535	0.215
	Intra-abdominal infection [n (%)]	4 (2.47%)	13 (8.23%)	5.273	0.022
	Intestinal obstruction [n (%)]	5 (3.09%)	14 (8.86%)	4.775	0.029
	Total [n (%)]	30 (18.70%)	62 (39.24%)	16.767	< 0.001
Three Year	Anastomotic leak [n (%)]	10 (6.17%)	15 (9.49%)	1.225	0.268
	Pulmonary infection [n (%)]	7 (4.32%)	12 (7.59%)	1.535	0.215
	Urinary retention [n (%)]	9 (5.56%)	14 (8.86%)	1.310	0.252
	Intra-abdominal infection [n (%)]	5 (3.09%)	14 (8.86%)	4.775	0.029
	Intestinal obstruction [n (%)]	7 (4.32%)	17 (10.76%)	4.780	0.029
	Total [n (%)]	38 (23.46%)	72 (45.57%)	17.338	< 0.001
Five Year	Anastomotic leak [n (%)]	11 (6.79%)	22 (13.92%)	4.401	0.036
	Pulmonary infection [n (%)]	9 (5.56%)	19 (12.03%)	4.193	0.041
	Urinary retention [n (%)]	10 (6.17%)	21 (13.29%)	4.632	0.031
	Intra-abdominal infection [n (%)]	7 (4.32%)	17 (10.76%)	4.780	0.029
	Intestinal obstruction [n (%)]	9 (5.56%)	19 (12.03%)	4.193	0.041
	Total [n (%)]	46 (28.40%)	98 (62.03%)	36.552	< 0.001

Table 4. Comparison of oncological outcomes between two groups

	Parameters	NOSES Group (n = 162)	TLS Group (n = 158)	t/ χ^2	P
One Year	DFS [n (%)]	146 (90.12%)	134 (84.81%)	2.065	0.151
	OS [n (%)]	154 (95.06%)	142 (89.87%)	3.104	0.078
	Local Recurrence Rate [n (%)]	8 (4.94%)	13 (8.23%)	1.412	0.235
	Distant Metastasis Rate [n (%)]	10 (6.17%)	16 (10.13%)	1.675	0.196
	Quality of Life Score Results	88.12±8.34	85.23±10.45	2.731	0.007
Three Year	DFS [n (%)]	122 (75.31%)	101 (63.92%)	4.908	0.027
	OS [n (%)]	130 (80.25%)	109 (68.99%)	5.364	0.021
	Local Recurrence Rate [n (%)]	16 (9.88%)	24 (15.19%)	2.065	0.151
	Distant Metastasis Rate [n (%)]	19 (11.73%)	28 (17.72%)	2.293	0.13
	Quality of Life Score Results	85.15±10.33	79.24±12.41	4.620	< 0.001
Five Year	DFS [n (%)]	97 (59.88%)	73 (46.20%)	6.006	0.014
	OS [n (%)]	113 (70.34%)	88 (55.70%)	6.766	0.009
	Local Recurrence Rate [n (%)]	24 (15.12%)	32 (20.25%)	1.639	0.201
	Distant Metastasis Rate [n (%)]	29 (17.90%)	44 (27.85%)	4.494	0.034
	Quality of Life Score Results	80.17±12.30	72.20±15.43	5.098	< 0.001

DFS: Disease-Free Survival; OS: Overall Survival.

highlights the superior prognosis associated with NOSES. Calibration curves demonstrated high predictive accuracy, with strong concordance between predicted probabilities and actual outcomes at multiple time points. These findings underscore the clinical utility of the nomogram and reinforce the advantages of NOSES in managing stage II-III rectal cancer.

Discussion

One of the most notable findings of this study was the superior intraoperative performance of NOSES. Compared with TLS, NOSES resulted in significantly shorter operative times and less intraoperative blood loss. This advantage is likely attributable to the minimally invasive

Table 5. Multivariate regression analysis of treatment regimens and therapeutic efficacy

Influencing factors	OR (95% CI)	P
Treatment regimen (NOSES/TLS) - Quality of Life Score Results at 1 year (%)	1.45 (1.10-1.89)	0.008
Treatment regimen (NOSES/TLS) - DFS at 3 years (%)	1.67 (1.23-2.27)	< 0.001
Treatment regimen (NOSES/TLS) - OS at 3 years (%)	1.55 (1.12-2.16)	0.009
Treatment regimen (NOSES/TLS) - Quality of Life Score Results at 3 years (%)	1.38 (1.05-1.82)	0.022
Treatment regimen (NOSES/TLS) - DFS at 5 years (%)	1.70 (1.24-2.33)	< 0.001
Treatment regimen (NOSES/TLS) - OS at 5 years (%)	1.60 (1.16-2.21)	0.005
Treatment regimen (NOSES/TLS) - Distant Metastasis Rate at 5 years (%)	0.72 (0.54-0.96)	0.024
Treatment regimen (NOSES/TLS) - Quality of Life Score Results at 5 years (%)	1.32 (1.01-1.73)	0.045

OR: Odds Ratio.

nature of NOSES, which eliminates the need for abdominal incisions to extract specimens [16]. By avoiding large wounds, NOSES reduces tissue trauma, thereby enhancing procedural efficiency [17]. These benefits are consistent with outcomes in other surgical specialties, where minimally invasive techniques are associated with improved recovery and reduced operative burden [18].

In terms of postoperative recovery, the NOSES group demonstrated clear advantages. Patients experienced earlier return of bowel function, including quicker passage of flatus and recovery of bowel sounds [19]. These indicators suggest that NOSES imposes less physiological stress than TLS, facilitating faster resumption of normal gastrointestinal function [20]. The reduced trauma associated with NOSES likely contributes to decreased inflammation and pain, resulting in shorter recovery times and quicker return to daily activities [21].

Postoperative pain assessment also favored the NOSES group. Patients reported significantly lower VAS scores, indicating milder pain experiences. This may be due to the avoidance of large abdominal incisions, which typically involve greater disruption of nerves and musculature [22]. Additionally, the less visible surgical trauma and absence of an external scar may contribute to psychological benefits, enhancing patient satisfaction and reducing perceived discomfort [23-25].

The incidence of postoperative complications was significantly lower in the NOSES group. This could be attributed to the reduced surgical trauma and preservation of anatomical structures. Traditional laparoscopic techniques may increase the risk of infection, wound dehiscence,

or incisional hernia due to the required abdominal incisions [26]. By maintaining the integrity of the abdominal wall, NOSES reduces opportunities for pathogen entry and tissue disruption, contributing to a more favorable complication profile [27].

Long-term outcomes further support the benefits of NOSES. Patients in the NOSES group exhibited better DFS and OS, along with a lower rate of distant metastasis. These findings may reflect improved oncologic resection quality and more precise lymphadenectomy enabled by better intraoperative visualization. Additionally, the less invasive nature of NOSES may reduce systemic inflammatory responses, potentially preserving immune function and decreasing the likelihood of residual tumor cell dissemination [28].

Quality of life scores were consistently higher in the NOSES group across all follow-up intervals. This may be a consequence of reduced complications, less pain, and faster physical and emotional recovery. Prior studies have shown that less invasive procedures are strongly associated with improved quality of life outcomes [29]. The ability to return to normal activities without prolonged convalescence has meaningful impacts on both psychological well-being and social functioning [30, 31].

Multivariate regression analysis reinforced these findings, confirming NOSES as an independent predictor of improved long-term outcomes, including DFS, OS, and quality of life. These consistent benefits across multiple endpoints suggest that NOSES is a more effective and patient-friendly surgical strategy for stage II-III rectal cancer.

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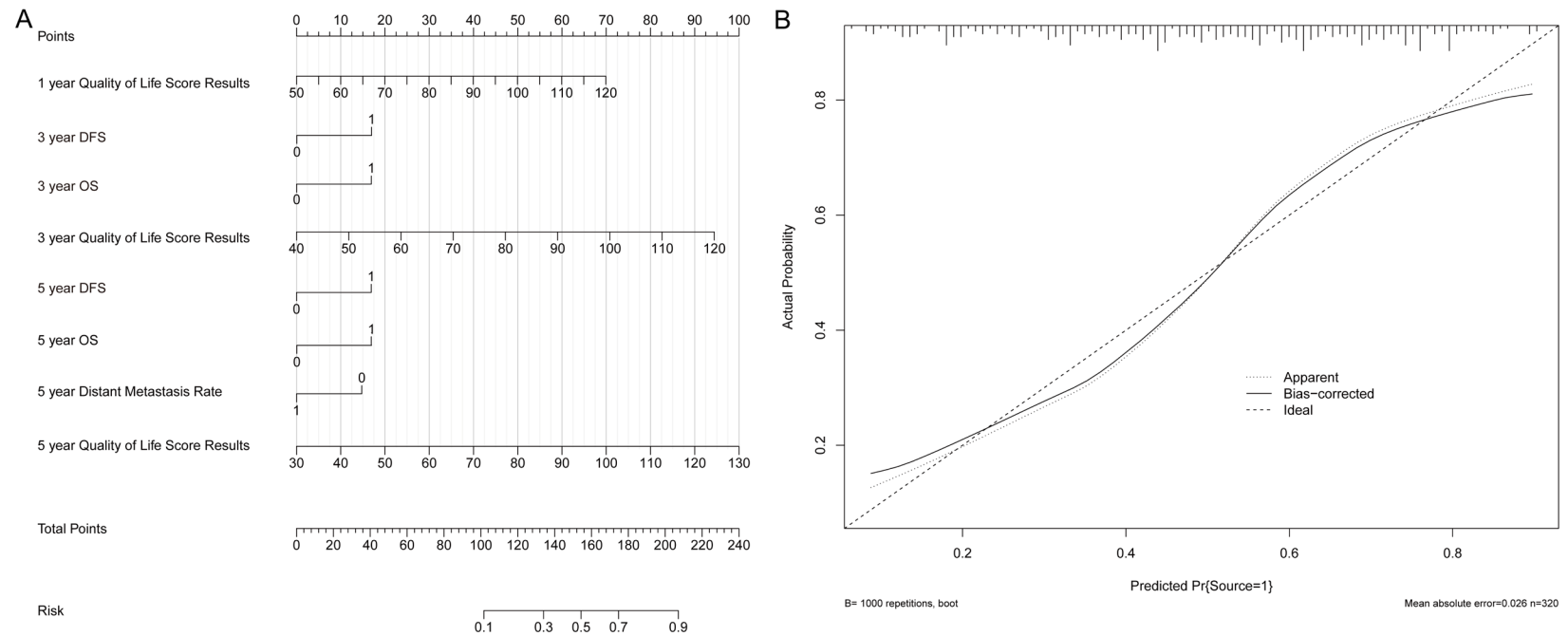


Figure 4. Nomogram development and validation. A. Nomogram; B. Calibration curve.

Furthermore, NOSSES aligns with the principles of patient-centered care in modern surgical oncology. Its emphasis on minimal invasiveness, functional preservation, and optimized recovery trajectories addresses not only clinical efficacy but also the holistic experience of the patient. The potential of NOSSES to reduce hospital stay, healthcare costs, and resource utilization while improving outcomes underscores its clinical value [32].

In conclusion, this study highlights the superiority of NOSSES over TLS in several key domains for the treatment of stage II-III rectal cancer. Although both approaches offer comparable long-term survival, NOSSES confers additional advantages in terms of operative efficiency, reduced postoperative complications, accelerated recovery, and enhanced quality of life. These findings support the continued integration of NOSSES into clinical practice and its inclusion in future treatment guidelines.

However, this study has limitations. Its retrospective design may introduce inherent biases, including selection and information bias, which could affect the generalizability of the results. The relatively small sample size and single-center scope limit the applicability of the findings to broader populations. Additionally, the lack of randomization and potential confounders - such as variability in surgeon expertise and perioperative protocols - may influence the observed outcomes. Although the follow-up period was adequate for assessing primary endpoints, it may not fully capture long-term survival effects or late-onset complications.

Future research should include large-scale, multicenter, prospective randomized controlled trials to validate these findings and provide stronger evidence for the adoption of NOSSES in routine surgical management of rectal cancer.

Disclosure of conflict of interest

None.

Address correspondence to: Xiaoning Qin, The Second Hospital of Hebei Medical University, No. 215, Heping West Road, Shijiazhuang 050000, Hebei, China. E-mail: 28503024@hebmu.edu.cn; a51981297@163.com

References

- [1] Quezada-Díaz FF, Bercz A, Escobar JL, Caire N, Díaz-Feldman LE, Manriquez E and Carvajal G. No operation after short-course radiotherapy followed by consolidation chemotherapy in locally advanced rectal cancer (NOAHS-ARC): study protocol for a prospective, phase II trial. *Int J Colorectal Dis* 2025; 40: 69.
- [2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 countries. *CA Cancer J Clin* 2021; 71: 209-249.
- [3] Houwen BBSL, Hartendorp F, Giotis I, Hazewinkel Y, Fockens P, Walstra TR and Dekker E; POLAR study group; *on behalf of the POLAR study group. Computer-aided classification of colorectal segments during colonoscopy: a deep learning approach based on images of a magnetic endoscopic positioning device. *Scand J Gastroenterol* 2023; 58: 649-655.
- [4] Liao YS, Chiu HY, Huang FH, Chang YH, Huang YM, Wei PL, Wang W, Hung CS and Tung HH. Prehabilitation interventions in patients undergoing colorectal cancer surgery: a systematic review and meta-analysis. *J Am Geriatr Soc* 2025; 73: 2262-2277.
- [5] Bedrikovetski S, Murshed I, Fitzsimmons T, Traeger L, Price TJ, Penniment M, Selva-Nayagam S, Vather R and Sammour T. Total neoadjuvant therapy in early-onset rectal cancer: a multicentre prospective cohort study. *Colorectal Dis* 2025; 27: e70059.
- [6] Pagano E, Pellegrino L, Robella M, Castiglione A, Brunetti F, Giacometti L, Rolfo M, Rizzo A, Palmisano S, Meineri M, Bachini I, Morino M, Allaix ME, Mellano A, Massucco P, Bellomo P, Polastri R, Ciccone G and Borghi F; ERAS-colorectal Piemonte group. Implementation of an enhanced recovery after surgery protocol for colorectal cancer in a regional hospital network supported by audit and feedback: a stepped wedge, cluster randomised trial. *BMJ Qual Saf* 2024; 33: 363-374.
- [7] Capoccia Giovannini S, Vierstraete M, Frascio M, Camerini G, Muysoms F and Stabilini C. Systematic review and meta-analysis on robotic assisted ventral hernia repair: the ROVER review. *Hernia* 2025; 29: 95.
- [8] Efetov SK, Cao Y, Panova PD, Khlusov DI and Shulutko AM. Reduced-port laparoscopic right colonic resection with D3 lymph node dissection and transvaginal specimen extraction (NOSSES Vlla) for right colon cancer: clinical features. *Tech Coloproctol* 2024; 29: 34.

- [9] Cao Y, He M, Liu Z, Chen K, Denis K 1st, Zhang J, Zou J, Semchenko BS and Efetov SK. Evaluation of the efficacy of natural orifice specimen extraction surgery versus conventional laparoscopic surgery for colorectal cancers: a systematic review and meta-analysis. *Colorectal Dis* 2025; 27: e17279.
- [10] Zhang Q, Wang M, Ma D, Zhang W, Wu H, Zhong Y, Zheng C, Ju H and Wang G. Short-term and long-term outcomes of natural orifice specimen extraction surgeries (NOSES) in rectal cancer: a comparison study of NOSES and non-NOSES. *Ann Transl Med* 2022; 10: 488.
- [11] Cubiella J, Marzo-Castillejo M, Mascort-Roca JJ, Amador-Romero FJ, Bellas-Beceiro B, Clofent-Vilaplana J, Carballal S, Ferrándiz-Santos J, Gimeno-García AZ, Jover R, Mangas-Sanjuán C, Moreira L, Pellisè M, Quintero E, Rodríguez-Camacho E and Vega-Villaamil P; Sociedad Española de Medicina de Familia y Comunitaria y Asociación Española de Gastroenterología. Clinical practice guideline. Diagnosis and prevention of colorectal cancer. 2018 Update. *Gastroenterol Hepatol* 2018; 41: 585-596.
- [12] Keller J, Bassotti G, Clarke J, Dinning P, Fox M, Grover M, Hellström PM, Ke M, Layer P, Malagelada C, Parkman HP, Scott SM, Tack J, Simren M, Törnblom H and Camilleri M; International Working Group for Disorders of Gastrointestinal Motility and Function. Expert consensus document: advances in the diagnosis and classification of gastric and intestinal motility disorders. *Nat Rev Gastroenterol Hepatol* 2018; 15: 291-308.
- [13] Crichton NJCN. Visual analogue scale (VAS). *J Clin Nurs* 2001; 10: 706.
- [14] Fayers P and Bottomley A; EORTC Quality of Life Group; Quality of Life Unit. Quality of life research within the EORTC - the EORTC QLQ-C30. European organisation for research and treatment of cancer. *Eur J Cancer* 2002; 38 Suppl 4: S125-133.
- [15] King MT. The interpretation of scores from the EORTC quality of life questionnaire QLQ-C30. *Qual Life Res* 1996; 5: 555-567.
- [16] Huang X, Wei R, Li Q, Qiu X, Li P and He W. Development and prospects of natural orifice specimen extraction surgery for colorectal cancer: a review article. *Int J Surg* 2025; 111: 2973-2989.
- [17] Sugita H, Nakanuma S, Tokoro T, Takei R, Okazaki M, Kato K, Takada S, Makino I and Yagi S. Effectiveness of pure laparoscopic right hepatectomy with a combined anterior and cranio-ventral approach for a giant hemangioma in a young woman. *Clin J Gastroenterol* 2025; 18: 492-498.
- [18] Oldani A, Cesana G, Uccelli M, Ciccarese F, Giorgi R, De Carli SM, Villa R and Olmi S. Surgical outcomes of rectal resection: our 10 years experience. *J Laparoendosc Adv Surg Tech A* 2019; 29: 820-825.
- [19] Wu B, Zhu JT, Lin HX, Dai YH, Lin TS, Huang AL, Chen YN, Li YW, Wang HB, Chen YF, Chen DH, Yu HD, You J and Hong QQ. Is intraperitoneal isoperistaltic side-to-side anastomosis a safe surgical procedure in radical colon cancer surgery. *World J Gastrointest Oncol* 2025; 17: 99124.
- [20] Yuan CD, Zhou BZ, Wang NY, Wan QQ and Hu ZZ. Evidence-based control of stress response on intraoperative physiological indexes and recovery of patients undergoing gastrointestinal surgery. *World J Gastroenterol* 2025; 31: 102331.
- [21] Chi P and Wang XJ. Historical evolution and ultimate goal of minimally invasive surgery for colorectal cancer. *Zhonghua Wei Chang Wai Ke Za Zhi* 2022; 25: 675-681.
- [22] Xu H, Peng G, Zeng X, Zhang P, Zhang A, Huang W, Guo Y and Wu T. Laparoscopic choledochal cyst excision and Roux-en-Y choledochojejunostomy in adults. *J Vis Exp* 2025.
- [23] Qi W, Zhou R, Qiu Q and Cui J. Relationship between core symptoms, function, and quality of life in colorectal cancer patients: a network analysis. *Qual Life Res* 2025; 34: 1723-1734.
- [24] Gleaves X, Tan JKH, Peh CH, Koh WL, Lau J, Lieske B, Cheong WK, Chan DKH and Tan KK. Risk factors for non-clinical prolonged lengths of stay after elective colorectal surgery. *Sci Rep* 2025; 15: 9184.
- [25] Zheng B, Wang Q, Wei M, Yue Y and Li X. Which site is better for prophylactic ileostomy after laparoscopic rectal cancer surgery? By the specimen extraction site or new site: a systematic review and meta-analysis. *Front Oncol* 2023; 13: 1116502.
- [26] Oudmaijer CAJ, Muller K, van Straalen E, Minnee RC, Kimenai DJAN, Reinders MEJ, van de Wetering J, IJzermans JNM and Terkivatan T. Long-term double-J stenting is superior to short-term single-J stenting in kidney transplantation. *PLoS One* 2025; 20: e0317991.
- [27] Sun Q, Wu H, Yao J, Wang W and Xu K. Different methods of Natural Orifice Specimen Extraction Surgery (NOSES) in laparoscopic anterior resection for rectal and low sigmoid colon cancer: a retrospective study. *World J Surg* 2025; 49: 1184-1192.
- [28] Rowe DG, O'Callaghan E, Yoo S, Dalton JC, Woo J, Owolo E, Dalton T, Johnson MO, Goodwin AN, Crowell KA, Kaplan S, Erickson MM and Goodwin CR. Perioperative trends in distress among cancer patients: a systematic review and meta-analysis. *Cancer Med* 2025; 14: e70456.

- [29] Chandramohan K, Mohandas M, Muralee M, Wagh MS, George PS, Geethakumari BS and Mayadevi L. Study of changes in quality of life after rectal cancer surgery using FACT-C questionnaire. *Indian J Surg Oncol* 2025; 16: 172-181.
- [30] McKigney N, Waldenstedt S, Gonzalez E, van Rees JM, Thaysen HV, Angenete E, Velikova G, Brown JM and Harji DP; LRRC-QoL Collaborators. Survivorship issues in long-term survivors of locally recurrent rectal cancer: a qualitative study. *Colorectal Dis* 2025; 27: e70051.
- [31] Lee TG, Ryoo SB, Oh HK, Cho YB, Kim CH, Lee JH, Ahn HM, Shin HR, Choi MJ, Jo MH, Kim DW and Kang SB. Longitudinal quality of life assessment after laparoscopic colorectal cancer surgery using the gastrointestinal quality of life index questionnaire: a multicentre prospective study. *Colorectal Dis* 2025; 27: e70060.
- [32] Li WW, Ding DB, Liang RP, Huang H, Zhao Y and Wei B. Completely laparoscopic radical treatment of distal gastric cancer through natural orifice specimen extraction surgery: past, present, and future. *Zhonghua Wei Chang Wai Ke Za Zhi* 2024; 27: 1172-1177.