Am J Cancer Res 2022;12(7):3148-3163
www.ajcr.us /ISSN:2156-6976/ajcr0140816

Original Article

Three-dimensional versus two-dimensional laparoscopic surgery for rectal cancer: better promote postoperative sexual and urinary function of a propensity-matched study

Fang-Hai Han[1*], Sheng-Ning Zhou[1*], Guang-Yu Zhong[1*], Jia-Nan Tan[1], Jing Huang[2], Han Gao[1], Zhi-Tao Chen[1], Jian-Kun Zhu[1], Shi-Lin Zhi[1], Jin-Tao Zeng[1], Bin Yang[1]

[1]*Department of Gastrointestinal Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China;* [2]*Thyroid and Parathyroid Surgery Center, West China Hospital of Sichuan University, Chengdu 610041, China.* [*]*Equal contributors.*

Received November 28, 2021; Accepted May 25, 2022; Epub July 15, 2022; Published July 30, 2022

Abstract: Laparoscopic total mesorectal excision (TME) with autonomic nerve preservation (ANP) is a common procedure for rectal cancer (RC), associated with a high prevalence of postoperative urogenital and anorectal dysfunctions. Compared to 2D laparoscopy, 3D laparoscopy provides better depth perception of the surgical field and hand-eye coordination to achieve better outcomes. We compared the performance of 2D and 3D laparoscopy on preserving urogenital and anorectal function in TME+ANP surgery for rectal cancer using propensity-score matching. Data were collected from consecutive male patients who underwent 3D or 2D laparoscopic TME+ANP for primary RC at our institution between March 2012 and December 2020. The primary outcome was sexual and urinary function 1 year after surgery. A total of 450 male patients were eligible. After 1:1 matching, 146 cases were included in each group for analysis. One year after surgery, the prevalence of sexual dysfunction (International Index of Erectile Function score <26) was 8.22% in the 3D laparoscopic group and 44.52% in the 2D laparoscopic group, respectively (P=0.000) and a significant difference in the incidence of urinary retention was observed (n=3 and 24, respectively (P=0.000)). Moreover, blood loss, operative time, duration of hospital stay, and the time to first flatus in the 3D laparoscopic group were significantly less than in the 2D laparoscopic group. In conclusion, 3D laparoscopic TME is associated with lower incidences of postoperative sexual and urinary dysfunction than 2D laparoscopic TME for rectal cancer in male patients.

Keywords: Rectal cancer, total mesorectal excision, laparoscopic, autonomic nerve preservation, sexual and urinary function

Introduction

Colorectal cancer (CRC) is well-established as the third most common cancer type worldwide [1-3], with an estimated 1.88 million new cases of primary CRC reported in 2020 [4]. In recent years, the overall incidence rate has exhibited a slow but steady increase in China, with around 380,000 new cases of colon cancer and 180,000 new cases of rectal cancer (RC) each year [5, 6]. Accordingly, CRC represents a global health challenge that harms public health.

Since its introduction by Heald et al. [7] in the 1980s, total mesorectal excision (TME) has become the mainstay of treatment for mid and low RCs since it improves survival and reduces the risk of local recurrence [8, 9]. Conventional surgery for RC is associated with the risk of autonomic nerve injury during dissection of the abdominopelvic cavity, including the superior hypogastric plexus (SHP), bilateral hypogastric nerves (HGNs), pelvic plexus (PP), and neurovascular bundles (NVBs), leading to sexual, urinary dysfunctions and anorectal dysfunction [10-12], which seriously affect patient quality of life.

In recent years, laparoscopic surgery for RC has gained increasing popularity given that it is technically feasible and oncologically safe [13-15]. The laparoscopic approach provides a magnified and well-illuminated image of the surgical field, thereby reducing the risk of injuries to autonomic nerves. However, much controversy surrounds the benefits of laparoscopy regarding sexual and urinary dysfunctions. Several studies claim no significant difference in postoperative sexual and urinary dysfunctions [16, 17], which may be attributed to the difference in accuracy between 3D and 2D laparoscopy not being emphasized. Compared with 2D laparoscopy, 3D laparoscopy provides a three-dimensional view and higher resolution of the surgical field. Many fine anatomical structures, such as fascia and pelvic autonomic nerve, can be identified in 3D laparoscopy but are challenging to find with 2D laparoscopy, given the lack of depth perception. C. A. Fleming et al. [18] identified favorable outcomes for urinary and erectile function in men who undergo robotic (3D) compared with conventional 2D laparoscopic surgery for rectal cancer. However, few studies have studied the differences in outcomes between 3D and 2D laparoscopy in postoperative urogenital and anorectal function.

Based on the anatomy of the abdominopelvic fascia and autonomic nervous system (ANS), along with the application of high-definition 3D laparoscopy, we compared the effect of 2D and 3D laparoscopy on preserving urogenital and anorectal function in TME+ANP surgery. Furthermore, we clarified the safety and feasibility of 3D laparoscopic TME+ANP by comparing its functional and oncological outcomes with patients that underwent conventional 2D surgery in a large, retrospective cohort study of male patients with RC using propensity-score matching.

Patients and methods

Ethical approval of the study protocol

The protocol for this retrospective study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital (Sun Yat-sen University, Guangzhou, China). All patients provided written informed consent before surgical procedures were carried out.

Inclusion criteria

The inclusion criteria were: (i) primary RC diagnosed as an adenocarcinoma by colonoscopy with pathological evidence; (ii) the lower margin of the tumor was within 12 cm of the anal verge; (iii) the clinical stage was T1-3N0-2M0; (iv) the preoperative International Index of Erectile Function (IIEF) score was 26-30, and International Prostate Symptom Score (IPSS) was 0-7; (v) the American Society of Anesthesiologists score was I-III; (vi) questionnaires were completed, and follow-up data were available.

Exclusion criteria

The exclusion criteria were: (i) multivisceral resection; (ii) retroperitoneal or pelvic surgery; (iii) lateral dissection of pelvic lymph nodes; (iv) conversion from laparoscopic to open surgery; (v) multiple CRCs; (vi) number of harvested lymph nodes <12; (vii) history of treatment for other malignancies; (viii) emergency surgery.

Data

Data from consecutive male patients with primary RC admitted to the Gastrointestinal Surgery Department of Sun Yat-sen Memorial Hospital from March 2012 to December 2020 with laparoscopic radical resection were retrospectively collected and analyzed. According to the different surgical methods, patients were divided into a conventional 2D laparoscopic TME+ANP group and a 3D laparoscopic TME+ANP group.

Neo-adjuvant chemoradiotherapy (CRT) was undertaken for patients with clinical T3+ and N+ stages. The patients received RT (50.4 Gy) plus capecitabine for 6 weeks, and surgery was carried out 4 weeks after CRT. Preoperative procedures (bowel preparation, intravenous injection of second-generation cephalosporins and metronidazole before incision) were carried out routinely in accordance with standard procedures. All patients underwent the same regimen of neoadjuvant chemoradiotherapy.

Surgical procedures

All surgical procedures were carried out by a single experienced surgeon with the same surgical team that performed more than 1,000 laparoscopic colorectal excisions. All procedures were in accordance with the principles of TME. The sequence of surgical steps for the 3D laparoscopic TME+ANP and 2D laparoscopic TME+ANP group was identical, except for the preservation of the abdominopelvic ANS.

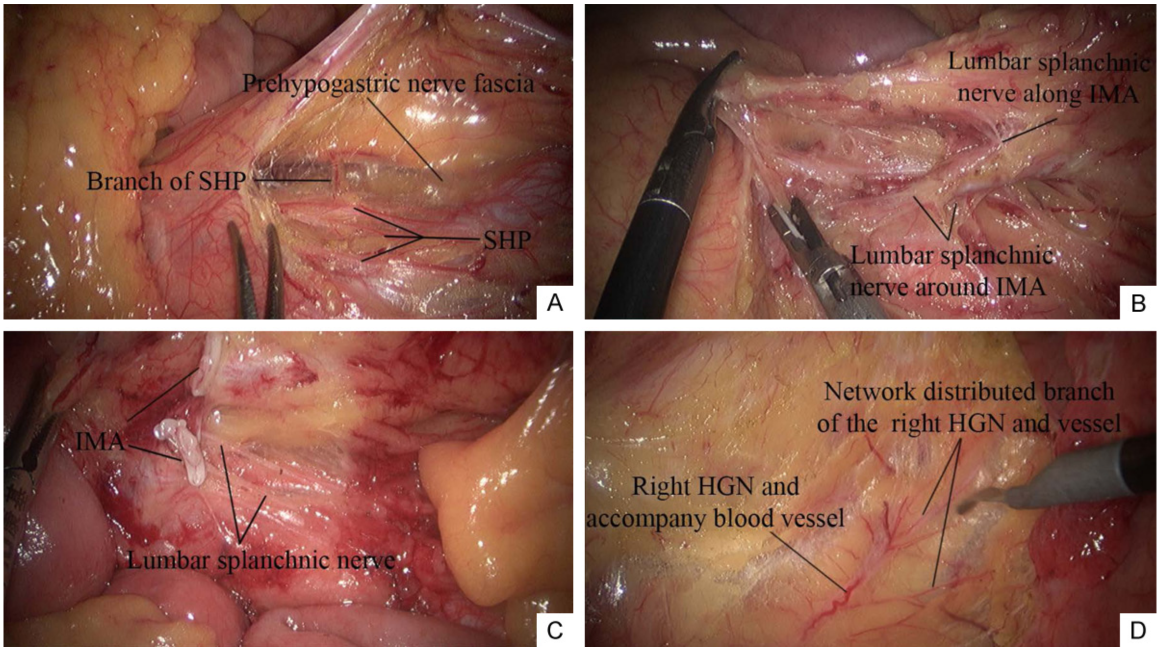

Figure 1. Preservation of the abdominal autonomic nervous system. A. The fascia of the prehypogastric nerve and the SHP and intermembranous nerve branches are preserved. B. Nerve branch surrounding the sympathetic trunk at the root of the IMA in a network-like manner, especially the left lumbar splanchnic nerve attached to the left side of the IMA. C. The root of the IMA is cut off, and the lumbar splanchnic nerve around the root of the IMA is preserved. The sympathetic nerve trunk accompanying the IMA is seen, and the vascular nerve sheath is resected along the IMA. D. Small blood vessels are visible along with the autonomic trunk and branches.

Aesculap Braun 3D laparoscopy was used in the 3D laparoscopic TME+ANP group, and Olympus 2D laparoscopy was used in the 2D laparoscopic TME+ANP group.

3D laparoscopic TME+ANP group

The patient was placed in a modified lithotomy position, and five laparoscopic ports were placed. A thorough examination of the abdominopelvic cavity was undertaken to rule out metastatic disease. A peritoneal incision was made at the level of the abdominal aortic bifurcation 2 cm above the intersection line between the mesocolon and the retroperitoneum. The SHP and its blood supply were carefully recorded (**Figure 1A**). The peritoneum was incised up to the origin of the inferior mesenteric artery (IMA). From the bottom to the top, we could see part of the sympathetic trunks wrapped around the root of the IMA in a network-shaped fashion, and the other part ran along with the IMA, forming the vascular nerve sheath (**Figure 1B**). We dissected the sigmoidal branches of the lumbar splanchnic nerves (especially the branches from the right lumbar splanchnic nerves) while preserving the pre-hypogastric nerve fascia (PHGNF) and HGN network. After skeletonization and IMA division, the left vascular nerve sheath running along the IMA was identified and divided (**Figure 1C**). Then, the surgical assistant grasped the distal end of the IMA and retracted it ventrally to extend the dissection plane between the mesocolon and PHGNF. We noted small blood vessels accompanying the trunk and branches of the autonomic nerve, supplying blood to nerve fibers (**Figure 1D**). The space between the sigmoid mesocolon and PHGNF was dissected laterally to the lateral wall of the sigmoid mesocolon. The left ureter and left gonadal vessels were underneath the PHGNF, which was smooth on both sides with no fat tissue. The direction of microvessels in the mesentery was different from that in the retroperitoneum. Subsequently, we placed a gauze in this space as a marker of the lateral boundary. The mesentery lateral to the sigmoid colon was dissected to allow complete mobilization.

After the rectum had been retracted cephalad and ventrally, we dissected the fascia of the rectum from the PHGNF, and the bilateral HGNs were visible. The left HGN gave rise to

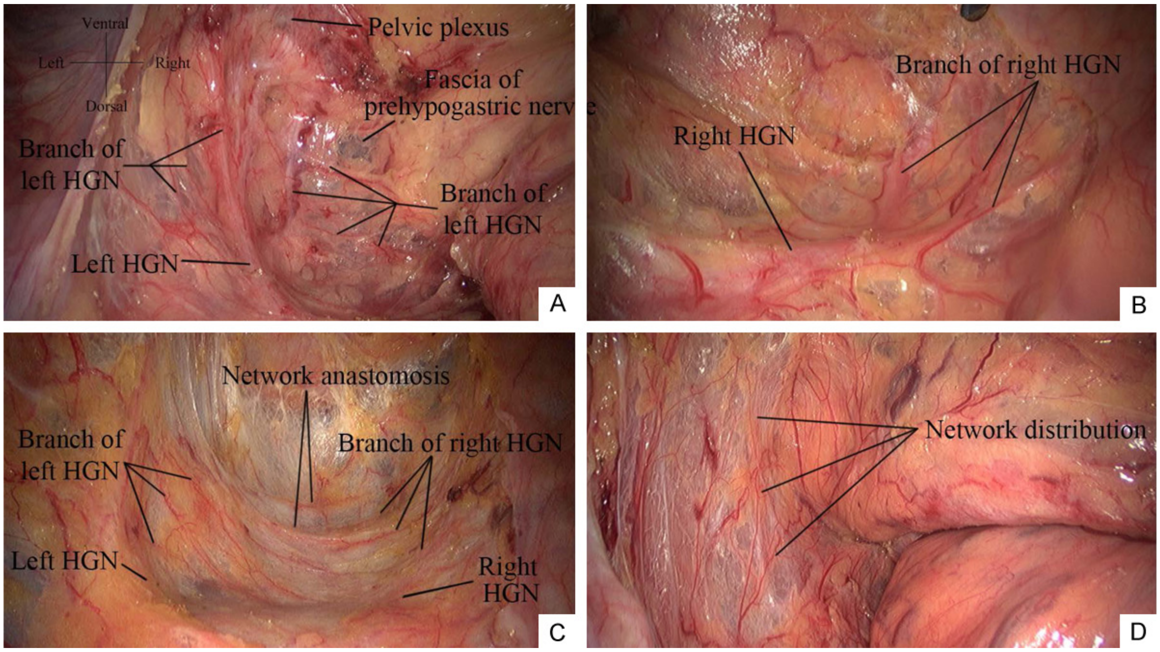

Figure 2. The left and right HGN give rise to small network-like nerve branches and anastomose with each other. A. Left HGN and pelvic plexus, small nerve branches to the pelvic sidewall, showing network-like anastomosis. B. Right HGN is divided into 4 trunks; each trunk emits small nerve branches to the pelvic sidewall that anastomose with each other. C. There are many small nerve branches between the left and right HGN, which exhibit a network-like anastomosis and travel in the fascia of the prehypogastric nerve. D. Small nerves in the fascia of the prehypogastric nerve of the left pelvic wall exhibit a network distribution and anastomose with each other. HGN: hypogastric nerve.

some small nerve branches in the pelvic wall to form a network-shaped communication (**Figure 2A**). In some cases, 3 to 5 main branches were issued from the HGN, while small branches from the HGN ran to the pelvic wall and mesorectum (**Figure 2B**). These small nerve branches on both sides communicated in a network-shaped fashion and each branch was accompanied by a small vessel (**Figure 2C**). On the left, small nerve branches within the PHGNF were distributed in a network-shaped fashion (**Figure 2D**).

After dissecting the anterolateral space and posterolateral space of the lateral ligament, we cauterized the small vessels in the lateral ligament (**Figure 3A**). Some nerve branches branched out from the PP, and vessels ran to the rectum under the lateral ligament (**Figure 3B**). We dissected the nerve branches to the rectum while preserving nerves to the seminal vesicle, prostate gland and corpus cavernosum. The NVBs were preserved lateral to the Denonviller's fascia (**Figure 3C**). When dissecting to the level of the levator ani, nerve branches running to the levator ani were preserved. At the anterior wall of the rectum, we dissected between the rectal fascia and Denonvillier's fascia to the inferior margin of the prostate gland and preserved small nerve branches running to the prostatic capsule. The dissection proceeded to the lateral space of the rectum, and the branches of HGNs and sacral nerves 2, 3 and 4 could be subsequently observed (S2, S3 and S4, respectively) (**Figure 3D**). Several small nerve branches within the pelvic fascia branched and communicated in a network-shaped fashion.

After low anterior resection of the rectum had been completed, the mesorectum was dissected ≥5 cm below the lower edge of the tumor. The rectum was transected using an endolinear stapler. An end-to-end colorectal anastomosis was made using standard double-stapling methods. A diverting ileostomy was necessary for neoadjuvant chemoradiotherapy (nCRT) patients.

2D laparoscopic TME+ANP group

Resection was conducted according to TME principles. The ANP method involved identifying and preserving the SHP, bilateral HGNs, PP, and NVBs as much as possible.

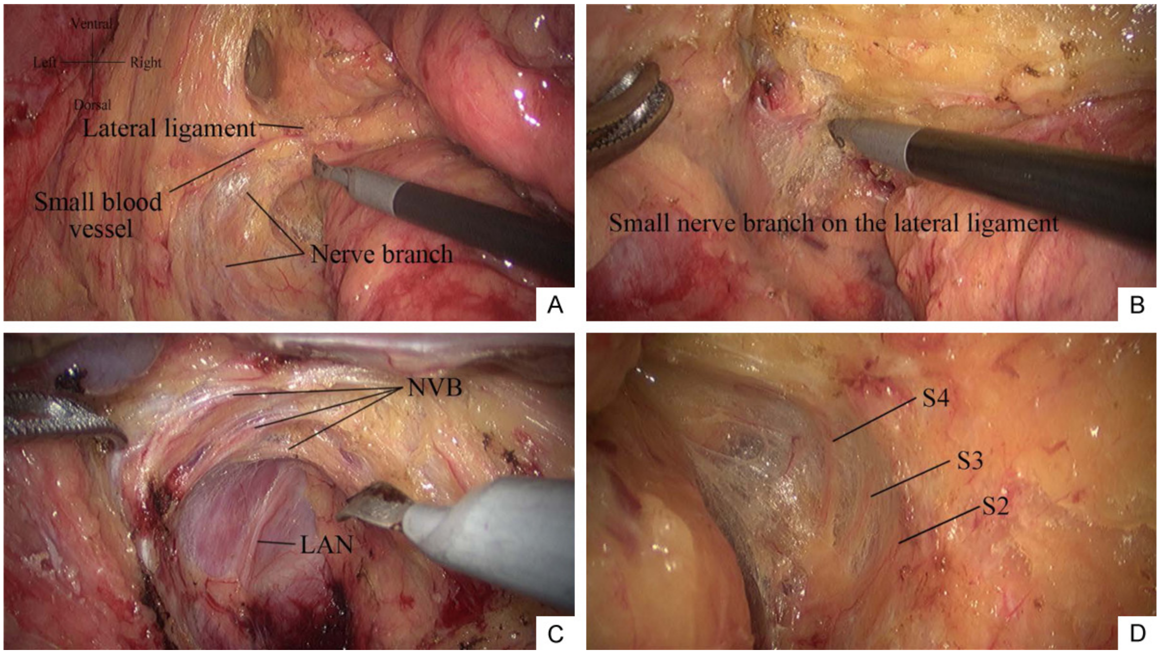

Figure 3. Small branching vessel and nerve branches from the pelvic plexus to the rectum. The NVB in the left pelvis and the left and right pelvic plexus emit nerves and branches to the levator ani muscle and the S2, S3, and S4 nerve branches. A. Small blood vessels and nerves in the left ligament are seen. The small nerve branches exhibit a network distribution in the pelvic sidewall behind the lateral ligament. B. Cutting the upper part of the lateral ligament showed the pelvic plexus nerve distribution to the small branches of the lower rectum. C. The NVB and pelvic plexus on the left side emit nerve branches distributed to the levator ani muscle. D. Pelvic splanchnic nerve S2, S3, S4. NVB: neurovascular bundle; LAN: levator ani nerve.

Postoperative specimens were assessed macrographically. TME quality and proximal and distal margins were evaluated, and lymph nodes were collected. TME quality was assessed by two experienced pathologists in accordance with the Quirke criteria [19]. The postoperative pathological staging (pTNM) was assessed according to the 8th edition of the American Joint Committee on Cancer (AJCC) Staging Manual.

Outcomes

The primary outcome of our study was the prevalence of sexual and urinary dysfunctions 12 months after surgery. The IIEF was used for evaluation of sexual function (preoperatively and at 3, 6 and 12 months after surgery) with a score of 26-30 defined as "normal", 22-25 as "mildly abnormal", 17-21 as "mild to moderately abnormal", 11-16 as "moderately abnormal" and 6-10 as "severely abnormal". The IPSS score, the maximum rate of urine flow (Q_{max}) and residual urine in the bladder were used to evaluate urinary function (preoperatively and at 3, 6 and 12 months after surgery). An IPSS score of 0-7 was defined as "mildly abnormal", 8-19 as "moderately abnormal" and 20-35 as "severely abnormal". The Q_{max} was measured with a urinometer (Siemens, Munish, Germany), and the mean value of the three tests was taken, with <15 mL/s indicating "abnormal urination". The residual urine in the bladder was quantified by ultrasound (General Electric, Boston, MA, USA), and the mean value was obtained from three measurements. Urine retention was defined as residual urine >50 mL [20].

The secondary outcomes were visibility of autonomic nerves, operative time, blood loss, TME extent, number of harvested lymph nodes, circumferential resection margin (CRM), course of postoperative recovery, morbidity, and 30-day mortality. The ANS (including the SHP; HGNs; inferior hypogastric plexus (IHP); pelvic splanchnic nerves (PSNs); PP; NVBs; nerves in the branches of the levator ani; sympathetic trunk at the IMA level) was observed intraoperatively by surgeons under laparoscopy and documented by photographs. Nerve visibility was evaluated by two experienced colorectal surgeons independently. If their preliminary judgments were different, the visibility of ANS was finally determined through consultation and reviewing the surgical video. The Kappa value was used to evaluate the interobserver differences.

Statistical analyses

Statistical analyses were carried out using SPSS 21.0 (IBM, Armonk, NY, USA). Two-sided t-tests were used for continuous variables. The chi-square or Fisher's exact test was used to compare categorical variables. IIEF and IPSS differences within each group were assessed by the paired-sample t-test. IIEF and IPSS differences at any time point between the two groups were compared using two-sided t-tests. A *P*-value <0.05 was statistically significant. Logistic regression was used for univariate and multivariate analyses, and variables with a *P*-value <0.10 during univariate analysis were incorporated into multivariate analysis.

To overcome selection bias between two groups, propensity score matching was conducted using R v2.10.0.15 (R, Vienna, Austria). One-to-one matching was done using the nearest-neighbor matching method with a caliper of 0.2. Patients with extreme propensity scores were excluded. Differences between the matched groups were further analyzed to assess sexual function and urinary function.

Results

Study cohort

938 consecutive patients with primary RC in the Department of Gastrointestinal Surgery in Sun Yat-sen Memorial Hospital underwent laparoscopic TME from March 2012 to December 2020. 516 male patients that met the inclusion criteria were initially included. 66 cases were then excluded based on the exclusion criteria. Finally, a total of 450 cases (304 in the 2D laparoscopic TME+ANP group and 146 in the 3D laparoscopic TME+ANP group) were included for statistical analysis. Propensity-score matching was conducted to adjust for the following parameters age, clinical T and N stages, preoperative erectile function according to the IIEF, and preoperative IPSS score. After 1:1 matching, 146 cases in the 2D laparoscopic TME+ANP group were chosen for further analyses (Figure S1).

Patient characteristics

The baseline data of patients at clinical are shown in **Table 1**. Significant differences in age, clinical stage and clinical N (cN) stage were initially found between the two groups. After propensity score matching, patient characteristics in the two groups were well-balanced.

Perioperative outcomes and histopathological characteristics

The perioperative outcomes and histopathological characteristics of the two groups are shown in **Table 2A**. Blood loss and operative time were significantly less in the 3D laparoscopic TME+ANP group compared with the 2D laparoscopic TME+ANP group (35.51±16.31 vs. 45.79±23.53 mL, P=0.000; 176.98±37.19 vs. 186.27±42.42 min, P=0.048), whereas no significant differences in the proportion of diverting ileostomies, distance from the anastomosis to the anus, and TME quality were found. Besides, there was no significant difference in the number of harvested lymph nodes, positive lymph nodes, and the pTNM stage between the two groups.

As shown in **Table 2B**, there was no significant difference in the prevalence of postoperative complications between the two groups. However, the duration of hospital stay (8.86±2.46 vs. 9.83±3.00 days, P=0.0028) and the time to first flatus (2.87±0.86 vs. 3.36±0.97 days, P=0.000) in the 3D laparoscopic TME+ANP group was significantly shorter than the 2D laparoscopic TME+ANP group.

Assessment of sexual function and urinary function

A kappa value of 0.93 was obtained, suggesting that the visibility of the ANS evaluated by two surgeons was highly consistent (Table S1). Details on the visibility of each ANS structure intraoperatively are shown in **Table 3A**. No significant difference was found in the visibility of the SHP and HGNs between the two groups. Significant differences in the visibility of the IHP, PSN, PP, NVB, branch of the levator ani and sympathetic trunks at the IMA level were found between the 3D and 2D laparoscopic TME+ANP group.

The sexual and urinary functions of patients preoperatively and 3, 6, and 12 months after

Table 1. Patient demographics and clinical characteristics

	Before matching			After matching		
	3D group (n=146)	2D group (n=304)	*P*-value	3D group (n=146)	2D group (n=146)	*P*-value
Age (years)	56.54±9.29	58.52±8.19	0.023*	56.54±9.29	57.84±8.41	0.215
BMI (kg/m^2)	22.69±3.45	23.13±3.09	0.172	22.69±3.45	23.21±3.12	0.174
ASA score			0.576			0.616
1	93 (63.70%)	181 (59.54%)		93 (63.70%)	93 (63.70%)	
2	44 (30.14%)	97 (31.91%)		44 (30.14%)	41 (28.08%)	
3	9 (6.16%)	26 (8.55%)		9 (6.16%)	12 (8.22%)	
Tumor distance from AV			0.099			0.240
low ≤8 cm	87 (59.59%)	156 (51.32%)		87 (59.59%)	77 (52.74%)	
Middle 8-12 cm	59 (40.41%)	148 (48.68%)		59 (40.41%)	69 (47.26%)	
Tumor size (cm)	4.12±1.50	4.21±1.37	0.525	4.12±1.50	4.21±1.37	0.592
Preoperative CEA (ng/ml)			0.840			0.100
≤5.0	72 (49.32%)	153 (50.33%)		72 (49.32%)	86 (58.90%)	
>5.0	74 (50.68%)	151 (49.67%)		74 (50.68%)	60 (41.10%)	
Clinical stage			0.023*			0.136
I	81 (55.48%)	130 (42.76%)		81 (55.48%)	64 (43.84%)	
II	22 (15.07%)	46 (15.13%)		22 (15.07%)	29 (19.86%)	
III	43 (29.45%)	128 (42.11%)		43 (29.45%)	53 (36.30%)	
cT stage			0.197			0.078
1	22 (15.07%)	39 (12.83%)		22 (15.07%)	19 (13.01%)	
2	68 (46.58%)	121 (39.80%)		68 (46.58%)	52 (35.62%)	
3	56 (38.35%)	144 (47.37%)		56 (38.35%)	75 (51.37%)	
cN stage			0.029*			0.180
0	103 (70.55%)	176 (57.89%)		103 (70.55%)	90 (61.64%)	
1	24 (16.44%)	64 (21.05%)		24 (16.44%)	26 (17.81%)	
2	19 (13.01%)	64 (21.05%)		19 (13.01%)	30 (20.55%)	
nCRT	65 (41.55%)	149 (49.01%)	0.372	65 (41.55%)	75 (51.37%)	0.241
IPSS score	1.88±2.09	2.27±2.11	0.070	1.88±2.09	1.73±1.81	0.510
IIEF Erectile score	27.95±1.64	27.69±1.55	0.072	27.97±1.53	27.97±1.55	1.000

Data presented as absolute number of patients (%) or mean ± standard deviation. ASA: American Society of Anesthesiologist's classification; BMI: body mass index; nCRT: neo-adjuvant chemoradiatherapy; AV: anal verge; CEA: carcinoembryonic antigen; IPSS: international prostate symptom score; IIEF: international index of erectile function. *, P<0.05.

surgery are shown in **Table 3B**. No significant difference was found between the two groups regarding the preoperative erectile function score (IIEF). However, scores obtained in the 3D laparoscopic TME+ANP group were significantly higher than in the 2D laparoscopic TME+ANP group at 3, 6 and 12 months after surgery, which indicated better postoperative sexual function and faster recovery in the 3D group compared to the 2D group. The IIEF score decreased significantly immediately after the surgical procedure and recovered slowly (**Figure 4**). Similar findings were noted in scores for orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction within the IIEF. One year after surgery, the prevalence of sexual dysfunction (erectile-function score <26) was 8.22% in the 3D laparoscopic TME+ANP group and 44.52% in the 2D laparoscopic TME+ANP group, respectively (P=0.000). The trend for the IPSS score was identical to sexual-function scores. Three patients in the 3D laparoscopic TME+ANP group and twenty-four cases in the 2D laparoscopic TME+ANP group developed urinary retention and were diagnosed with residual urine in the bladder 1 year after surgery, respectively (P=0.000).

Our results showed that the IIEF score in the 3D laparoscopic group was significantly higher than in the 2D laparoscopic group at 12 mon-

Table 2. Perioperative results and short-term outcomes

	3D group (n=146)	2D group (n=146)	*P*-value
A. Perioperative results and pathological findings			
Surgical procedure			0.386
LAR	79 (54.11%)	88 (60.27%)	
uLAR	47 (32.19%)	41 (28.08%)	
Parks	9 (6.16%)	8 (5.48%)	
ISR	11 (7.53%)	9 (6.16%)	
diverting ileostomy	46 (31.51%)	53 (36.30%)	0.460
Anastomotic height (cm)	4.63±1.59	4.90±1.49	0.135
Operative time (min)	176.98±37.19	186.27±42.42	0.048*
Blood loss (ml)	35.51±16.31	45.79±23.53	0.000**
Degree of TME			0.498
complete	127 (86.99%)	123 (84.25%)	
near-complete	15 (10.27%)	17 (11.64%)	
incomplete	4 (2.74%)	6 (4.11%)	
Pathological Stage			0.968
I	78 (53.42%)	78 (53.42%)	
II	25 (17.12%)	24 (16.44%)	
III	43 (29.45%)	44 (30.14%)	
Pathological T category			0.850
1	20 (13.70%)	23 (15.75%)	
2	69 (47.26%)	66 (45.21%)	
3	52 (35.62%)	53 (36.30%)	
4	5 (3.42%)	4 (2.74%)	
Pathological N category			0.747
0	103 (70.4%)	102 (70.4%)	
1	24 (17.6%)	21 (15.7%)	
2	19 (11.9%)	23 (13.8%)	
Harvested lymph node	18.23±6.31	18.21±4.86	0.983
Positive lymph node	1.84±4.73	1.97±3.88	0.797
Histological type			0.998
Poorly differentiated	42 (28.77%)	43 (29.45%)	
Well-moderately differentiated	104 (71.23%)	103 (70.55%)	
Adjuvant chemotherapy	57 (39.04%)	51 (34.93%)	0.793
Positive lower margin	1 (0.68%)	2 (1.37%)	0.800
positive CRM	3 (2.05%)	3 (2.05%)	1.000
B. Short-term outcomes			
Length of stay (days)	8.86±2.46	9.83±3.00	0.003**
Time to first flatus (days)	2.87±0.86	3.36±0.97	0.000**
Duration of catheter (days)	4.85+1.28	5.16+1.49	0.059
Morbidity	47 (28.93%)	57 (32.08%)	0.371
Major bleeding	1 (0.68%)	1 (0.68%)	
Intra-abdominal abscess	9 (6.16%)	12 (8.22%)	
Ileus	8 (5.48%)	7 (4.79%)	
Anastomotic leakage	7 (4.79%)	11 (7.53%)	
Cardiac problem	1 (0.68%)	3 (3.05%)	
Wound infection	6 (4.11%)	9 (6.16%)	
Lung infection	12 (8.22%)	12 (8.22%)	
Deep venous thrombosis	3 (2.05%)	1 (0.68%)	
30-days mortality	0 (0.00%)	1 (0.6%)	1.000

Data presented as the absolute number of patients (%) or mean ± standard deviation. LAR: Low anterior resection; uLAR: ultra-low anterior resection; ISR: Intersphincteric resection; TME: total mesorectal excision; CRM: circumferential resection margin. *, P<0.05; **, P<0.01.

Table 3. Sexual and urinary function

A. Visibility of autonomic nerves intraoperatively

	3D group (n=146)	2D group (n=146)	*P*-value
SHP	123 (84.25%)	114 (78.08%)	0.261
HGN	138 (94.52%)	136 (93.15%)	0.912
IHP	114 (78.08%)	75 (51.37%)	0.000**
PSN	62 (42.47%)	28 (19.18%)	0.000**
PP	107 (73.29%)	73 (50.00%)	0.000**
NVB	103 (70.55%)	66 (45.21%)	0.000**
Branch of levator ani	46 (31.51%)	16 (10.96%)	0.000**
Sympathic trunk at the IMA level	123 (84.25%)	87 (59.59%)	0.000**

B. Postoperative sexual and urinary function

	Preoperative	3 month	6 month	1 year	*P*-value[A]
IIEF score (3D group)					
Erectile function	27.97±1.53	20.75±3.67	25.27±3.12	26.99±2.47	0.000**
Orgasmic function	9.14±0.85	6.96±1.46	8.21±1.41	8.87±1.10	0.018*
Sexual desire	9.13±0.72	6.81±1.52	8.08±1.30	8.84±1.13	0.008**
Intercourse satisfaction	13.62±1.19	10.42±2.06	12.39±1.93	13.26±1.78	0.045*
Overall satisfaction	9.04±0.89	6.80±1.47	8.17±1.37	8.69±1.17	0.004**
Total	68.90±2.82	51.73±5.67	62.12±5.27	66.64±4.99	0.000**
IIEF score (2D group)					
Erectile function	27.97±1.55	18.43±4.00	20.47±3.96	25.05±3.12	0.000**
Orgasmic function	9.16±0.71	6.25±1.77	6.90±1.76	8.19±1.62	0.000**
Sexual desire	9.14±0.75	6.12±1.66	6.90±1.62	8.16±1.50	0.000**
Intercourse satisfaction	13.71±1.09	9.48±2.31	10.79±2.33	12.95±1.64	0.000**
Overall satisfaction	9.08±0.74	6.29±1.76	6.98±1.52	8.35±1.37	0.000**
Total	68.90±2.39	46.58±5.96	52.03±6.07	62.71±5.68	0.000**
IPSS score (3D group)	1.88±2.09	2.25±2.59	2.07±2.25	2.00±2.14	0.639
IPSS score (2D group)	1.73±1.81	2.28±2.55	2.13±2.31	2.22±2.30	0.138
Residual urine (3D group)					1.000
≤50 ml	143 (97.95%)	111 (76.03%)	139 (95.21%)	143 (97.95%)	
>50 ml	3 (2.05%)	35 (23.97%)	7 (4.79%)	3 (2.05%)	
Residual urine (2D group)					0.000**
≤50 ml	144 (98.63%)	107 (73.29%)	117 (80.14%)	122 (83.56%)	
>50 ml	2 (1.37%)	39 (26.71%)	29 (19.86%)	24 (16.44%)	
Qmax (3D group)					1.000
≥15 ml/s	141 (99.4%)	146 (91.8%)	156 (98.1%)	157 (98.7%)	
<15 ml/s	5 (0.6%)	13 (8.2%)	3 (1.9%)	2 (1.3%)	
Qmax (2D group)					0.000**
>15 ml/s	141 (96.58%)	112 (76.71%)	131 (89.73%)	132 (90.41%)	
<15 ml/s	5 (3.42%)	34 (23.29%)	15 (10.27%)	14 (9.59%)	

SHP: superior hypogastric plexus; IHP: inferior hypogastric plexus; HGN: hypogastric nerve; PSN: pelvic splanchnic nerves; PP: pelvic plexus; NVB: neurovascular bundle; IMA: inferior mesenteric artery. [A]Comparision between 1-year after the operation and preoperation by paired-sample t-test; *, P<0.05; **, P<0.01.

ths after surgery. Further subgroup analysis of clinical characteristics showed no significant difference in IIEF score between the two groups in patients >65 years of age and patients with anastomotic leakage (**Table 4**). In other subgroup analyses, IIEF scores in the 3D laparoscopic group were significantly higher than in the 2D laparoscopic group 12 months after surgery. Univariate and multivariate analyses were then performed to identify factors influ-

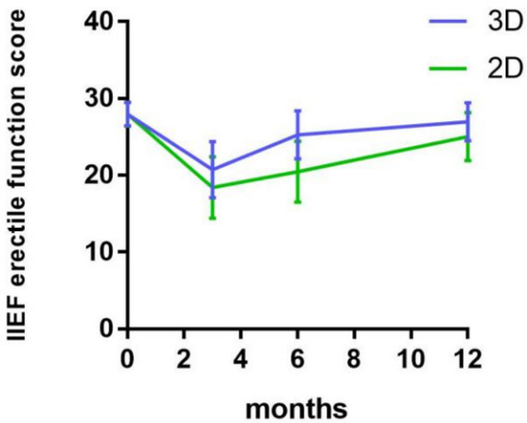

Figure 4. Changes in IIEF erectile function score in 3D laparoscopic group and 2D laparoscopic group (Charts with error bars corresponding to the 95% CI).

encing the IIEF score 12 months after surgery. The logistic regression analysis identified 3D laparoscopy and age as independent factors that could increase the postoperative IIEF score of patients who underwent TME (**Table 5**).

Assessment of anorectal function

Data on the anorectal function of patients preoperatively and at 3, 6, and 12 months after surgery are shown in **Table 6**. No significant difference was found between the two groups in the preoperative and 3-month Wexner scores. 6 months and one year after surgery, the Wexner score in the 3D laparoscopic TME+ANP group was significantly lower than in the 2D laparoscopic TME+ANP group ($P<0.05$).

Discussion

TME with autonomic-nerve preservation (ANP) has become the standard surgical procedure for RC. However, there are no generally accepted surgical indications or standard surgical procedures regarding ANP for patients with RC, and criteria for visual assessment of ANP are lacking, making it challenging to guarantee the efficacy of ANP. Quality of life after surgery for RC should be regarded as an equally essential indicator in addition to traditional outcome measures, as the overall survival rate of patients with rectal cancer has improved.

Over the years, significant inroads have been achieved in surgical methods and surgical equipment, leading to improved outcomes of surgical treatment of RC. Most importantly, Heald and colleagues [9, 21] proposed TME to change the surgical principles of RC. The significance of this surgical approach lies in the introduction of the concept of mesentery and the recognition that metastases are primarily within the mesentery. Total mesorectal excision is accomplished by sharp dissection along the holy plane. However, in the Heald era, TME for rectal cancer was mainly performed through traditional open surgery; accordingly, it was challenging to complete the entire operation under direct vision. Much confusion surrounds current understanding of the course of the pelvic autonomic nerve at the fascia level.

The fascia structure of the ANS is reportedly more complex than previously thought [22]. Studies on the layer distribution of the ANS have yielded inconsistent findings. Some scholars have suggested that autonomic nerves run in the adipose tissue between the fascia, in the fascia propria of the rectum, or behind the pelvic parietal fascia. Kinugasa and colleagues [22, 23] provided histological evidence of the PHGNF covering the bilateral HGNs and the PP and proposed the concept of a "urogenital-hypogastric sheath". PHGNF preservation is important for TME+ANP because the accompanying vessels and small communicating nerve branches run underneath it. Consistent with 3D magnetic resonance imaging (MRI) of pelvic ANS in anatomic studies of cadavers, we found that the pelvic ANS shows a network distribution.

The progress achieved in surgical equipment has paved the road for innovation and optimization of surgical concepts. The invention and clinical application of 3D laparoscopy optimize the characteristics of flat display and poor resolution of 2D laparoscopy [24]. Importantly, a high-definition surgical field allows visualization of many anatomical structures, such as the fascial layers and fine nerves, that were not previously observed during surgery and enhances the accuracy of surgical manipulation. Indeed, the three-dimensional presentation and high resolution facilitate nerve protection when performing TME in the narrow pelvic cavity. Based on the structure of the fascia during the 3D laparoscopic TME operation and

Table 4. Subgroup analysis of IIEF erectile function score

Factor	IIEF erectile function score		
	3D	2D	*P*-value
Age (year)			
≤65	27.41±1.68	25.20±2.75	0.000**
>65	24.74±4.30	24.43±4.36	0.800
BMI (kg/m^2)			
<24	27.01±2.38	24.95±3.24	0.000**
≥24	26.94±2.66	25.20±2.95	0.002**
Tumor distance from AV			
low ≤8 cm	27.01±2.62	24.74±2.88	0.000**
Middle 8-12 cm	26.95±2.27	25.41±3.35	0.003**
Tumor size (cm)			
<4	26.69±3.41	25.02±3.21	0.009**
≥4	27.18±1.58	25.08±3.08	0.000**
nCRT			
N	27.14±2.13	25.14±3.23	0.000**
Y	26.80±2.85	24.97±3.03	0.000**
Anastomotic height (cm)			
<6 cm	26.95±2.59	24.66±3.25	0.000**
≥6 cm	27.06±2.27	25.78±2.74	0.012*
Diverting ileostomy			
N	26.89±2.39	25.15±3.18	0.000**
Y	27.20±2.66	24.89±3.03	0.000**
Degree of TME			
Complete	26.90±2.57	25.08±2.93	0.000**
Not-complete	27.58±1.68	24.91±4.04	0.011*
Anastomotic leakage			
N	26.96±2.52	24.99±3.13	0.000**
Y	27.43±1.27	25.91±2.91	0.210
Clinical stage			
I	27.14±2.13	25.25±3.25	0.000**
II+III	26.80±2.85	24.90±3.02	0.000**

Data presented as absolute number of patients (%) or mean ± standard deviation. BMI: body mass index; nCRT: neo-adjuvant chemoradiatherapy; AV: anal verge; IIEF: international index of erectile function. *, P<0.05; **, P<0.01.

anatomic research of the abdominopelvic ANS, we propose a new surgical technique under 3D laparoscopic surgery called TME+network-ANP, which could be an essential milestone for RC surgery. Our study elicited five main findings. First, we raised a hitherto undocumented concept of network-ANP in 3D laparoscopic TME for RC, and the key points of the surgical procedure were described in detail. Moreover, we found that preserving the main trunk of the abdominopelvic ANS and nerve branches, small communicating branches, NVBs, and the nerve branches distributed to the levator ani is essential to optimally preserve ANS integrity. Besides, the blood supply of the ANS must be maintained to prevent ischemic injury to the nervous system after surgery. In addition, the PHGNF covers the pelvic ANS. After the PHGNF was dissected from the rectal fascia, the pelvic ANS could be preserved completely. Finally, propensity-score matching was performed to eliminate the influence of preoperative variables, which could affect postoperative sexual function and urinary function.

Complete preservation of the pelvic ANS, including the sympathetic trunks around IMA, bilateral HGNs, PSNs, PP, NVBs, nerve branches innervating the levator ani, and small communicating branches, is vital for preserving sexual and urinary function and the defecation reflex. Damage to any of these can cause urination and sexual dysfunction. However, injuries may be difficult to avoid due to individual variations of ANS in the 2D laparoscopy TME group. Importantly, many tiny nerve structures can be visualized under 3D laparoscopy. It is well-established that HGN branches are extremely complex due to the heterogeneity in branch types and sizes. Moreover, S2, S3 and S4 give off small branches that communicate with each other, with the communicating branches exhibiting a network distribution. The nerve branches of NVBs communicate in a network manner and innervate the seminal vesicle, prostate gland, neck of the prostate gland, cavernous body of the penis, and the lower rectum. Anatomical variations of the pelvic ANS have been found in cadaveric anatomy studies similar to those observed in our clinical practice [25]. Difficulties in nerve identification can cause nerve injury if the patient is obese, has a narrow or deep pelvis, bleeds during surgery, or with poor surgical field exposure. Small nerve branches and their accompanying vessels are difficult to identify and preserve when carrying out 2D laparoscopic TME+ANP since they are not visible due to the low-definition images. During 3D laparoscopy TME+ANP surgery, the ANS branches and

Table 5. Variables of IIEF erectile function score according to logistics regression

Variable	Univariate		Multivariate	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	0.95 (0.92-0.98)	0.000**	0.95 (0.91-0.98)	0.0048**
BMI	0.98 (0.91-1.07)	0.70		
Laparoscopic approach	0.11 (0.06-0.22)	0.000**	0.12 (0.06-0.23)	0.000**
nCRT	0.80 (0.48-1.35)	0.41	--	--
AV distance	0.99 (0.86-1.13)	0.84	--	--
cT	0.63 (0.42-0.93)	0.022*	0.62 (0.33-1.17)	0.14
cN	0.86 (0.62-1.20)	0.39	--	--
cTNM	0.77 (0.58-1.03)	0.077	1.07 (0.66-1.73)	0.79
Anastomotic height	1.06 (0.90-1.26)	0.47	--	--
Tumor size	1.03 (0.86-1.23)	0.77	--	--
Diverting ileostomy	0.93 (0.54-1.61)	0.80	--	--
Anastomic leakage	3.02 (0.68-13.43)	0.15	--	--
Bleed	0.99 (0.98-1.00)	0.025*	1.00 (0.99-1.01)	0.89

BMI: body mass index; nCRT: neo-adjuvant chemoradiatherapy; AV: anal verge; IIEF: international index of erectile function. *, P<0.05; **, P<0.01.

Table 6. Perioperative anorectal function

	Preoperative	3 month	6 month	1 year	*P*-value
Wexner score					0.000**
3D group	3.43±1.67	11.17±3.23	9.07±2.37	7.03±2.37	
2D group	3.51±1.43	11.42±3.05	10.07±2.44	8.08±2.20	

Data presented as absolute number of patients (%) or mean ± standard deviation. **, P<0.01.

accompanying vessels surrounding the remnant rectum and mesorectum were preserved, including the nerve branches from the PP to the levator ani. The network-ANP surgery was successfully conducted based on knowledge of the pelvic anatomy, 3D MRI imaging and our intraoperative observations.

Overall, our findings substantiate that preserving ANS under direct vision is the most reliable approach. Current evidence suggests that ANS visibility intraoperatively is related to sexual and urinary dysfunctions [26]. Kauff and colleagues reported a significant difference in the prevalence of urinary dysfunction with (2.1-22.4%) and without (22.4-79.1%) visibility of the ANS [27]. According to videos of surgical procedures, postoperative sexual and urinary dysfunctions are often caused by an unclear surgical field, which leads to injuries to the abdominopelvic ANS [28]. Questionnaires among 368 surgeons of the European Society of Endoscopic Surgery about laparoscopic TME for RC [29] reported different degrees of visibility for ANS structures, including the SHP (57.6%), IHP (43.5%), HGNs (81.2%), NVBs (31.8%), PSNs (12.9%) and the sympathetic trunk at the IMA level (34.1%). In the present study, 3D laparoscopy TME+ANP could improve ANS visibility. In the 3D laparoscopy TME+ANP group, the visibility of ANS structures, including SHP, IHP, HGNs, NVBs, PSNs, the sympathetic trunk around the IMA root and branches from the PP to levator ani was 84.25%, 78.08%, 94.52%, 70.55%, 42.47%, 84.25% and 31.51%, respectively. According to our experience, using high-definition 3D laparoscopy, dissecting along the correct fascia space, keeping the surgical field clear, prompt hemostasis of minor bleeding, and clear exposure of the surgical field by assistants, are essential to achieve good surgical outcomes. Each anatomic marker of the ANS should be identified carefully in a magnified view for recognition and protection of the PP, NVBs and PSNs.

It is generally accepted that there are two surgical-dissection planes along the posterior and lateral sides of the rectum. The inner plane is between the fascia propria of the rectum and PHGNF. The outer plane is between the PHGNF and parietal fascia of the pelvic cavity. Given that there is no precise dissection plane during conventional TME+ANP surgery, complete preservation of the nerve trunks, small branches and accompanying blood vessels of the pelvic ANS is difficult. Compared with 2D laparoscopy TME+ANP, the prevalence of sexual and urinary dysfunctions was significantly lower in the 3D laparoscopy TME+ANP group. Further subgroup analysis of clinical characteristics showed no significant difference in IIEF score between the two groups in patients >65 years of age and patients with anastomotic leakage. However, this finding might be due to the low number of cases of anastomotic leakage. Importantly, it should be borne in mind that 3D laparoscopy may not improve sexual function in patients older than 65 at 12 months after surgery. A logistic regression analysis identified 3D laparoscopy and age as independent factors associated with increased postoperative IIEF scores in patients who underwent TME. Our results suggest that in patients with rectal cancer at age ≤65, 3D laparoscopy TME+ANP can improve postoperative sexual function. Nevertheless, the prevalence of sexual dysfunction in the 3D laparoscopy TME+ANP group was 8.22%, which may be attributed to the following reasons. First of all, high ligation of the IMA was carried out in all patients. Consistently, Mari et al. reported that the prevalence of sexual dysfunction 9 months after surgery for RC in a high-ligation group was significantly higher than in the low-ligation group. Moreover, neoadjuvant CRT and adjuvant chemotherapy are well-established to exert certain effects on postoperative sexual and urinary functions of patients with RC [30]. After neoadjuvant radiotherapy and chemotherapy, tissue edema, thickening of the fascia, and widening of the intermembrane space can occur. The separation in the intermembranous space under 3D laparoscopy can reduce bleeding and preserve PHGNF integrity to improve network retention after ANP. Last but not least, complete preservation of NVBs anatomically and technically is challenging [31], especially if the tumor is on the anterior wall of the lower rectum. At present, the anatomy and function of NVBs remain poorly understood. Kiyoshima and colleagues [32] reported that NVB formation in the NVB region was present in only 52% of patients, and intraoperative blood loss was related to postoperative sexual and urinary dysfunctions. The prevalence of urinary dysfunction was increased with more intraoperative blood loss during surgery of lower RC [33]. In our study, the volume of blood loss in the 3D laparoscopy TME+ANP group and 2D laparoscopy group was 35.51±16.31 and 45.79±23.53 mL, respectively. Importantly, accurate dissection of the plane between the fascia propria of the rectum and the PHGNF led to less blood loss, reduced hospital stay, and lower incidence of urogenital and anorectal dysfunctions. The high definition of the surgical field under 3D laparoscopy and less blood loss also shortened the operative time.

Importantly, the extent of radical resection was not compromised in the 3D laparoscopy TME+ANP group. No significant differences in the total number of harvested lymph nodes, pathologically positive lymph nodes, the integrity of the specimen after TME, positive CRM, or distal resection margin were found between groups.

The application of 3D laparoscopy TME+ANP surgery can preserve the main trunk and branches of the ANS and maintain the blood supply of nerves, especially for the PP, PSNs, NVBs, the nerves of the levator ani and their small branches, which can reduce the prevalence of postoperative urogenital and anorectal dysfunctions and improve the quality of life of RC patients.

The main limitation of our study is that this is a single-center retrospective study, and unavoidable biases may have affected our findings to a certain extent. Evidence is lacking from large, randomized clinical trials comparing sexual and urinary functions after laparoscopic and open resection of RC. Long-term outcomes require further follow-up and analysis, ideally in a multiple-center randomized control trial. Given that only male patients were investigated, the conclusions of this study cannot be generalized to all rectal cancer patients.

Conclusions

3D laparoscopic TME can better promote postoperative sexual and urinary function than 2D laparoscopic TME in male patients with rectal cancer.

Acknowledgements

This study was funded by the Basic Research Plan of Guangzhou Science and Technology Plan Project (Item Number: 202002020082).

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Fang-Hai Han and Bin Yang, Department of Gastrointestinal Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510000, Guangdong, China. E-mail: fh_han@163.com (FHH); yyzsu@163.com (BY)

References

[1] Siegel RL, Miller KD and Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019; 69: 7-34.

[2] Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, Dicker DJ, Chimed-Orchir O, Dandona R, Dandona L, Fleming T, Forouzanfar MH, Hancock J, Hay RJ, Hunter-Merrill R, Huynh C, Hosgood HD, Johnson CO, Jonas JB, Khubchandani J, Kumar GA, Kutz M, Lan Q, Larson HJ, Liang X, Lim SS, Lopez AD, MacIntyre MF, Marczak L, Marquez N, Mokdad AH, Pinho C, Pourmalek F, Salomon JA, Sanabria JR, Sandar L, Sartorius B, Schwartz SM, Shackelford KA, Shibuya K, Stanaway J, Steiner C, Sun J, Takahashi K, Vollset SE, Vos T, Wagner JA, Wang H, Westerman R, Zeeb H, Zoeckler L, Abd-Allah F, Ahmed MB, Alabed S, Alam NK, Aldhahri SF, Alem G, Alemayohu MA, Ali R, Al-Raddadi R, Amare A, Amoako Y, Artaman A, Asayesh H, Atnafu N, Awasthi A, Saleem HB, Barac A, Bedi N, Bensenor I, Berhane A, Bernabé E, Betsu B, Binagwaho A, Boneya D, Campos-Nonato I, Castañeda-Orjuela C, Catalá-López F, Chiang P, Chibueze C, Chitheer A, Choi JY, Cowie B, Damtew S, das Neves J, Dey S, Dharmaratne S, Dhillon P, Ding E, Driscoll T, Ekwueme D, Endries AY, Farvid M, Farzadfar F, Fernandes J, Fischer F, G/Hiwot TT, Gebru A, Gopalani S, Hailu A, Horino M, Horita N, Husseini A, Huybrechts I, Inoue M, Islami F, Jakovljevic M, James S, Javanbakht M, Jee SH, Kasaeian A, Kedir MS, Khader YS, Khang YH, Kim D, Leigh J, Linn S, Lunevicius R, El Razek HMA, Malekzadeh R, Malta DC, Marcenes W, Markos D, Melaku YA, Meles KG, Mendoza W, Mengiste DT, Meretoja TJ, Miller TR, Mohammad KA, Mohammadi A, Mohammed S, Moradi-Lakeh M, Nagel G, Nand D, Le Nguyen Q, Nolte S, Ogbo FA, Oladimeji KE, Oren E, Pa M, Park EK, Pereira DM, Plass D, Qorbani M, Radfar A, Rafay A, Rahman M, Rana SM, Søreide K, Satpathy M, Sawhney M, Sepanlou SG, Shaikh MA, She J, Shiue I, Shore HR, Shrime MG, So S, Soneji S, Stathopoulou V, Stroumpoulis K, Sufiyan MB, Sykes BL, Tabarés-Seisdedos R, Tadese F, Tedla BA, Tessema GA, Thakur JS, Tran BX, Ukwaja KN, Uzochukwu BSC, Vlassov VV, Weiderpass E, Wubshet Terefe M, Yebyo HG, Yimam HH, Yonemoto N, Younis MZ, Yu C, Zaidi Z, Zaki MES, Zenebe ZM, Murray CJL and Naghavi M. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the global burden of disease study. JAMA Oncol 2017; 3: 524-548.

[3] Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, Stein KD, Alteri R and Jemal A. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin 2016; 66: 271-289.

[4] 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.

[5] Chen WQ, Sun KX, Zheng RS, Zeng HM, Zhang SW, Xia CF, Yang ZX, Li H, Zou XN and He J. Cancer incidence and mortality in China, 2014. Chin J Cancer Res 2018; 30: 1-12.

[6] Chen WQ, Zheng RS, Baade PD, Zhang SW, Zeng HM, Bray F, Jemal A, Yu XQ and He J. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115-132.

[7] Heald RJ, Husband EM and Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? Br J Surg 1982; 69: 613-616.

[8] Enker WE, Merchant N, Cohen AM, Lanouette NM, Swallow C, Guillem J, Paty P, Minsky B, Weyrauch K and Quan SH. Safety and efficacy of low anterior resection for rectal cancer: 681 consecutive cases from a specialty service. Ann Surg 1999; 230: 544-552; discussion 552-4.

[9] Heald RJ and Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet 1986; 1: 1479-1482.

[10] Hendren SK, O'Connor BI, Liu M, Asano T, Cohen Z, Swallow CJ, Macrae HM, Gryfe R and McLeod RS. Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. Ann Surg 2005; 242: 212-223.

[11] Maurer CA, Z'Graggen K, Renzulli P, Schilling MK, Netzer P, Brae HM, Gryfe R and McLeod RS. Preon preserves male genital function compared with conventional rectal cancer surgery. Br J Surg 2001; 88: 1501-1505.

[12] Havenga K, Enker WE, McDermott K, Cohen AM, Minsky BD and Guillem J. Male and female sexual and urinary function after total mesorectal excision with autonomic nerve preservation for carcinoma of the rectum. J Am Coll Surg 1996; 182: 495-502.
[13] Stevenson AR, Solomon MJ, Lumley JW, Hewett P, Clouston AD, Gebski VJ, Davies L, Wilson K, Hague W and Simes J; ALaCaRT Investigators. Effect of laparoscopic-assisted resection vs. open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA 2015; 314: 1356-1363.
[14] Bonjer HJ, Deijen CL, Abis GA, Cuesta MA, van der Pas MH, de Lange-de Klerk ES, Lacy AM, Bemelman WA, Andersson J, Angenete E, Rosenberg J, Fuerst A and Haglind E; COLOR II Study Group. A randomized trial of laparoscopic versus open surgery for rectal cancer. N Engl J Med 2015; 372: 1324-1332.
[15] Jeong SY, Park JW, Nam BH, Kim S, Kang SB, Lim SB, Choi HS, Kim DW, Chang HJ, Kim DY, Jung KH, Kim TY, Kang GH, Chie EK, Kim SY, Sohn DK, Kim DH, Kim JS, Lee HS, Kim JH and Oh JH. Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. Lancet Oncol 2014; 15: 767-774.
[16] Jayne DG, Brown JM, Thorpe H, Walker J, Quirke P and Guillou PJ. Bladder and sexual function following resection for rectal cancer in a randomized clinical trial of laparoscopic versus open technique. Br J Surg 2005; 92: 1124-1132.
[17] Quah HM, Jayne DG, Eu KW and Seow-Choen F. Bladder and sexual dysfunction following laparoscopically assisted and conventional open mesorectal resection for cancer. Br J Surg 2002; 89: 1551-1556.
[18] Fleming CA, Cullinane C, Lynch N, Killeen S, Coffey JC and Peirce CB. Urogenital function following robotic and laparoscopic rectal cancer surgery: meta-analysis. Br J Surg 2021; 108: 128-137.
[19] Quirke P, Durdey P, Dixon MF and Williams NS. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumour spread and surgical excision. Lancet 1986; 2: 996-999.
[20] Oelke M, Höfner K, Jonas U, de la Rosette JJ, Ubbink DT and Wijkstra H. Diagnostic accuracy of noninvasive tests to evaluate bladder outlet obstruction in men: detrusor wall thickness, uroflowmetry, postvoid residual urine, and prostate volume. Eur Urol 2007; 52: 827-834.
[21] Stelzner S, Heinze T, Nikolouzakis TK, Torge Mees S, Witzigmann H and Wedel T. Perirectal fascial anatomy: new insights into an old problem. Dis Colon Rectum 2021; 64: 91-102.
[22] Kinugasa Y, Murakami G, Suzuki D and Sugihara K. Histological identification of fascial structures posterolateral to the rectum. Br J Surg 2007; 94: 620-626.
[23] Li PF, Liu P, Chen CL, Duan H, Qiao WJ and Ognami OH. The 3D reconstructions of female pelvic autonomic nerves and their related organs based on MRI: a first step towards neuronavigation during nerve-sparing radical hysterectomy. Eur Radiol 2018; 28: 4561-4569.
[24] Curtis NJ, Conti JA, Dalton R, Rockall TA, Allison AS, Ockrim JB, Jourdan IC, Torkington J, Phillips S, Allison J, Hanna GB and Francis NK. 2D versus 3D laparoscopic total mesorectal excision: a developmental multicentre randomised controlled trial. Surg Endosc 2019; 33: 3370-3383.
[25] Seracchioli R, Mabrouk M, Mastronardi M, Raimondo D, Arena A, Forno SD, Mariani GA, Billi AM, Manzoli L, O'Guin WM and Lemos N. Anatomic cartography of the hypogastric nerves and surgical insights for autonomic preservation during radical pelvic procedures. J Minim Invasive Gynecol 2019; 26: 1340-1345.
[26] Kneist W, Kauff DW, Juhre V, Hoffmann KP and Lang H. Is intraoperative neuromonitoring associated with better functional outcome in patients undergoing open TME? Results of a case-control study. Eur J Surg Oncol 2013; 39: 994-999.
[27] Kauff DW, Kronfeld K, Gorbulev S, Wachtlin D, Lang H and Kneist W. Continuous intraoperative monitoring of pelvic autonomic nerves during TME to prevent urogenital and anorectal dysfunction in rectal cancer patients (NEUROS): a randomized controlled trial. BMC Cancer 2016; 16: 323.
[28] Ito M, Kobayashi A, Fujita S, Mizusawa J, Kanemitsu Y, Kinugasa Y, Komori K, Ohue M, Ota M, Akazai Y, Shiozawa M, Yamaguchi T, Akasu T and Moriya Y; Colorectal Cancer Study Group of Japan Clinical Oncology Group. Urinary dysfunction after rectal cancer surgery: results from a randomized trial comparing mesorectal excision with and without lateral lymph node dissection for clinical stage II or III lower rectal cancer (Japan clinical oncology group study, JCOG0212). Eur J Surg Oncol 2018; 44: 463-468.
[29] Cheung YM, Lange MM, Buunen M and Lange JF. Current technique of laparoscopic total mesorectal excision (TME): an international questionnaire among 368 surgeons. Surg Endosc 2009; 23: 2796-2801.
[30] Brændengen M, Tveit KM, Bruheim K, Cvancarova M, Berglund Å and Glimelius B. Late patient-reported toxicity after preoperative radiotherapy or chemoradiotherapy in non-

resectable rectal cancer: results from a randomized phase III study. Int J Radiat Oncol Biol Phys 2011; 81: 1017-1024.
[31] Bertrand MM, Macri F, Mazars R, Droupy S, Beregi JP and Prudhomme M. MRI-based 3D pelvic autonomous innervation: a first step towards image-guided pelvic surgery. Eur Radiol 2014; 24: 1989-1997.
[32] Kiyoshima K, Yokomizo A, Yoshida T, Tomita K, Yonemasu H, Nakamura M, Oda Y, Naito S and Hasegawa Y. Anatomical features of periprostatic tissue and its surroundings: a histological analysis of 79 radical retropubic prostatectomy specimens. Jpn J Clin Oncol 2004; 34: 463-468.
[33] Wallner C, Lange MM, Bonsing BA, Maas CP, Wallace CN, Dabhoiwala NF, Rutten HJ, Lamers WH, Deruiter MC and van de Velde CJ; Cooperative Clinical Investigators of the Dutch Total Mesorectal Excision Trial. Causes of fecal and urinary incontinence after total mesorectal excision for rectal cancer based on cadaveric surgery: a study from the Cooperative Clinical Investigators of the Dutch total mesorectal excision trial. J Clin Oncol 2008; 26: 4466-4472.

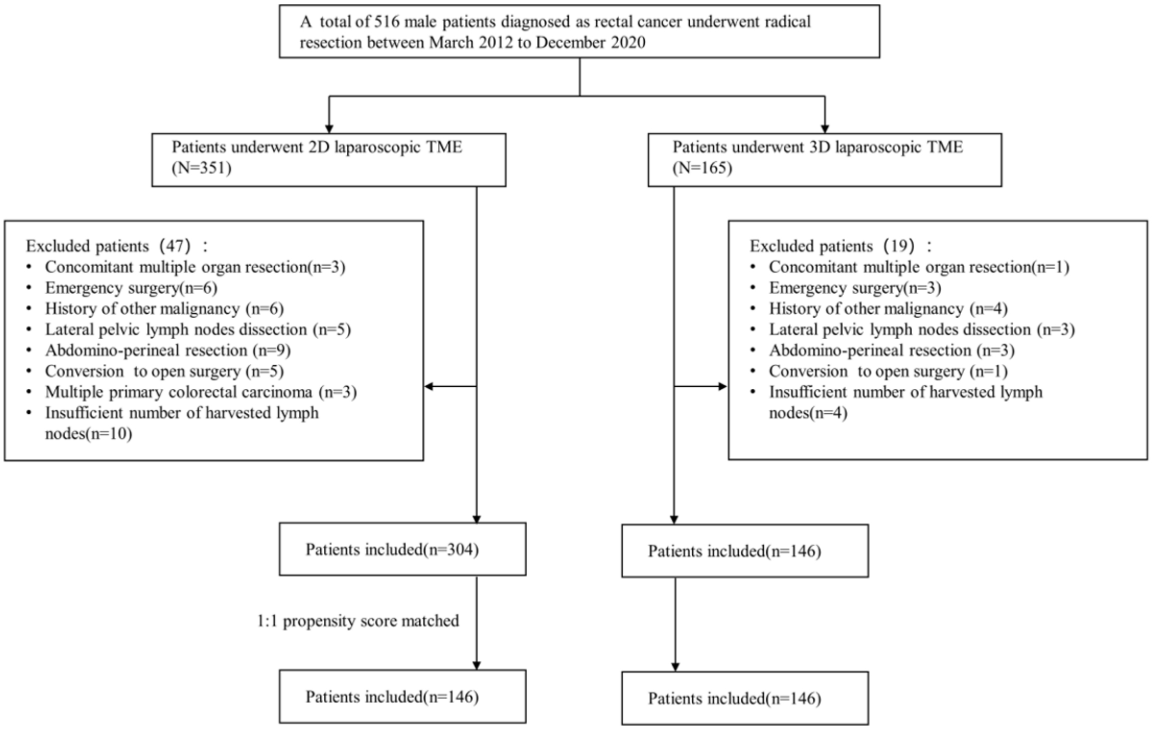

Figure S1. Study cohort.

Table S1. Pelvic autonomic nerve coincidence rate

Surgeon 1 / Surgeon 2	SHP	HGN	IHP	PSN	PP	NVB	Branch of levator ani	Sympathic trunk at the IMA level	Non-visible
SHP	123	2	0	0	0	0	0	3	3
HGN	0	138	1	2	0	0	0	0	0
IHP	0	0	114	1	0	0	0	0	0
PSN	0	2	0	62	3	0	0	0	6
PP	0	0	0	5	107	4	0	0	0
NVB	0	0	0	0	5	103	0	0	1
Branch of levator ani	0	0	0	0	4	0	46	0	5
Sympathic trunk at the IMA level	4	0	0	0	0	0	0	123	4
Non-visible	0	0	0	5	0	2	5	4	291

SHP: superior hypogastric plexus; IHP: inferior hypogastric plexus; HGN: hypogastric nerve; PSN: pelvic splanchnic nerves; PP: pelvic plexus; NVB: neurovascular bundle; IMA: inferior mesenteric artery.