



## Oncological Outcomes of Robotic-Assisted Surgery With High Dissection and Selective Ligation Technique for Sigmoid Colon and Rectal Cancer

#### OPEN ACCESS

#### Edited by:

Jiankun Hu, Sichuan University, China

#### Reviewed by:

Ziv Radisavljevic, Brigham and Women's Hospital and Harvard Medical School, United States Giovanni Battista Levi Sandri, San Camillo-Forlanini Hospital, Italy

#### \*Correspondence:

Jaw-Yuan Wang Jawyuanwang@gmail.com Ching-Wen Huang cy614112@ms14.hinet.net

#### Specialty section:

This article was submitted to Surgical Oncology, a section of the journal Frontiers in Oncology

Received: 07 June 2020 Accepted: 15 September 2020 Published: 21 October 2020

#### Citation:

Yin T-C, Su W-C, Chen P-J, Chang T-K, Chen Y-C, Li C-C, Hsieh Y-C, Tsai H-L, Huang C-W and Wang J-Y (2020) Oncological Outcomes of Robotic-Assisted Surgery With High Dissection and Selective Ligation Technique for Sigmoid Colon and Rectal Cancer. Front. Oncol. 10:570376. doi: 10.3389/fonc.2020.570376 Tzu-Chieh Yin<sup>1,2,3</sup>, Wei-Chih Su<sup>3</sup>, Po-Jung Chen<sup>3,4</sup>, Tsung-Kun Chang<sup>3</sup>, Yen-Cheng Chen<sup>3</sup>, Ching-Chun Li<sup>3</sup>, Yi-Chien Hsieh<sup>3</sup>, Hsiang-Lin Tsai<sup>3,5</sup>, Ching-Wen Huang<sup>3,5\*</sup> and Jaw-Yuan Wang<sup>3,5,6,7,8\*</sup>

<sup>1</sup> Division of General and Digestive Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>2</sup> Department of Surgery, Kaohsiung Municipal Tatung Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>3</sup> Division of Colorectal Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>4</sup> Division of Colorectal Surgery, Department of Surgery, Department of Surgery, Kaohsiung Municipal Hsiaokang Hospital, Kaohsiung, Taiwan, <sup>6</sup> Department of Surgery, Faculty of Medicine, College of Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>6</sup> Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>7</sup> Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>8</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>8</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>8</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>8</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research, Kaohsiung University, Kaohsiung, Taiwan, <sup>9</sup> Center for Cancer Research

**Background:** Curative resection of sigmoid colon and rectal cancer includes "high tie" of the inferior mesenteric artery (IMA). However, IMA ligation compromises blood flow to the anastomosis, which may increase the complication rate. We present preliminary experiences of operative and oncologic outcomes of patients with rectal or sigmoid colon cancer who underwent robotic surgery employing the high dissection and selective ligation technique.

**Methods:** Over May 2013 to April 2017, 113 stage I–III rectal or sigmoid colon cancer patients underwent robotic surgery with the single-docking technique at one institution. We performed D3 lymph node dissection and low-tie ligation of the IMA (i.e., high dissection and selective ligation technique). Clinicopathological features, perioperative parameters, and postoperative outcomes were retrospectively analyzed. Overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan–Meier method.

**Results:** Sphincter preservation rate was 96.3% in rectal cancer patients. Median number of harvested lymph nodes was 12. Apical nodes were pathologically harvested in 84 (82.4%) patients. R0 resection was performed in 108 (95.6%) patients. Overall complication rate was 17.7%; but most complications were mild and the patients recovered uneventfully. Estimated 5-year OS was 86.1% and 3-year DFS was 79.6% after median follow-up periods of 49.1 months (range, 5.3–85.3).

1

**Conclusions:** High dissection of the IMA and selective ligation of the major feeding vessel to the sigmoid colon or rectum can be safely performed using da Vinci Surgical System, yielding favorable clinical, and oncologic outcomes in rectal or sigmoid colon cancer treatment.

Keywords: selective ligation of IMA, sigmoid colon cancer, rectal cancer, robotic surgery, oncologic outcomes

#### INTRODUCTION

Total mesorectal excision (TME) surgery, notably improves the clinical outcomes, has served as the essential procedure for patients with rectal cancer since it was first described by Heald and Ryall in 1982 (1). MacFarlane et al. (2) reported a 5-year local recurrence rate of 5% in patients who underwent TME surgery alone. Moreover, in patients with locally advanced rectal cancer (LARC), local recurrence rate is substantially reduced by preoperative concurrent chemoradiotherapy (CCRT). A German study reported that the 5-year cumulative incidence of local relapse was 6% in patients who received preoperative CCRT (3, 4). Similar results were reported in other studies (5–7), and preoperative CCRT with subsequent surgical intervention has been highly recommended as the treatment for patients with of LARC (8).

Laparoscopic rectal surgery with TME is highly technically dependent and requires skilled surgeons experienced in minimal invasive surgery (9, 10). The robotic system (da Vinci Surgical System, Intuitive Surgical, Inc., Sunnyvale, CA, USA) has several strengths including high-definition three-dimensional magnified vision, the surgeon-controlled camera platform, the meticulous articulatory instruments, and steady traction provided by the robotic arm. Operation in the confined and narrow space such as pelvic cavity can be performed more easily and precisely. Robotic colon surgery, which was first performed in 2002 (11), is expected to address the disadvantages of conventional laparoscopic colorectal surgery. Compared with laparoscopic surgery, robotics rectal cancer surgery is more favorable in regarding to clinical and short-term oncological outcomes and is suggested in several studies (12-15). Even in patients of LARC or mid to low rectal cancer received CCRT, robotic rectal surgery is still associated with at least comparable short-term surgical outcomes (16-18).

Conventionally, high ligation of the inferior mesenteric artery (IMA) is one of the important surgical steps in rectal or sigmoid colon cancer surgery. However, this technique may reduce blood flow in the bowel and increase the risk of ischemia and anastomosis leakage (19). In a study of patients with rectal cancer following preoperative CCRT, Huang et al. (20) observed that robotic surgery with the technique of high dissection and low ligation resulted in a sufficient number of harvested lymph nodes and a low rate of anastomotic leakage. Because the high dissection and selective ligation of IMA branches theoretically preserves more blood supply to the anastomosis, we intend to apply this technique by using the robotic system in patients with rectal cancer or sigmoid colon cancer and evaluate their perioperative surgical, pathologic, and oncologic outcomes.

## MATERIALS AND METHODS

#### **Patients**

This is a single-institution retrospective study. Patients with stage I-III rectal or sigmoid colon cancer underwent robotic surgery with the single-docking technique were enrolled into this study. This study was approved by the institutional review board of our hospital. Informed consent was obtained from each patient before the robotic surgery was performed. Over May 2013 to April 2017, 113 consecutive patients were included in the study and analyzed. These patients routinely underwent diagnostic colonoscopy and abdominal and pelvic computed tomography (CT) or magnetic resonance imaging for preoperative staging. Patients with T3/T4 or N+ rectal cancer received preoperative CCRT. A biweekly 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) chemotherapy regimen or a fluoropyrimidine-based regimen was used for CCRT in patients with LARC. Longcourse radiotherapy was concurrently administered according to our protocol (20, 21). The total radiation dose was delivered in a range of 45-50.4 Gy using a daily fraction of 1.8-2.0 Gy. All patients received external-beam radiotherapy with either three-dimensional conformal or intensity-modulated radiation therapy. Most of the robotic-assisted surgery with the singledocking technique were scheduled  $\sim$ 8–12 weeks after completion of radiotherapy (22).

Clinicopathological features and perioperative parameters or outcomes, including age, sex, histological type, TNM classification, time interval between completion of preoperative radiotherapy and robotic surgery, tumor location (distance from the anal verge), American Society of Anesthesiologists classification, and body mass index (BMI), were collected and evaluated. The TNM classification was defined according to the American Joint Commission on Cancer (AJCC)/International Union Against Cancer (UICC) criteria (23). The tumor regression grade (TRG) was assessed according to the AJCC system (24). Perioperative outcomes, including surgical procedures, time consumed in docking, console and operation, estimated blood loss, time of the first flatus passage, time of resuming soft diet, length of hospital stay, and pain score (visual analog scale) at the first postoperative day, were collected and evaluated.

Patients were regularly followed up after operation, which included the collection of clinical outcome and survival status data. History-taking and physical examinations were performed every 3 months postoperatively. Serum carcinoembryonic antigen levels were measured every 2–3 months postoperatively. Colonoscopy was carried out around 1 year after surgery. A repeat colonoscopy was generally recommended at 3



years. In patients with stage II–III disease, abdominal, and pelvic CT scans were executed annually for 3 consecutive years postoperatively.

## **Surgical Procedures**

The da Vinci Si surgical system was docked over the left flank of the patient. We used medial to lateral fashion to ligate and divide the branches of inferior mesenteric artery and vein. First, a peritoneal incision at the level of the sacral promontory was performed. The dissection was then extended cranially and caudally. We fully explored the IMA from the abdominal aorta to the converging of the left colic artery (LCA) and IMA. Lymphoadipose tissues here were skeletonized and stripped easily with the use of the da Vinci Surgical System to complete the lymph nodes dissection over the root of IMA. We performed dissection of the D3 lymph node (from the level of the IMA entering the abdominal aorta to the branching of the LCA) and low-tie ligation of the IMA with preservation of the LCA in all patients; this technique also known as the high dissection and low ligation technique (20). Transection was executed below the junction of IMA and LCA. The superior rectal artery (SRA) was also preserved during anterior resection (AR) if the tumor was located in the proximal sigmoid colon. In addition, the sigmoid artery was preserved in case of rectal cancer with redundant sigmoid colon (Figure 1). The inferior mesenteric vein (IMV) was identified but was not transected immediately. The IMV was ligated and divided only if excess tension was noted during the colonic anastomosis. The splenic flexure was not routinely mobilized if its mobilization was also dependent on the tension of the anastomosis. Totally robotic-assisted TME with the singledocking technique was performed on patients of rectal cancer as described previously (22).

After complete mobilization of the sigmoid colon, mesocolon, entire rectum and TME, AR using the hand-sewn or doublestapled technique, low anterior resection (LAR) using the double-stapled technique, intersphincteric resection (ISR) with coloanal anastomosis as well as protective diverting colostomy, or abdominoperineal resection (APR) was performed accordingly. A specimen was then extracted and resected transanally after ISR. Finally, a conventional laparoscope was used to meticulously inspect for the abdominal and pelvic cavity, and a drain tube was placed in the cul-de-sac.

## **Statistical Analysis**

All data were statistically analyzed using JMP for Windows (version 13.0; SAS Institute, Cary, NC, USA). Continuous variables are presented as median and their quartiles, and dichotomous variables are denoted by numbers and percentages. A t test was used to analyze continuous variables, and the Chi-square test was used for univariate statistical analysis. All patients were followed up until their death, final follow-up, or May 31, 2020. The survival plot was calculated using the Kaplan-Meier method.

**TABLE 1** Baseline characteristics and perioperative outcomes of 113 patients with rectal or sigmoid colon cancer who underwent totally robotic-assisted TME with the high dissection and selective ligation technique.

Characteristics				
Age (years, median) (range)	62 (28–88)			
Sex				
Male	69 (61.1%)			
Female	44 (38.9%)			
BMI (IQR)	24.0 (22.1–26.2)			
Distance from anal verge, rectum only (cm, median) (IQR)	5 (3–7)			
Pre-operative CCRT				
Yes	79 (69.9%)			
No	34 (30.1%)			
Pre-operative chemotherapy regimen				
FOLFOX	58 (73.4%)			
Fluoropyrimidine-based	21 (26.6%)			
Time interval (days, median) (range)	82 (41–203)			
ASA classification				
II	64 (56.6%)			
III	49 (43.4%)			
Tumor location				
Sigmoid colon	9 (17.9%)			
Recotosigmoid colon	22 (31.6%)			
Rectum	82 (50.5%)			
Procedure				
AR	9 (8.0%)			
LAR	66 (58.4%)			
ISR	35 (31.0%)			
APR	3 (2.7%)			
Protective colostomy (except APR)	44 (40%)			
Docking time (min, median) (IQR)	5 (4–6)			
Console time (min, median) (IQR)	205 (168–244)			
Operation time (min, median) (IQR)	320 (280–436)			
Estimate blood loss (mL, median) (IQR)	80 (50–145)			
Time to flatus passage (day, median) (IQR)	2 (1, 2)			
Time to resume soft diet (day, median) (IQR)	4 (3,4)			
Postoperative LOS (day, median) (range)	6 (5–32)			
POD1 VAS pain score (median) (IQR)	3 (3–4)			

BMI, body mass index; TME, total mesorectal excision; CCRT, concurrent chemoradiotherapy; ASA, American Society of Anesthesiologists; AR, anterior resection; LAR, low anterior resection; ISR, intersphincteric resection; APR, abdominoperineal resection; LOS, length of stay, POD1: postoperative day 1.

#### RESULTS

#### Patients Characteristics and Perioperative Outcomes

The baseline characteristics and perioperative outcomes of 113 patients with rectal or sigmoid colon cancer who underwent robotic-assisted surgery using the high dissection and selective ligation technique are summarized in **Table 1**. The median age and BMI of the patients was 62 (range, 28–88) years and 24.0 (IQR, 22.1–26.2) kg/m<sup>2</sup>, respectively. Of the 113 patients, 82 (50.5%), 22 (31.6%), and 9 (17.9%) had rectal, rectosigmoid, and

**TABLE 2** | Postoperative complications of 113 patients with rectal or sigmoid

 colon cancer who underwent totally robotic-assisted TME with the high dissection

 and selective ligation technique.

Complications	Number (%)	Management
Postoperative bleeding	1 (0.9%)	Laparotomy
Anastomosis leakage	4 (3.5%)	Loop transverse colostomy
Intraabdominal infection/abscess	2 (1.8%)	1 CT guide drainage
		1 Conservative treatment
Coloanal anastomosis stenosis	5 (4.4%)	Colonoscopic dilation
Urethral injury	1 (0.9%)	Conservative treatment
Postoperative lleus	3 (2.7%)	Conservative treatment
Pulmonary complication	3 (2.7%)	Conservative treatment
Urinary tract infection	1 (0.9%)	Conservative treatment
Total	20 (17.7%)	

TME, total mesorectal excision.

sigmoid colon cancers, respectively. The median distance of the tumor from the anal verge was 5 (IQR, 3–7) cm in patients with rectal cancer. The most frequent surgical procedure was LAR (66, 58.4%), followed by ISR with coloanal anastomosis (35, 31.0%), and APR (3, 2.7%).

Finally, 44 patients (40%) had protective diverting colostomy after surgery, including 35 patients and 9 patients who underwent ISR and LAR, respectively. Sphincter preservation rate was 79/82 (96.3%) in patients with rectal cancer. The median estimated blood loss, including tissue fluid after CCRT, was 80 mL. The median time of the first flatus passage and resuming soft diet was 2 and 4 days postoperative, respectively, and the median length of postoperative hospital stay was 6 (range, 5–32) days.

#### **Postoperative Complications**

Postoperative complications are summarized in Table 2. Postoperative complications were observed in 13 patients with 20 episodes (17.7%). One (0.9%) patient developed intraabdominal bleeding and unstable hemodynamic condition postoperatively; a laparotomy was subsequently performed, during which bleeding from the mesocolon was noted. Anastomosis leakage occurred in 4 (3.5%) patients who underwent LAR with the double-stapled technique. 3 of them were male, 3 had preoperative CCRT and protective diverting stoma was not created simultaneously in these 4 patients. Loop colostomy of the transverse colon was subsequently performed. Five (4.4%) patients developed stenosis of coloanal anastomosis and underwent colonoscopic balloon dilation. Urethral injury during ISR was noted in one patient (0.9%). All postoperative ileus, pulmonary complications, and urinary tract infection were of grades I-II according to the Clavien-Dindo classification, and the patients recovered after conservative treatment. Furthermore, no 30-day hospital mortality occurred.

# Clinicopathological Features and Oncological Outcomes

The pathological characteristics and oncological outcomes of all 113 patients are summarized in **Table 3**. Most of the patients had

**TABLE 3** | Pathological characteristics and oncological outcomes of 113 patients with rectal or sigmoid colon cancer who underwent totally robotic-assisted TME with the high dissection and selective ligation technique.

#### **Clinical staging**

Tumor depth	
T1	2 (1.8%)
Τ2	23 (20.4%)
ТЗ	73 (64.6%)
Τ4	15 (12.3%)
Lymph node metastasis	
NO	52 (46.0%)
N1	38 (33.6%)
N2	23 (20.4%)
AJCC Stage	
I	22 (19.5%)
II	30 (26.5%)
III	61 (54.0%)
Pathological outcomes	
Histology	
WD	15 (13.4%)
MD	94 (83.9%)
PD	3 (2.7%)
Tumor size	
<5 cm	102 (90.3%)
≥5 cm	11 (9.7%)
– Tumor size (cm. median) (IQR)	2.5 (1.2–3.2)
Tumor depth	
TO	31 (27.4%)
Tis	1 (0.9%)
T1	21 (18.6%)
T2	25 (22.1%)
ТЗ	32 (28.3%)
T4	3 (2.7%)
Lymph node metastasis	
NO	87 (77.0%)
N1	19 (16.8%)
N2	7 (6.2%)
AJCC stage	
0	30 (26,5%)
1	38 (33.6%)
11	19 (16.8%)
10	26 (23.0%)
Pathological response grade (in 79 CCRT)	· · · · · · · · · · · · · · · · · · ·
0	28 (36.8%)
1	32 (42.1%)
2	10 (13.2%)
3	6 (7.9%)
Lymph node harvested (median) (IQR)	- ( )
With CCRT	10 (8–14)
Without CCRT	17 (12–21)
Apical node harvested	84 (82.4%)
Apical node harvested (median) (IOR)	2 (1-4)
Positive apical node	3 (3.6%)
	- (,-)
	(Continued,

#### TABLE 3 | Continued

Clinical staging	
Length of bowel resected (median) (IQR)	10.5
	(9.0–12.5)
Distance of distal resection margin, rectum only	2.0 (1.1–3.0)
(cm, median) (IQR)	
Distance of circumferential resection margin, rectum only (cm, median) (IQR)	1.0 (0.4–1.5)
Distal resection margin	
Free	112 (99.1%)
Positive	1 (0.9%)
Circumferential resection margin	
Free	109 (96.5%)
Positive	4 (3.5%)
Resection degree	
R0	108 (95.6%)
R1	5 (4.4%)
Oncological outcomes	
Follow up periods (month, median) (range)	49.1
	(5.3–85.3)
R0 resection	
Locoregional recurrence	8 (7.4%)
Distant metastasis	12 (11.1%)
Liver	2 (1.9%)
Lung	6 (5.6%)
Chest wall + adrenal gland	1 (0.9%)
Chest wall + bone	1 (0.9%)
Non-regional LN	2 (1.9%)
R1 resection	
Locoregional recurrence	3 (60%)
Distant metastasis	4 (80%)
Liver	2 (40%)
Lung	1 (20%)
Peritoneal carcinomatosis	1 (20%)

TME, total mesorectal excision; AJCC, American Joint Commission on Cancer; WD, well-differentiated; MD, moderately-differentiated; PD, poorly-differentiated; CCRT, concurrent chemoradiotherapy.

LARCs in preoperative clinical staging including T3 in 73 (64.6%) patients, T4 in 15 (12.3%) patients, or N+ in 61 (54.0%) patients. Therefore, preoperative CCRT was carried out in 79 (69.9%) patients, including FOLFOX regimen in 58 (73.4%) patients and fluoropyrimidine-based regimen in 21 (26.6%) patients. The median number of harvested lymph nodes and apical lymph nodes was 12 (IQR, 8-17) and 2 (IQR, 1-4), respectively. However, metastatic apical lymph node was found in only 3 (3.6%) patients. The median distance of the circumferential resection margin (CRM) and the distal resection margin (DRM) was 1.0 and 2.0 cm, respectively. CRM and DRM involvement were noted in 4 (3.5%) and 1 (0.9%) patients, respectively. R0 resection (microscopic tumor clearance) was accomplished in 108 (95.6%) patients. Pathologic complete response (pCR) of the primary tumor was observed in 28 (36.8%) of the 79 patients who received preoperative CCRT. In total, 28 (36.8%), 32 (42.1%), 10 (13.2%), and 6 (7.9%) patients revealed complete (TRG 0), moderate (TRG 1), minimal (TRG 2), and poor (TRG 3) response, respectively. The median time interval between



radiotherapy completion and robotic surgery was 82 (range, 41–203) days.

Of 108 patients who underwent R0 resection, local recurrence, and distant metastases happened in 8 (7.4%) and 12 (11.1%) patients, respectively. At a median follow-up duration of 49.1 (range, 5.3–85.3) months, the estimated 5-year overall survival (OS) was 86.1% and 3-year disease-free survival (DFS) was 79.6%, respectively (**Figure 2**).

## DISCUSSION

The completeness of TME is the indication of the qualification of rectal cancer surgery. CRM involvement and DRM distance constitute the two crucial parameters of TME completeness. Moreover, CRM involvement may be a prognostic factor for local recurrence and survival (25-28). In this study, the rate of CRM and DRM involvement were 3.5 and 0.9%, with a median distance of 1.0 and 2.0cm, respectively. These were comparable to that reported in a previous study (0-16.1% of CRM involvement and 1.5-3.9 cm of DRM distance) (22). The odds of achieving R0 resection in rectal cancer patients increased with the use of robotic-assisted surgery (29). The robotic platform also reduced the difficulty of accomplishing R0 resection in cancer requiring extensive resection (30). In current study, R0 resection for all cases was performed in 108 of 113 patients (95.6%). Of the 108 patients who underwent R0 resection, local recurrence and distant metastasis occurred in 8 (7.4%) and 12 (11.1%), respectively.

Although 69 of our patients (61.1%) were men and 75 (66.4%) of our patients had middle to low rectal cancers (tumor located at  $\leq$ 10 cm from the anal verge) with a median distance of 5 cm from the anal verge, we did not routinely mobilize the splenic flexure in most of them. Precise dissection during the TME procedure could still be executed when using our single-docking technique. Splenic flexure was mobilized only as required to achieve a tension-free anastomosis (31, 32). However, a comparable DRM

distance and favorable negative rates of CRM were reached. The introduction of extended oxaliplatin-based chemotherapy and a longer interval between radiotherapy completion and robotic surgery might have contributed to the success (8, 33). The sphincter preservation rate in patients with rectal cancer in our study was 96.3%, comparable to that reported by Kim et al. (18) and Saklani et al. (16). The anastomosis leakage rate (3.5%) in our study was lower than that reported in literature (7.1–16%) (34–37) even though protective diverting colostomy was performed in only 44 (55.7%) of 79 patients who underwent sphincter preservation surgery. Cautiously protective diverting stoma performing in high risk patients may further decrease the leakage rate.

The status of lymph node metastasis is a key factor for predicting the prognoses of patients with colorectal cancer (CRC). The AJCC/UICC recommends that at least 12 lymph nodes should be examined for each surgical specimen of CRC (23). However, the guidelines were mainly based on colon cancer studies. Patients with rectal cancer and older patients with distally located early colon cancer were less likely to meet the recommended lymph node yield (i.e., 12) (38). Moreover, the number of harvested lymph nodes essentially decreased after preoperative CCRT (median, 4–14) (39). In the present study, the median number of harvested lymph nodes after neoadjuvant CCRT was 10 (range, 8–14), which is consistent with previous results (39).

IMA ligation level remains a controversial topic. To obtain sufficient lymph nodes is the main purpose of high ligation of the IMA for better survival and adequate staging. However, this technique may result in bowel ischemia and subsequent anastomosis leakage and/or stenosis due to reduced blood flow in the colon. Recently, some surgeons suggest the technique of low ligation of the IMA with preservation of the LCA (19, 34, 40). In addition, the metastatic rate of lymph nodes around the IMA was reported to be 0.3–8.6% in patients with rectal cancer (41). In the present study, we performed high dissection of the TABLE 4 | Studies regarding the high dissection and selective ligation technique published since 2013.

Study	Country (year)	Patient number	Tumor location	Description of the technique	Comparison
(37)	Japan (2013)	155	Middle and low rectum	LCA preserving	Operative outcome, complications, OS RFS
(42)	Japan (2014)	120	Sigmoid colon and RS colon, T3	Low ligations with preservation of the LCA	Operative outcome, OS, DFS
(35)	Japan (2015)	49	Rectum	Low-ligation of IMA	Defecatory function, QoL, leakage rate, LN harvested
(43)	Japan (2016)	147	Sigmoid colon and rectum	Low tie with lymph node dissection	OS, DFS, complications
(44)	Japan (2018)	142	Sigmoid colon and upper rectum	IMA preservation	Operative outcome, LN harvested, OS, DFS
Present study	Taiwan (2020)	113	Sigmoid colon and rectum	High dissection and selective ligation technique	Operative outcomes, complications, pathologic outcomes, OS, DFS

LCA, left colic artery; OS, overall survival; DFS, disease free survival; RS, rectosigmoid; IMA, inferior mesenteric artery; QoL, quality of life; LN, lymph node.

IMA and selective ligation of the major feeding vessel to the sigmoid colon or rectum. Apical lymph nodes were identified in 84 (82.4%) of 102 patients, and the median number of harvested apical lymph nodes was 2 (range, 1–4). However, positive apical lymph node metastasis was observed in only three patients (3.6%). Therefore, we obtained results comparable to those in the literature, including sufficient harvesting rate and number of harvested apical lymph nodes, with this technique (35, 36, 42). The routine ligation of IMA might be re-considered if it remained as a standard operative procedure.

Studies regarding high dissection and selective ligation are briefly summarized in **Table 4**. Our technique was similar to that described in the literature, including low ligation of the IMA, IMA preservation, LCA preservation, low tie with lymph node dissection, and low ligation with preservation of the LCA (35, 37, 42–44). This technique was mostly used in AR and LAR for stage I–III sigmoid colon or rectal cancer during lymph node dissection at the root of the IMA. Oncologic outcome and complication rate were the most pertinent points in these studies. OS (42, 43) and DFS (42–44) were not inferior to those in patients who received standard high ligation technique procedures even in N+ or  $\geq$ T3 disease (42). In some cases with proximal sigmoid colon cancer, both the LCA and SRA were preserved (44) and the DFS was unaltered.

Anastomotic leakage rate was as low as 3.5% in the present study with the robotic-assisted high dissection and selective ligation technique. Nevertheless, complication and anastomotic leakage rates revealed equivalent outcomes for the high-tie and low-tie techniques for sigmoid colon and rectal cancer surgery in the study of Yasuda et al. (43). Favorable anastomotic leakage rate (7.4 vs. 13.2%; hazard ratio 0.269 (0.131–0.550); P < 0.001) was observed in LCA preservation during laparoscopic-assisted sphincter-preserving rectal surgery (37). A low complication rate, including only 6% anastomotic leakage rate, was also achieved in a study by Liang et al. (34) by using the robotic approach to perform D3 lymph node dissection over the IMA with preservation of the LCA for the treatment of distal rectal cancer.

This study has some limitations. First, this was a singleinstitution retrospective study including only 113 patients. Second, the median interval of follow-up was 49.1 months; however, the 3-year local control rate (89.4%) and the 3-year distant metastasis control rate (84.7%) were comparable with those reported in related studies.

## CONCLUSIONS

Robotic-assisted high dissection and selective ligation of the IMA yields low postoperative complication rates, enables the harvesting of sufficient lymph nodes, and provides equivalent oncologic outcome compared with the conventional high ligation technique. R0 resection remains one of the most critical elements for locoregional control and the reduction of distant metastasis. This effective and safe surgical technique, with favorable oncological outcomes, is suggested for the potential treatment option for patients with stage I–III rectal cancer or sigmoid cancer.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## **ETHICS STATEMENT**

The studies involving human participants were reviewed and approved by Institutional Review Board of Kaohsiung Medical University Hospital. The patients/participants provided their written informed consent to participate in this study.

## **AUTHOR CONTRIBUTIONS**

T-CY, being the first author of this manuscript, designed this study, analyzed the data, and wrote the manuscript. W-CS, P-JC, T-KC, Y-CC, C-CL, Y-CH, H-LT, and C-WH made substantial contributions in terms of the data acquisition, interpretation and statistical analyses, in addition to assisting with the manuscript preparation. J-YW, being the

corresponding author for this manuscript, also participated in the study design and coordination, in addition to making critical revisions to the manuscript. All authors have reviewed and approved submission of the final version of the manuscript.

#### ACKNOWLEDGMENTS

This work was supported by grants through funding from the Ministry of Science and Technology (MOST 109-2314-B-037-035, MOST 109-2314-B-037-040, MOST 109-2314-B-037-046-MY3) and the Ministry of Health and

#### REFERENCES

- Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery-the clue to pelvic recurrence? *Br J Surg.* (1982) 69:613–6. doi: 10.1002/bjs.1800691019
- MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. Lancet. (1993) 341:457–60. doi: 10.1016/0140-6736(93)90207-W
- Sauer R, Liersch T, Merkel S, Fietkau R, Hohenberger W, Hess C, et al. Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer: results of the German CAO/ARO/AIO-94 randomized phase III trial after a median follow-up of 11 years. *J Clin Oncol.* (2012) 30:1926– 33. doi: 10.1200/JCO.2011.40.1836
- Sauer R, Becker H, Hohenberger W, Rodel C, Wittekind C, Fietkau R, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. (2004) 351:1731–40. doi: 10.1056/NEJMoa 040694
- McCarthy K, Pearson K, Fulton R, Hewitt J. Pre-operative chemoradiation for non-metastatic locally advanced rectal cancer. *Cochrane Database Syst Rev.* (2012) 12:CD008368. doi: 10.1002/14651858.CD008368.pub2
- Bosset JF, Calais G, Mineur L, Maingon P, Radosevic-Jelic L, Daban A, et al. Enhanced tumorocidal effect of chemotherapy with preoperative radiotherapy for rectal cancer: preliminary results–EORTC 22921. J Clin Oncol. (2005) 23:5620–7. doi: 10.1200/JCO.2005.02.113
- Gerard JP, Conroy T, Bonnetain F, Bouche O, Chapet O, Closon-Dejardin MT, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. J Clin Oncol. (2006) 24:4620–5. doi: 10.1200/JCO.2006.06.7629
- Huang MY, Huang CW, Wang JY. Surgical treatment following neoadjuvant chemoradiotherapy in locally advanced rectal cancer. *Kaohsiung J Med Sci.* (2019) 36:152–9. doi: 10.1002/kjm2.12161
- van der Pas MH, Haglind E, Cuesta MA, Furst A, Lacy AM, Hop WC, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): shortterm outcomes of a randomised, phase 3 trial. *Lancet Oncol.* (2013) 14:210– 8. doi: 10.1016/S1470-2045(13)70016-0
- Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopicassisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet.* (2005) 365:1718–26. doi: 10.1016/S0140-6736(05)66545-2
- Weber PA, Merola S, Wasielewski A, Ballantyne GH. Telerobotic-assisted laparoscopic right and sigmoid colectomies for benign disease. *Dis Colon Rectum.* (2002) 45:1689–94; discussion 95–6. doi: 10.1007/s10350-004-7261-2
- Baek JH, Pastor C, Pigazzi A. Robotic and laparoscopic total mesorectal excision for rectal cancer: a case-matched study. *Surg Endosc.* (2011) 25:521– 5. doi: 10.1007/s00464-010-1204-x
- Park JS, Choi GS, Lim KH, Jang YS, Jun SH. S052: a comparison of robotassisted, laparoscopic, and open surgery in the treatment of rectal cancer. *Surg Endosc.* (2011) 25:240–8. doi: 10.1007/s00464-010-1166-z

Welfare (MOHW107-TDU-B-212-123006, MOHW107-TDU-B-212-114026B, MOHW108-TDU-B-212-133006, MOHW109-TDU-B-212-134026, MOHW109-TDU-B-212-114006) and funded by the health and welfare surcharge on tobacco products, and the Kaohsiung Medical University Hospital (KMUH108-8R34, KMUH108-8R35, KMUH108-8M33, KMUH 108-8M35, KMUH108-8M36, KMUH-DK109003, KMUH-DK109005~3, KMUHS10903) and KMU Center for Cancer Research (KMU-TC108A04-02) as well as and a KMU Cohort Research Center Grant (KMU-TC109B05), Kaohsiung Medical University. In addition, this study was supported by the Grant of Taiwan Precision Medicine Initiative, Academia Sinica, Taiwan, R.O.C.

- Hellan M, Ouellette J, Lagares-Garcia JA, Rauh SM, Kennedy HL, Nicholson JD, et al. Robotic rectal cancer resection: a retrospective multicenter analysis. *Ann Surg Oncol.* (2015) 22:2151–8. doi: 10.1245/s10434-014-4278-1
- Kim JY, Kim NK, Lee KY, Hur H, Min BS, Kim JH. A comparative study of voiding and sexual function after total mesorectal excision with autonomic nerve preservation for rectal cancer: laparoscopic versus robotic surgery. *Ann Surg Oncol.* (2012) 19:2485–93. doi: 10.1245/s10434-012-2262-1
- Saklani AP, Lim DR, Hur H, Min BS, Baik SH, Lee KY, et al. Robotic versus laparoscopic surgery for mid-low rectal cancer after neoadjuvant chemoradiation therapy: comparison of oncologic outcomes. *Int J Colorectal Dis.* (2013) 28:1689–98. doi: 10.1007/s00384-013-1756-z
- Huang YM, Huang YJ, Wei PL. Outcomes of robotic versus laparoscopic surgery for mid and low rectal cancer after neoadjuvant chemoradiation therapy and the effect of learning curve. *Medicine (Baltimore)*. (2017) 96:e8171. doi: 10.1097/MD.00000000008171
- Kim YS, Kim MJ, Park SC, Sohn DK, Kim DY, Chang HJ, et al. Robotic versus laparoscopic surgery for rectal cancer after preoperative chemoradiotherapy: case-matched study of short-term outcomes. *Cancer Res Treat.* (2016) 48:225– 31. doi: 10.4143/crt.2014.365
- Lange MM, Buunen M, van de Velde CJ, Lange JF. Level of arterial ligation in rectal cancer surgery: low tie preferred over high tie. A review. *Dis Colon Rectum.* (2008) 51:1139–45. doi: 10.1007/s10350-008-9328-y
- Huang CW, Yeh YS, Su WC, Tsai HL, Choy TK, Huang MY, et al. Robotic surgery with high dissection and low ligation technique for consecutive patients with rectal cancer following preoperative concurrent chemoradiotherapy. *Int J Colorectal Dis.* (2016) 31:1169–77. doi: 10.1007/s00384-016-2581-y
- Huang CM, Huang CW, Ma CJ, Yeh YS, Su WC, Chang TK, et al. Predictive value of FOLFOX-based regimen, long interval, hemoglobin levels and clinical negative nodal status, and post-chemoradiotherapy CEA levels for pathological complete response in patients with locally advanced rectal cancer after neoadjuvant chemoradiotherapy. J Oncol. (2020) 2020:9437684. doi: 10.1155/2020/9437684
- Huang CW, Tsai HL, Yeh YS, Su WC, Huang MY, Huang CM, et al. Robotic-assisted total mesorectal excision with the singledocking technique for patients with rectal cancer. *BMC Surg.* (2017) 17:126. doi: 10.1186/s12893-017-0315-x
- Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th Edition of the AJCC Cancer Staging Manual and the Future of TNM. *Ann* Surg Oncol. (2010) 17:1471–4. doi: 10.1245/s10434-010-0985-4
- Mace AG, Pai RK, Stocchi L, Kalady MF. American Joint Committee on Cancer and College of American Pathologists regression grade: a new prognostic factor in rectal cancer. *Dis Colon Rectum.* (2015) 58:32– 44. doi: 10.1097/DCR.00000000000266
- Adam IJ, Mohamdee MO, Martin IG, Scott N, Finan PJ, Johnston D, et al. Role of circumferential margin involvement in the local recurrence of rectal cancer. *Lancet.* (1994) 344:707–11. doi: 10.1016/S0140-6736(94)92206-3

- 26. Quirke P, Steele R, Monson J, Grieve R, Khanna S, Couture J, et al. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. *Lancet.* (2009) 373:821– 8. doi: 10.1016/S0140-6736(09)60485-2
- Quirke P. Training and quality assurance for rectal cancer: 20 years of data is enough. *Lancet Oncol.* (2003) 4:695– 702. doi: 10.1016/S1470-2045(03)01248-8
- Kwak JM, Kim SH. Robotic surgery for rectal cancer: an update in 2015. Cancer Res Treat. (2016) 48:427–35. doi: 10.4143/crt.2015.478
- Fransgaard T, Pinar I, Thygesen LC, Gogenur I. Association between robotassisted surgery and resection quality in patients with colorectal cancer. Surg Oncol. (2018) 27:177–84. doi: 10.1016/j.suronc.2018.03.003
- Shin US, Nancy You Y, Nguyen AT, Bednarski BK, Messick C, Maru DM, et al. Oncologic outcomes of extended robotic resection for rectal cancer. *Ann Surg* Oncol. (2016) 23:2249–57. doi: 10.1245/s10434-016-5117-3
- Brennan DJ, Moynagh M, Brannigan AE, Gleeson F, Rowland M, O'Connell PR. Routine mobilization of the splenic flexure is not necessary during anterior resection for rectal cancer. *Dis Colon Rectum.* (2007) 50:302–7; discussion 7. doi: 10.1007/10350-006-0811-z
- Dilday JC, Gilligan TC, Merritt CM, Nelson DW, Walker AS. Examining utility of routine splenic flexure mobilization during colectomy and impact on anastomotic complications. *Am J Surg.* (2019) 219:998– 1005. doi: 10.1016/j.amjsurg.2019.07.030
- 33. Huang CM, Huang MY, Tsai HL, Huang CW, Ma CJ, Yeh YS, et al. An observational study of extending FOLFOX chemotherapy, lengthening the interval between radiotherapy and surgery, and enhancing pathological complete response rates in rectal cancer patients following preoperative chemoradiotherapy. *Therap Adv Gastroenterol.* (2016) 9:702– 12. doi: 10.1177/1756283X16656690
- 34. Liang JT, Lai HS. Surgical technique of robotic D3 lymph node dissection around the inferior mesenteric artery with preservation of the left colic artery and autonomic nerves for the treatment of distal rectal cancer. *Surg Endosc.* (2014) 28:1727–33. doi: 10.1007/s00464-013-3340-6
- Matsuda K, Hotta T, Takifuji K, Yokoyama S, Oku Y, Watanabe T, et al. Randomized clinical trial of defaecatory function after anterior resection for rectal cancer with high versus low ligation of the inferior mesenteric artery. *Br J Surg.* (2015) 102:501–8. doi: 10.1002/bjs.9739
- 36. Fan YC, Ning FL, Zhang CD, Dai DQ. Preservation versus nonpreservation of left colic artery in sigmoid and rectal cancer surgery: a meta-analysis. *Int J Surg.* (2018) 52:269–77. doi: 10.1016/j.ijsu.2018. 02.054

- Hinoi T, Okajima M, Shimomura M, Egi H, Ohdan H, Konishi F, et al. Effect of left colonic artery preservation on anastomotic leakage in laparoscopic anterior resection for middle and low rectal cancer. *World J Surg.* (2013) 37:2935–43. doi: 10.1007/s00268-013-2194-3
- Chou JF, Row D, Gonen M, Liu YH, Schrag D, Weiser MR. Clinical and pathologic factors that predict lymph node yield from surgical specimens in colorectal cancer: a population-based study. *Cancer.* (2010) 116:2560– 70. doi: 10.1002/cncr.25032
- Persiani R, Biondi A, Gambacorta MA, Bertucci Zoccali M, Vecchio FM, Tufo A, et al. Prognostic implications of the lymph node count after neoadjuvant treatment for rectal cancer. *Br J Surg.* (2014) 101:133–42. doi: 10.1002/bjs.9341
- Cirocchi R, Trastulli S, Farinella E, Desiderio J, Vettoretto N, Parisi A, et al. High tie versus low tie of the inferior mesenteric artery in colorectal cancer: a RCT is needed. Surg Oncol. (2012) 21:e111–23. doi: 10.1016/j.suronc.2012.04.004
- Ubukata M, Itabashi M, Kameoka S. Japanese D3 lymph node dissection in low rectal cancer with inferior mesenteric lymph node metastases. World J Surg. (2014) 38:2724–9. doi: 10.1007/s00268-014-2617-9
- Yamamoto M, Okuda J, Tanaka K, Ishii M, Hamamoto H, Uchiyama K. Oncological impact of laparoscopic lymphadenectomy with preservation of the left colic artery for advanced sigmoid and rectosigmoid colon cancer. *Dig Surg.* (2014) 31:452–8. doi: 10.1159/000369938
- Yasuda K, Kawai K, Ishihara S, Murono K, Otani K, Nishikawa T, et al. Level of arterial ligation in sigmoid colon and rectal cancer surgery. World J Surg Oncol. (2016) 14:99. doi: 10.1186/s12957-016-0819-3
- 44. Maeda Y, Shinohara T, Futakawa N, Minagawa N, Sunahara M, Koyama R, et al. The oncologic outcomes of inferior mesenteric artery-preserving laparoscopic lymph node dissection for upper-rectal or sigmoid colon cancer. *J Laparoendosc Adv Surg Tech A*. (2018) 28:1352–8. doi: 10.1089/lap.2018.0201

**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright © 2020 Yin, Su, Chen, Chang, Chen, Li, Hsieh, Tsai, Huang and Wang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.