



Comparison of posterior rectal dissection techniques during rectosigmoid colon resection as part of cytoreductive surgery in patients with epithelial ovarian cancer: Close rectal dissection versus total mesorectal excision

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HIGHLIGHTS

- Clinical outcomes of posterior rectal dissection techniques were evaluated in patients with ovarian cancer.
- Compared to the traditional TME technique, CRD showed a low rate of anastomotic leakage and less frequent prolonged ileus.
- The pelvic recurrence and progression-free survival did not differ between the 2 groups.
- The CRD may be an alternative technique with less perioperative morbidity and equivalent oncologic outcomes.

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ABSTRACT

Objective. The aim of this study was to evaluate the clinical outcomes of close rectal dissection (CRD) compared with those of total mesorectal excision (TME) as the posterior rectal dissection procedure during rectosigmoid colectomy performed as part of cytoreductive surgery in patients with epithelial ovarian cancer.

Methods. We retrospectively reviewed the medical records of 163 patients who underwent posterior rectal dissection for rectosigmoid resection, including low anterior resection or subtotal colectomy, as part of ovarian cancer surgery from 2006 to 2018. The TME technique was mainly performed by colorectal surgeons, and the CRD technique preserving the mesorectal tissue was performed by an experienced gynecologic oncology surgeon. The patients were divided into the TME group and the CRD group, and their clinical outcomes were analyzed.

Results. A total of 163 patients with ovarian cancer underwent rectosigmoid colon resection. Among the patients, 87 (53.4%) underwent CRD and 76 (46.6%) underwent TME as the posterior rectal dissection technique. The disease severity according to FIGO stage ($p = .390$) and the residual disease status ($p = .412$) were not statistically different between the 2 groups. However, the postoperative incidences of anastomotic leakage ($p = .045$) and prolonged ileus (>7 days, $p = .055$) were higher in the TME group. The pelvic recurrence rate and progression-free survival did not differ between the 2 groups ($p = .663$ and $.790$, respectively).

Conclusions. Considering the perioperative outcomes, CRD may be an alternative technique for rectal dissection in ovarian cancer with less perioperative morbidity and equivalent oncologic outcomes.

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1. Introduction

Ovarian cancer remains the most lethal gynecologic cancer and is mainly diagnosed at an advanced stage [1]. Optimal cytoreductive surgery to no gross residual disease followed by platinum-based adjuvant chemotherapy has been the most effective therapeutic strategy in the treatment of advanced ovarian cancer [2,3]. Among various procedures

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for complete cytoreductive surgery, bowel surgery has been a crucial part of the debulking procedures for achieving no gross residual disease, as ovarian cancer often presents in an advanced stage and frequently involves the adjacent bowel [4–6]. By far, the most frequently involved bowel segment is the rectosigmoid colon, which needs to be removed for complete pelvic cytoreduction [7,8].

The total mesorectal excision (TME) technique has traditionally been used for rectosigmoid colon resection. It has been universally accepted as the preferred technique for surgical excision in rectal cancer [9]. Because the procedure completely removes the mesorectal tissues, TME results in lower rates of local recurrence in colorectal cancer [10,11]. However, the risks of anastomotic leakage and local infection have increased after the introduction of TME surgery [12,13]. In a study that recruited patients with benign diseases of the rectum, the close rectal dissection (CRD) technique was related to improved bowel function and lower frequency of anastomotic leakage. However, there are few studies on the techniques for posterior dissection of the rectosigmoid colon for patients with ovarian cancer. The biology of ovarian cancer differs from that of colorectal cancer, and ovarian cancer cells primarily disseminate within the peritoneal cavity and are superficially invasive in most cases [14]. Further, a positive margin status is not part of the treatment paradigm for ovarian cancer [15]. Therefore, the technique of posterior rectal dissection for patients with ovarian cancer needs to be examined.

In this study, we aimed to evaluate the clinical outcomes of CRD compared with those of TME as the posterior rectal dissection procedure during rectosigmoid colectomy as part of cytoreductive surgery in patients with epithelial ovarian cancer.

2. Materials and methods

In this retrospective study, patients with ovarian cancer who underwent rectosigmoid colon resection during cytoreductive surgery at Ajou University Hospital, Suwon, South Korea, from May 2005 to August 2018, were identified. In the study period, a total of 163 patients were identified to have undergone rectosigmoid colon surgery including low anterior resection (LAR) or subtotal colectomy as part of the debulking procedures. Patients were included consecutively regardless of the timing of debulking surgery (primary, interval, secondary, or tertiary debulking surgery). Moreover, patients who had 2-segment bowel surgeries including rectosigmoid resection were included. Except for patients with recurrent disease, most patients received paclitaxel (175 mg/m²) and carboplatin (area under the curve 5) for neoadjuvant or adjuvant chemotherapy. The study protocol was approved by the institutional review board.

For the posterior rectal dissection of the rectosigmoid colon, 2 techniques were adopted during the study period. One was TME in which the superior rectal artery was ligated and the dissection proceeded through the areolar avascular plane along the mesorectal fascia down to the pelvic floor. Another technique was CRD in which the superior rectal artery was not ligated, thus preserving the mesorectal tissue and vascular supply (Fig. 1). In CRD, the dissection was performed along the posterior rectal wall, generally by using advanced energy devices such as LigaSure® (Covidien Inc., Boulder, CO, USA) or Thunderbeat® (Olympus Medical Systems Corp., Tokyo, Japan). Both techniques were utilized in subtotal colectomy or LAR. The subtotal colectomy was defined as removal of the entire colon from terminal ileum to the sigmoid colon with ileorectal anastomosis. The TME technique was performed by experienced colorectal surgeons and the CRD technique was performed by an experienced gynecologic oncology surgeon during the study period. As a retrospective study, there were no institutional selection criteria for TME or CRD. Mainly, the technique was selected by the surgeon's preference. However, when bowel mucosal invasion was suspicious in the preoperative CT or Colonoscopy, we performed the TME technique. Since the TME technique was widely utilized in colorectal surgery, colorectal surgeons preferred the TME

technique. On the other hand, the gynecologic oncologic surgeon mainly focused on visual tumor removal and performed CRD preserving the mesorectum and around blood supply. After the surgery, bowel function was evaluated with simple abdominal radiography and diet was started after the patient had passed gas. Adjuvant chemotherapy was administered when the patient's wound healing was complete without any sign of infection and generally corresponded with completion of diet build-up. Most patients received adjuvant chemotherapy beginning 3–4 weeks postoperatively and discharged after the 1st adjuvant chemotherapy.

Clinical characteristics including age, histology, International Federation of Gynecology and Obstetrics (FIGO) stage, timing of surgery, and residual disease status were analyzed. The accompanying intestinal surgeries were also analyzed. For the evaluation of outcomes, the patients were divided into the TME group and the CRD group. Outcomes including packed red blood cell transfusion during surgery, operative time, anastomotic leakage, wound dehiscence, prolonged ileus (persisting for >7 days), hospital stay duration, and postoperative death within 30 days were evaluated. Lastly, pelvic recurrence rates and progression free survival rates were evaluated. Wound dehiscence was defined as the need to re-suture the wound after surgery. Anastomotic leakage was defined as drainage of fecal fluid or extravasations of anastomosis sites verified with computed tomography and the patients' clinical symptoms. Ileus was defined using the following criteria: nausea/vomiting, inability to tolerate diet, absence of flatus, abdominal distension, and features of ileus on imaging over 7 days.

Descriptive statistics were used to characterize the patient population and the type of intestinal surgery. The perioperative outcomes of the 2 groups were analyzed using the Mann-Whitney test or chi-square test. For the evaluation of risk of anastomotic leakage, univariate and multivariable analysis with logistic regression were performed to control for potential confounding variables. Survival analysis was performed with the Kaplan-Meier method. Progression-free survival was defined as the period from the date of surgery to the first observation of disease progression. Patients with no recurrence at the time of analysis, lost to follow-up for any reason or patients who died without progression were censored. All patients have monitored 3-month interval with a tumor marker. Abdominal computed tomography (CT) scan was performed when the tumor-marker elevated. When the CT scans show a suspicious result, positron emission tomography (PET) scan was also utilized. All the imaging results were interpreted with The Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Statistical analysis was performed with IBM SPSS Statistics for Windows (version 20.0; IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < .05$.

3. Results

A total of 163 patients were identified to have undergone posterior rectal dissection during the study period. The median age of the included patients was 56 years (range, 24–86 years). Most of the patients had FIGO stage III or IV disease with a serous histology (85.9%, 140 of 163). Rectosigmoid colon resection was performed mainly in primary debulking surgery (58.3%, 95 patients), followed by interval debulking surgery (37.4%, 61 patients) and secondary cytoreductive surgery (4.3%, 7 patients). Of the patients, 76 (46.6%) underwent TME and 87 (53.4%) underwent CRD as the posterior rectal dissection technique. After the cytoreductive surgeries, optimal cytoreductive surgeries were performed in 162 patients (99.4%), resulting in no gross residual disease in 133 patients (81.6%) and gross residual disease <1 cm in 29 patients (17.8%) (Table 1).

With respect to the type of intestinal surgery, 143 (87.7%) patients underwent LAR and 20 (12.3%) patients underwent subtotal colectomy. Among the patients who underwent LAR ($n = 143$), 26 patients had 2-segment bowel resection. The most common procedure was LAR with ileocectomy, followed by LAR with small-bowel resection, LAR with

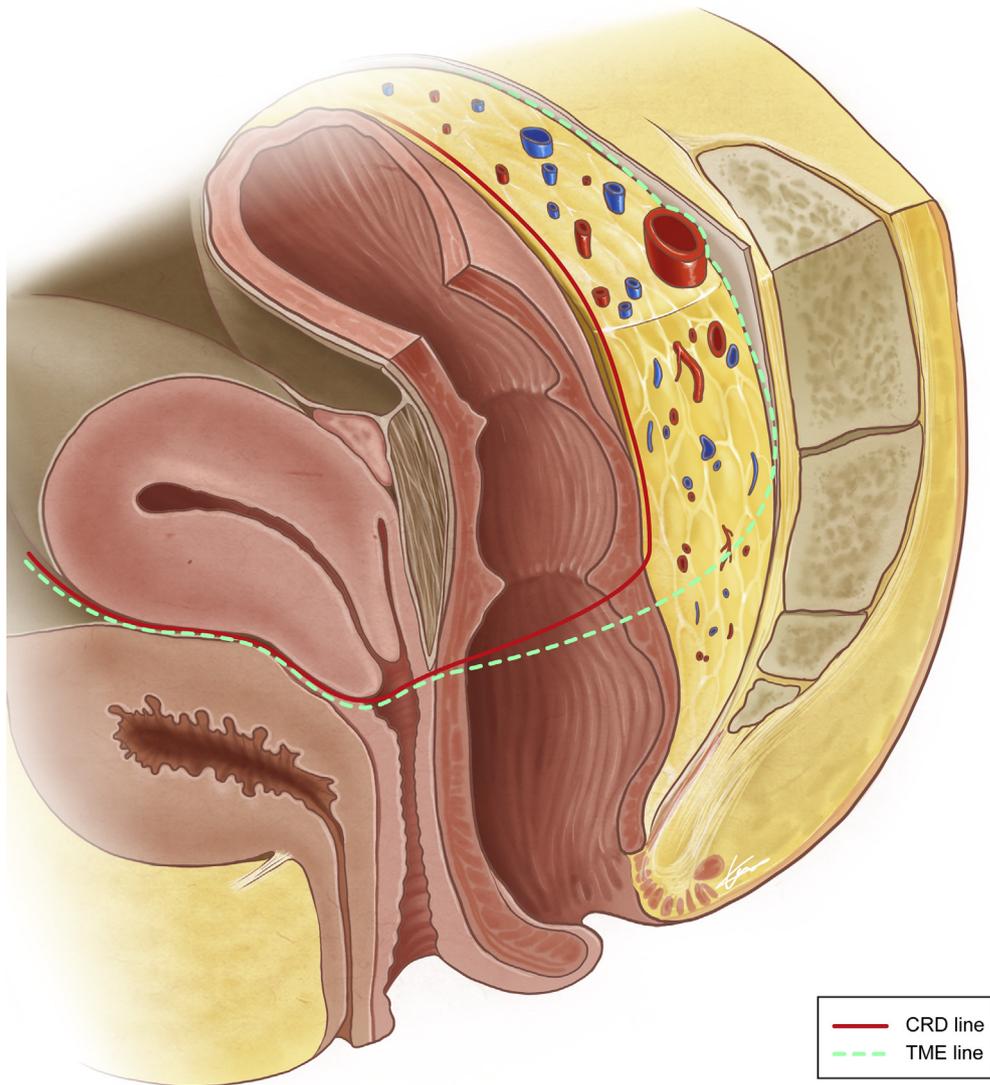


Fig. 1. Illustration of the dissection line of total mesorectal excision (TME) or close rectal dissection (CRD) for rectosigmoid colectomy.

right hemicolectomy, and LAR with transverse colon resection. Although most subtotal colectomies were performed in TME group ($p = .001$), 2-segment bowel resections were more common in the CRD group ($p = 0.077$). However, among patients who underwent LAR, the technique used was not statistically different ($p = .215$) (Table 2).

The perioperative outcomes were evaluated among patients who underwent TME or CRD. The incidence of intraoperative transfusion and the operative time were not different between the 2 groups. However, patients who underwent CRD had fewer anastomotic leakage events ($p = .045$). Also, although not significant, they had a lower incidence of prolonged ileus of >7 days, and shorter hospital stay ($p = .055$, and 0.096 , respectively). Events of anastomotic leakage were found in 2 patients who underwent subtotal colectomy, 1 patient who underwent LAR plus ileocecectomy, and 1 patient who underwent LAR plus transverse colon resection. The disease severity (FIGO stage), residual disease status, and short-term postoperative death incidence were not significantly different between the 2 groups. There was no procedure-related rectal injury in both groups (Table 3).

As risk factors for anastomotic leakage, postoperative hemoglobin level, subtotal colectomy and surgery type (TME) appeared in the univariate analysis. In multivariate analysis, only postoperative hemoglobin level remained as an independent risk factor (Table 4).

Recurrence after the surgery was compared between the 2 groups. The pelvic recurrence rate was not different between the 2 groups ($p = .663$). In the TME group ($n = 76$), 51 (67.1%) patients experienced disease recurrence and 6 patients experienced recurrence involving the pelvis (vaginal stump, pelvic lymph node, and perirectal area). In the CRD group ($n = 87$), 37 (42.5%) patients experienced disease recurrence and 3 patients experienced recurrence involving the pelvis (pelvic peritoneum). The progression-free survival time was not significantly different between the 2 groups (median, 22 vs. 26 months; $p = .790$) (Table 5) (Fig. 2).

4. Discussion

In this study, we analyzed the surgical outcomes of posterior rectal dissection techniques used in cytoreductive surgery for ovarian cancer. To our knowledge, this is the first report on rectal dissection techniques for patients with ovarian cancer. Among the techniques, CRD preserving the posterior mesorectum and vascular supply was related to improved perioperative outcomes in terms of anastomotic leakage rate or functional bowel recovery. Moreover, CRD showed comparable outcomes to the traditional TME technique in terms of local recurrence and progression-free survival.

Table 1
 Characteristics of patients who underwent posterior rectal dissection for rectosigmoid colon resection during cytoreductive surgery (N = 163).

Age (years), median, range	56 (24–86)
BMI	23.1 (17.7–31.3)
Medical co-morbidities	
Diabetes	12 (7.4%)
Cardiovascular disease	37 (22.7%)
Thromboembolic disease	2 (1.2%)
Liver disease	5 (3.1%)
Pulmonary disease	2 (1.2%)
Rheumatoid disease	3 (1.8%)
Thyroid disease	7 (4.3%)
Preoperative CA-125 (U/mL)	706.4 (10.5–9945.0)
Time of surgery	
Primary debulking surgery	95 (58.3%)
Interval debulking surgery	61 (37.4%)
Secondary cytoreductive surgery	7 (4.3%)
Technique of posterior rectal dissection	
TME	76 (46.6%)
CRD	87 (53.4%)
Intraoperative blood loss	1200 (200–9550)
RBC transfusion during operation (mL)	1000 (0–8250)
Histology	
Serous	140 (85.9%)
Non-serous	23 (13.1%)
FIGO stage	
I	18 (11.0%)
II	5 (3.1%)
III	103 (63.2%)
IV	37 (22.7%)
Residual disease	
NGR	133 (81.6%)
GR-1	29 (17.8%)
GR-B	1 (0.6%)
Interval from surgery to following chemotherapy (days)	19 (9–60)

Data are presented as median (range) or n (%).
 BMI, body mass index; TME, total mesorectal excision; CRD, close rectal dissection; FIGO, International Federation of Gynecology and Obstetrics; NGR, no gross residual disease; GR-1, gross residual disease <1 cm; GR-B, gross residual disease >1 cm.

For rectosigmoid colon resection, the TME technique has traditionally been utilized. It has been universally accepted as the preferred technique for surgical excision of rectal cancer [9]. The crucial point of TME is the excision of the entire rectum with blood vessels and surrounding lymph nodes within the visceral fascial layer. Because of the nature of this surgery, it has both advantages and disadvantages. As the procedure completely removes the mesorectal tissues, TME results in lower rates of local recurrence in colorectal cancer [10,11]. However, the risks of anastomotic leakage and local infection have increased after the introduction of TME surgery [12,13]. Compared with the CRD technique, after TME, the empty space resulting from the removal of mesorectal fat tissues are filled with pelvic fluid or hematoma. It has been reported that these components might act as risk factors for local infection and subsequent anastomotic leakage [13]. In our study, the frequency of anastomotic leakage was higher in the TME group (4 of 76, 5.3%) than in the CRD group (0 of 87, 0%) (p = .045). However, the TME technique itself was not an independent risk factor for anastomotic

Table 2
 Type of intestinal surgery and posterior rectal dissection technique (N = 163).

	TME (n = 76)	CRD (n = 87)	Total	p-Value
Subtotal colectomy	17 (22.4%)	3 (3.4%)	20 (12.3%)	0.001
LAR				
LAR only	51 (67.1%)	66 (75.9%)	117 (71.8%)	0.215
Two-segment resection	8 (10.5%)	18 (20.7%)	26 (15.9%)	0.077
LAR + ileocecectomy	3	11	14	
LAR + small-bowel resection	1	4	5	
LAR + right hemicolectomy	2	3	5	
LAR + transverse colon resection	2	0	2	

Data are presented as n (%).
 TME, total mesorectal excision; CRD, close rectal dissection; LAR, low anterior resection.

Table 3
 Patients characteristics and perioperative outcomes according to the posterior rectal dissection technique.

	TME (n = 76)	CRD (n = 87)	p-Value
Age	52 (31–78)	55 (24–86)	0.230
BMI	23.8 (17.8–30.5)	22.9 (17.7–31.3)	0.672
Medical co-morbidities			
Diabetes	4 (5.3%)	8 (9.2%)	0.383
Cardiovascular disease	18 (23.7%)	19 (21.8%)	0.779
Thromboembolic disease	0 (0%)	2 (2.3%)	0.499
Liver disease	2 (2.6%)	3 (3.4%)	1.000
Pulmonary disease	0 (0%)	2 (2.3%)	0.499
Rheumatoid disease	1 (1.3%)	2 (2.3%)	1.000
Thyroid disease	3 (3.9%)	4 (4.6%)	1.000
Intraoperative blood loss (mL)	1200 (300–9550)	1300 (200–6450)	0.917
RBC transfusion during operation (mL)	1000 (0–8250)	750 (0–5750)	0.116
Perioperative laboratory findings (g/dL)			
Albumin			
Preoperative	4.0 (2.3–5.0)	4.1 (2.6–4.7)	0.120
Postoperative (POD #1)	2.1 (1.2–3.4)	2.2 (1.0–3.8)	0.504
Hemoglobin			
Preoperative	12.1 (9.0–13.5)	11.3 (8.8–13.4)	0.111
Postoperative (POD #1)	12.8 (8.7–16.0)	12.6 (10.2–15.9)	0.772
Operative time (min)	430 (170–1060)	415 (190–680)	0.903
Anastomotic leakage	4 (5.3%)	0 (0%)	0.045
Wound dehiscence	0	2 (2.3%)	0.514
Prolonged ileus of >7 days	7 (9.2%)	3 (3.4%)	0.055
Hospital stay (days)	30 (15–80)	24 (10–91)	0.096
Residual disease			0.412
NGR	60 (78.9%)	73 (83.9%)	
GR-1	16 (21.1%)	13 (14.9%)	
FIGO stage			0.390
Stage I or II	12 (15.8%)	11 (12.6%)	
Stage III or IV	64 (84.2%)	76 (87.4%)	
Interval from surgery to following chemotherapy (days)	18 (11–60)	19 (9–32)	0.248
Number of adjuvant chemotherapy cycles	6 (1–9)	6 (2–8)	0.328
Postoperative death within 30 days	0	2 (2.3%)	0.112

Data are presented as median (range) or n (%).
 TME, total mesorectal excision; CRD, close rectal dissection; BMI, body mass index; RBC, red blood cell; POD, postoperative day; NGR, no gross residual disease; GR-1, gross residual disease <1 cm; FIGO, International Federation of Gynecology and Obstetrics.

leakage in multivariate analysis. Postoperative hemoglobin level was the most significant factor for anastomotic leakage. This result suggests the importance of adequate blood supply and tissue perfusion of anastomotic sites. Recent research suggests that mid and upper rectum is considerably more vascularized than the lower part, in which the posterior compartment might most vulnerable [16]. Moreover, available another data suggests that perfusion in the rectal stump than in the colonic limb may be more important for the integrity of the colorectal anastomosis

Table 4
Univariate and multivariate analysis for risk of anastomotic site leakage.

Risk factor	Univariate analysis	Multivariate analysis		
	p-value	HR	95% CI	p-Value
Age	0.232			
BMI	0.672			
Medical co-morbidities				
Diabetes	0.383			
Cardiovascular disease	0.779			
Thromboembolic disease	0.499			
Liver disease	1.000			
Pulmonary disease	0.499			
Rheumatoid disease	1.000			
Thyroid disease	1.000			
Preoperative CA-125	0.383			
Intraoperative estimated blood loss (mL)				
≤1200	Ref.			
>1200	0.997			
Intraoperative RBC transfusion (mL)				
≤1000	Ref.			
>1000	0.154			
Perioperative laboratory findings				
Albumin				
Preoperative	0.498			
Postoperative	0.306			
Hemoglobin				
Preoperative	0.624			
Postoperative	0.037	0.5	0.3–1.0	0.048
Operative time	0.903			
Surgery type				
LAR	0.215			
Two-segment resection	0.077			
Subtotal colectomy	0.001	7.6	0.9–63.7	0.061
Surgery technique				
TME	0.045	12.3	0.7–215.6	0.085
CRD	Ref.			
Wound dehiscence	1.000			
Prolonged ileus of >7 days	0.999			

HR, hazard ratio; CI, confidence interval; BMI, body mass index; RBC, red blood cell; LAR, lower anterior resection; TME, total mesorectal excision; CRD, close rectal dissection.

[17]. Considering the CRD technique preserves the rectal blood vessel in the mesorectum, it might be a reasonable alternative in terms of blood perfusion of the rectum without sacrificing oncologic outcome.

Currently, there have been few studies on the techniques for posterior dissection of the rectosigmoid colon, especially in patients with ovarian cancer. Nally et al. reported on the use of CRD in benign diseases of the rectum [18]. They performed a literature review on the CRD technique and analyzed the outcomes of CRD compared with those of TME in benign diseases of the rectum. The CRD technique was related to improved bowel and sexual function, as well as lower frequency of anastomotic leakage and infection. However, mesorectal tissue dissection was associated with a bleeding risk and potential risk of rectal wall injury. The CRD technique is sometimes considered time consuming with

Table 5
Recurrence rate in patients who underwent close rectal dissection or total mesorectal excision (N = 163).

	TME (n = 76)	CRD (n = 87)	p-Value
Recurrence site			0.663
Pelvis only	4 (5.3%)	1 (1.1%)	
Pelvis and middle/upper abdominal sites	2 (2.6%)	2 (2.3%)	
Middle or upper abdominal sites	45 (59.2%)	34 (39.1%)	
Total	51 (67.1%)	37 (42.5%)	
Progression-free survival, (95% CI), months	22 (14.0–30.0)	26 (17.4–34.5)	0.790

Data are presented as median (range) or n (%).

TME, total mesorectal excision; CRD, close rectal dissection; CI, confidence interval.

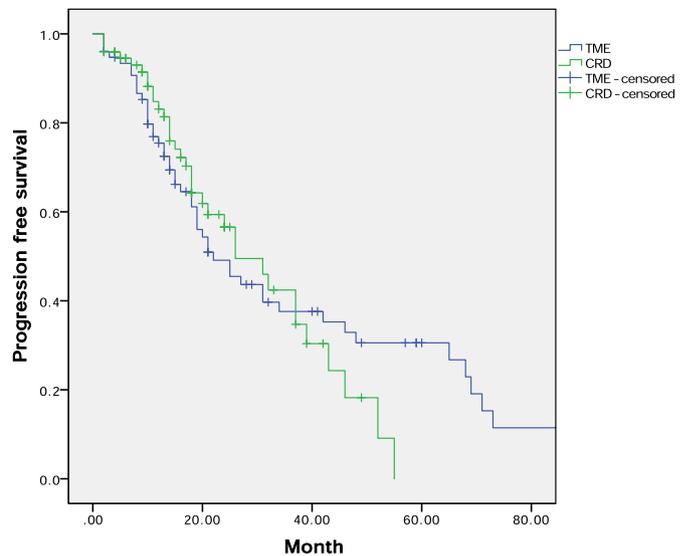


Fig. 2. Kaplan-Meier analysis of progression-free survival in patients who underwent total mesorectal excision (TME) or close rectal dissection (CRD) for posterior rectal dissection.

respect to the underlying vascular system of the perimuscular area. In contrast, during TME, bleeding might be minimized by controlling and dividing the inferior mesenteric artery at its aortic origin. However, this is no longer a worrisome problem, especially with the use of advanced hemostatic vessel sealing devices. In this study, although some patients had tumors on the mesorectal peritoneum, we performed mesorectal stripping, and mesorectal tissues were preserved with their vascular and neural supply in patients who underwent CRD. Consequently, there were no differences in bleeding events ($p = .116$) between the 2 groups, and prolonged ileus of >7 days occurred less frequently in the CRD group showing marginal statistical significance ($p = .055$). Moreover, there were no occurrences of intraoperative direct rectal injury in the CRD group during the study period.

Meanwhile, the dissemination of ovarian cancer is somewhat different from that of colorectal cancer. Especially, ascitic fluid and its flow dynamics are considered to be related to the dissemination mechanism. Tumor cells shed from the ovarian epithelium are disseminated in ascites and then flow in a clockwise pattern, resulting in peritoneal seeding [19]. Although ascites are related to peritoneal carcinomatosis, the biology of ovarian cancer differs from that of gastrointestinal tract cancers because ovarian cancer cells primarily disseminate within the peritoneal cavity and are superficially invasive in most cases [14]. Therefore, most of the lesions are superficial and resectable, allowing an effective surgical approach such as total peritonectomy or mesorectal stripping. Likewise, bowel involvement in ovarian cancer is mostly due to anterior lesions, whereas the posterior mesorectal tissues are seldom involved. As most patients with FIGO stage III or IV disease already have circulating peritoneal metastasis, microscopic margin status is not important like in colorectal cancer. Further, a positive margin status is not part of the treatment paradigm for ovarian cancer, as the surgical approach is focused on complete cytoreduction and achieving no gross residual disease rather than a clear margin status [15]. Accordingly, TME might be somewhat an overtreatment in patients with ovarian cancer who needs rectosigmoid colectomy, and CRD may be an alternative technique of colorectal surgery in these patients.

This study has several limitations. First, the retrospective nature of the study might inevitably induce a patient or treatment selection bias. Second, owing to the relatively small sample size, the findings should be confirmed in a larger patient cohort. Third, the long-term quality of bowel function was not evaluated and future studies are needed on this topic. However, we enrolled the patients consecutively

to minimize selection bias and the treatment was performed in a single institution with the same treatment policy during the study period.

In conclusion, TME might not be a suitable technique for rectosigmoid colon resection in ovarian cancer surgery. Considering the perioperative outcomes, CRD may be an alternative technique with less perioperative morbidity but with equivalent oncologic outcomes.

Conflict of interest statement

There are no conflicts of interest to disclose.

Author contributions

S.J. Chang contributed to the study design and critical revision of the manuscript. J.H. Son and T.W. Kong contributed to data analysis and manuscript writing. J. Kim and J. Shim contributed to data acquisition and analysis. J. Paek and H.S. Ryu contributed to study conception and critical revision of the manuscript. All authors approved the final manuscript.

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