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Outcomes of Laparoscopic Surgery in Colorectal Cancer Patients With Dialysis

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Abstract. *Background/Aim: To investigate the outcomes of laparoscopic surgery in colorectal cancer patients with dialysis. Patients and Methods: Fourteen dialysis (dialysis group) and 567 non-dialysis (non-dialysis group) patients who underwent laparoscopic and open surgery for colorectal cancer between April 2008 and December 2015 were included. Short-term and long-term outcomes were compared between the groups. A 1:2 propensity score matching was performed to compare long-term outcomes. Results: All the dialysis patients underwent laparoscopic surgery. There were no significant differences in operative outcomes and postoperative short-term outcomes between the two groups. In the whole cohort, overall survival of dialysis patients was shorter than that in the non-dialysis ones (p=0.020), while disease-free survival did not differ between the two groups. After matching, there was no significant difference between the groups in overall or disease-free survival. Conclusion: Laparoscopic colorectal cancer surgery for dialysis patients seems safe and feasible and associates with comparable short-term outcome and recurrence rate to non-dialysis patients.*

With the rapid growth of aging of the population in different societies, the number of patients with chronic kidney disease (CKD) who need to undergo dialysis is annually increasing worldwide, and it is estimated to continue to rise in the next years as well (1-3). It has been reported that CKD patients undergoing dialysis more frequently suffer from adverse postoperative outcomes, such as high morbidity rate and long hospital stay compared with those without receiving dialysis (4, 5). Postoperative complications and prognosis of patients on dialysis or patients with CKD have been implicated in some cancers (6, 7). CKD is associated with perioperative bleeding due to platelet dysfunction (8, 9). In addition, dialysis patients sometimes suffer from cardiovascular events as CKD is associated with an increased risk of cardiovascular diseases, such as myocardial infarction, heart failure, and stroke (9). In addition, dialysis patients have a tendency of acquiring an immune disorder (10). Once some infections (*e.g.*, pneumonia, anastomotic leakage, and surgical site infection (SSI) occur, the patients' clinical status is severely affected.

Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer-related death globally (11). Although different methods of surgery have been already proposed, laparoscopic surgery is rapidly becoming popular worldwide because of its superiority in short-term outcomes compared with open surgery. As previously reported, laparoscopic surgery for treatment of CRC could associate with shorter operative time, less intraoperative bleeding, and shorter postoperative hospital stay compared with open surgery (12). However, it is still unknown whether laparoscopic surgery can be effective in the treatment of CRC patients undergoing dialysis. Although Hu *et al.* have reported that the status of dialysis significantly increased postoperative morbidity, length of hospital stay, and mortality in CRC patients according to the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database (4), their study included several open surgeries.

We have already employed laparoscopic colorectal surgery for dialysis patients since 2008. In this study, we compared the surgical and oncological outcomes between dialysis patients who received laparoscopic surgery and non-dialysis patients who underwent open or laparoscopic surgery to

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Key Words: Dialysis, colorectal cancer, laparoscopic surgery, short-term outcome, overall survival.

Table I. *Patient and tumor characteristics*.

	Before matching			After matching		
	Non-dialysis (n=567)	Dialysis (n=14)	*p*-Value	Non-dialysis (n=28)	Dialysis (n=14)	*p*-Value
Age, median (range)	69.6 (28-95)	74.4 (64-83)	0.004	77.4 (64-93)	74.4 (64-83)	0.163
Sex, male, n (%)	334 (58.9)	7 (50.0)	0.504	14 (50.0)	7 (50.0)	1.000
BMI (kg/m^2), median (range)	22.5 (14.2-40.5)	20.7 (15.5-24.2)	0.080	23.0 (15.7-34.1)	20.8 (15.5-24.2)	0.031
Diabetes mellitus, n (%)	94 (16.6)	6 (42.9)	0.010	12 (42.9)	6 (42.9)	1.000
Hypertension, n (%)	248 (43.7)	12 (85.7)	0.001	23 (82.1)	12 (85.7)	0.770
ASA-PS, n (%)			<0.001			<0.001
<3	505 (89.0)	0 (0)		19 (67.9)	0 (0)	
≥3	62 (11.0)	14 (100)		9 (32.1)	14 (100)	
Tumor stage, n (%)			0.363			1.000
1 or 2	380 (67.0)	11 (78.5)		22 (78.6)	11 (78.5)	
3	187 (33.0)	3 (21.5)		6 (21.4)	3 (21.5)	
Approach, n (%)			0.056			N.S.
Open	118 (20.8)	0 (0)		0 (0)	0 (0)	
Laparoscopic	449 (79.2)	14 (100)		28 (100)	14 (100)	
Tumor location, n (%)			0.909			1.000
Colon	356 (62.8)	9 (64.2)		18 (64.3)	9 (64.2)	
Rectum	211 (37.2)	5 (35.8)		10 (35.7)	5 (35.8)	

BMI: Body mass index; ASA-PS: the American Society of Anesthesiologists-physical status; NS: not significant.

evaluate whether the less invasive laparoscopic surgery could be applied to dialysis patients.

Patients and Methods

Study subjects. We therefore investigated 840 patients who underwent surgery for CRC in Kobe University Hospital (Kobe, Japan) from April 1, 2008 to December 31, 2015 retrospectively. Of these, patients who underwent curative surgery on primary colorectal adenocarcinoma were eligible for analysis. However, the cases who had disseminated cancer, recurrent tumor, or underwent transanal endoscopic surgery were excluded. A total of 581 patients were eventually included in the present study. There were 14 patients who underwent dialysis (dialysis group), while the remaining 567 patients did not receive dialysis (non-dialysis group). The operative and postoperative outcomes were compared between these two groups. Patients were assigned into the dialysis group if they had chronic renal failure, and required hemodialysis at the day of surgery. Dialyses were performed by a nephrologist in the previous day of surgery and every two or three days after surgery at our hospital. After curative surgery, patients were investigated by blood testing every three or six months, contrast-enhanced computed tomography (CT) scan every six months, and colonoscopy every year. Tumor stage was determined according to the ninth edition of Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma. Perioperative complications within 30 days from surgery were evaluated according to the Clavien–Dindo classification (13).

Median follow-up period was 1438 days, and written informed consent was obtained from all the participants. This study was approved by the Ethics Committee of Kobe University Hospital as well.

Propensity score matching. To decrease the biases, originating from patients' characteristic, 1:2 propensity score matching was performed. Age (<65/65 years), sex (male/female), tumor location (colon/rectum), clinical cancer stage (stage I or II/stage III or IV), surgical procedure (open/laparoscopic), diabetes mellitus (yes/no), and hypertension (yes/no) were imported as independent variables into a multivariate logistic regression model. Dialysis status was included as a dependent variable. The nearest neighbor algorithm was used with a caliper of 0.2. No replacement was allowed and patients were matched only once.

Statistical analysis. Dialysis and other categorical variables (*e.g.*, patients' characteristics) were compared using chi-square test. The association of continuous variables in the two groups was analyzed by Student *t*-test. Disease-free survival (DFS) and overall survival (OS) were estimated by the Kaplan–Meier method and compared by log-rank test. The associations between postoperative complications and clinical factors were analyzed by multivariate logistic regression analysis. Tests were two-tailed and statistical significance was defined as $p<0.05$. All statistical analyses were performed by SPSS 22.0 software (IBM, Armonk, NY, USA)

Results

Table I shows the baseline characteristics of the patients and tumors. Dialysis patients were significantly older and more likely to have diabetes mellitus, hypertension, and severe systemic disease based on the American Society of Anesthesiologists (ASA-PS) physical status classification system than non-dialysis patients. There were no significant differences between the two groups in terms of sex, body mass index, tumor stage, and tumor location.

Table II. *Operative and postoperative results*.

	Non-dialysis (n=567)	Dialysis (n=14)	*p*-Value
Operative procedure, n (%)			0.967
Ileocecal resection	42 (7.4)	2 (14.2)	
Right hemicolectomy	120 (21.2)	3 (21.4)	
Transverse colectomy	29 (5.1)	0 (0)	
Left hemicolectomy	23 (4.0)	1 (8.3)	
Sigmoid colectomy	125 (22.0)	3 (21.4)	
Low anterior resection	162 (28.6)	4 (28.6)	
Abdominoperineal resection	47 (8.3)	1 (8.3)	
Hartmann's operation	17 (3.0)	0 (0)	
Total colectomy	2 (0.4)	0 (0)	
Operative time (min), median (range)	315.7 (105-1513)	262.5 (136-434)	0.201
Blood loss (ml), median (range)	306.2 (0-11068)	54.6 (0-200)	0.329
Blood transfusion (ml), median (range)	109.6 (0-5320)	0 (0-0)	0.353
Resected lymph nodes, median (range)	20.9 (0-192)	17.7 (2-39)	0.450
Complications			
Superficial SSI, n (%)	52 (9.1)	1 (7.1)	0.795
Deep SSI, n (%)	40 (7.0)	0 (0)	0.303
Ileus, n (%)	42 (7.4)	1 (7.1)	0.970
Pneumonia, n (%)	8 (1.4)	0 (0)	0.654
Postoperative death, n (%)	7 (1.2)	0 (0)	0.905
Postoperative hospital stay (days), median (range)	21.6 (5-188)	16.5 (11-26)	0.351

SSI: Surgical site infection.

The operative and postoperative results are shown in Table II. Although all 14 dialysis patients underwent laparoscopic surgery, differences in the rate of the undergoing laparoscopic surgery between the two groups was not statistically significant. There were no significant differences between the two groups in terms of operation time, blood loss, number of resected lymph nodes, and blood transfusion. There was also no significant increase in morbidities in dialysis patients compared with non-dialysis ones. Moreover, the length of postoperative hospital stay did not differ between the two groups.

The univariate logistic regression analysis showed that postoperative morbidity higher than grade III, based on Clavien–Dindo classification, was significantly associated with male patients, surgery for CRC, and open surgery, while association with dialysis was not confirmed (Table III). Among them, surgery for CRC and open surgery were also associated with severe morbidities by multivariate logistic regression analysis (Table III).

The Kaplan–Meier analysis showed that dialysis patients had significantly shorter OS than non-dialysis ones (Figure 1a). There were two cancer-related deaths and two non-cancer-related deaths because of pneumonia or enteritis in the dialysis patients. However, there was no significant difference in DFS between the two groups (Figure 1b). After applying 1:2 propensity score matching, no significant difference in OS was found between the two groups (Figure 2).

Discussion

In the present study, we analyzed the influences of laparoscopic colorectal surgery on dialysis and non-dialysis patients in a single institution. We found that there were no significant differences in operative results, postoperative complications, postoperative hospital stay, and mortality rate between the two groups. Hu *et al*. reported that dialysis status significantly contributes to postoperative morbidity, length of stay in hospital, and mortality in surgery for CRC by using the ACS-NSQIP database (4), and also reported that the rate of laparoscopic surgery in dialysis patients was only 33%. However, in the present study, all the dialysis patients received laparoscopic surgery. Hence, the difference in the results of these two studies might be attributed to the difference in the accomplishment rate of laparoscopic surgery.

In terms of laparoscopic surgery for dialysis patients, only a limited number of studies could be reached. Rao *et al*. reported that elective laparoscopic cholecystectomy in dialysis patients showed significantly higher rate of mortality and complication compared with non-dialysis patients (14). On the other hand, Lee *et al*. reported the safety of laparoscopic radical gastrectomy for gastric cancer patients with end-stage renal disease (15). They found that the postoperative morbidity for laparoscopic and open gastrectomy was comparable and no significant difference was observed in the long-term OS between the two groups.

Table III. *Association between postoperative complications and clinical factors.*

		Univariate analysis			Multivariate analysis		
	Number	HR	95%CI	*p*-Value	HR	95%CI	*p*-Value
Age		0.779	0.466-1.301	0.340			
<65	156						
≥65	425						
Gender		1.768	1.062-2.944	0.028	1.569	0.928-2.637	0.093
Female	240						
Male	341						
BMI (kg/m^2)		0.848	0.248-2.902	0.793			
<30	556						
≥30	25						
Dialysis		0.475	0.061-3.683	0.476			
No	567						
Yes	14						
Diabetes mellitus		0.923	0.488-1.746	0.806			
No	481						
Yes	100						
Hypertension		1.073	0.668-1.722	0.771			
No	321						
Yes	260						
ASA-PS		0.942	0.462-1.918	0.868			
<3	505						
≥3	76						
Tumor stage		1.538	0.949-2.495	0.081			
1 or 2	391						
3	190						
Surgical procedure		2.459	1.472-4.107	0.001	2.438	1.448-4.103	0.001
Laparoscopic	463						
Open	118						
Tumor location		2.077	1.291-3.343	0.003	1.969	1.210-3.204	0.006
Colon	365						
Rectum	216						

BMI: Body mass index; ASA-PS: the American Society of Anesthesiologists-physical status.

Laparoscopic surgery possesses the advantages of small incisions, as well as decreased blood loss, pain, and discomfort (16). Moreover, laparoscopic surgery is independently associated with a reduced SSI compared with open surgery (17). In the present study, multivariate logistic regression analysis showed that laparoscopic surgery is associated with less postoperative complications, and even in dialysis patients, effectively reduces postoperative complications.

The association between postoperative complications and poor cancer-related prognosis has been reported in esophageal cancer, gastric cancer, and also CRC (18-21). Postoperative intra-abdominal infectious complications and perioperative blood loss suppresses immune function (21, 22). This immune suppression is a possible contributing factor to cancer recurrence. For dialysis patients who are in an immune suppressive condition, an effort to decrease postoperative complication is of great importance and may result in a better prognosis. Consequently, laparoscopic surgery might be a helpful therapeutic approach for dialysis patients with CRC.

In the survival analysis, dialysis patients had significantly poorer OS than non-dialysis patients, however, there were no significant differences in DFS. Besides, 2 out of 4 deaths in the dialysis patients were caused by non-cancerous diseases, such as pneumonia and enteritis. In the presence of a difference in OS between the two groups due to their characteristics (*e.g.*, comorbidity or general condition), we performed the 1:2 propensity score matching to reduce the biases. As a result, the difference in OS between the two groups disappeared. Therefore, it cannot be concluded that the patients may have poor OS just because they undergo dialysis. Careful follow-up should also be taken if the patients have several comorbidities, such as hypertension or diabetes mellitus.

There are some limitations in this study. First, the sample size was small, thus the risk of perioperative complication in dialysis patients might be underestimated. Secondly, since all the surgeries in dialysis patients were performed laparoscopically, we were not able to compare laparoscopic

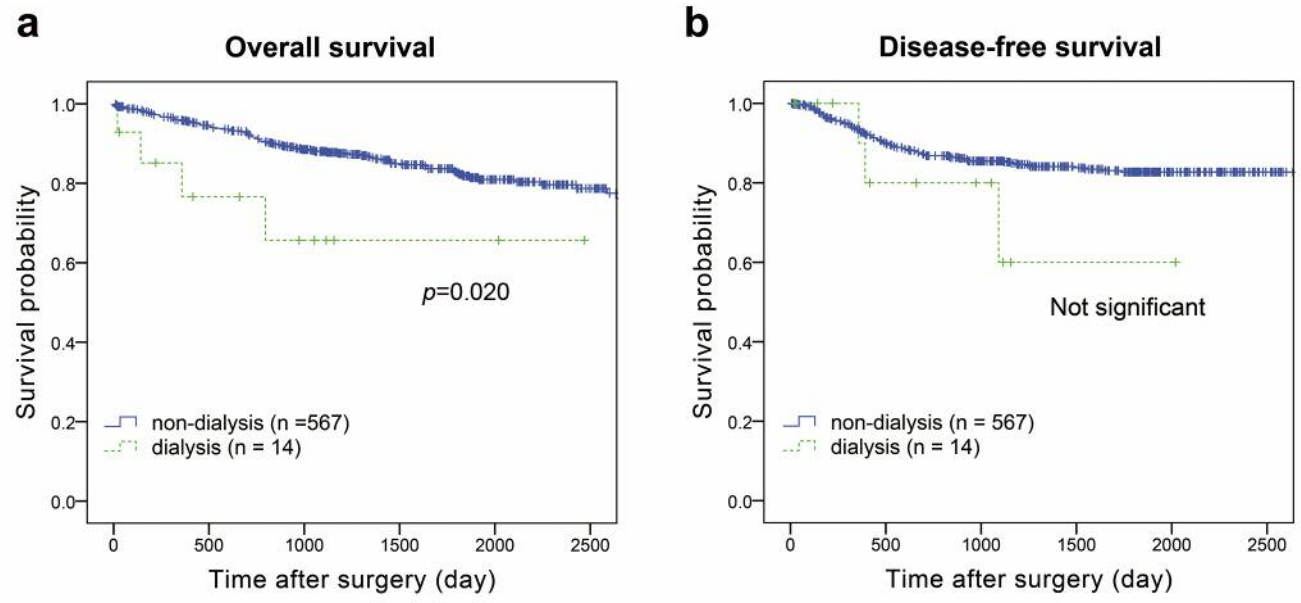

Figure 1. *Kaplan–Meier analysis of the overall survival (a) and disease-free survival (b) in all patients.*

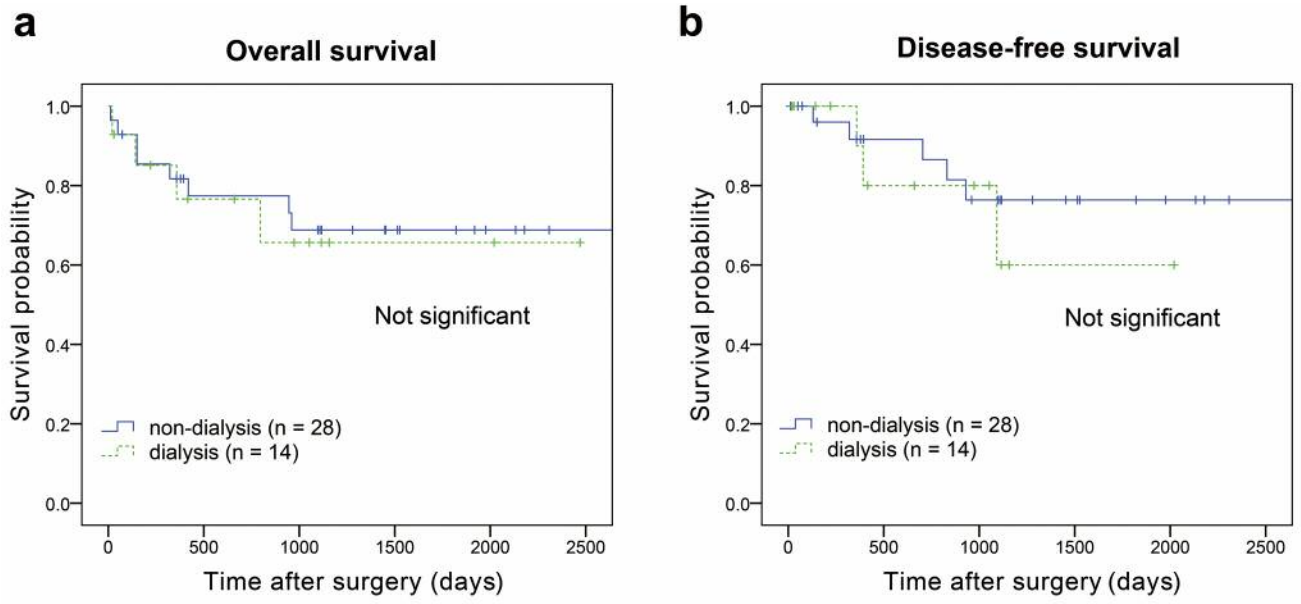

Figure 2. *Kaplan–Meier analysis of the overall survival (a) and disease-free survival (b) in matched patients.*

surgery with open surgery in dialysis patients. Despite these limitations, our study presented significant short- and long-term data for dialysis patients undergoing surgery for CRC in a single institution.

In conclusion, laparoscopic surgery for colorectal cancer patients with dialysis is safe and feasible with comparable short-term outcomes and recurrence rate to non-dialysis ones. Although careful selection of eligible patients needs to be carried out, it might possess the advantage of being minimally invasiveness.

Conflicts of Interest

The Authors declare that they have no conflicts of interest regarding this study.

Authors' Contributions

NH and TM designed the study. NH, TM, KY, HH, HS, MF and MY performed operation and collected data. NH wrote the initial draft of the manuscript. SK, TO, TN and SS contributed to analysis and interpretation of data. TM and YK critically reviewed the manuscript. All Authors approved the final version of the manuscript.

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