

Original Article

# The Clinical Outcomes of Surgical Resection for Primary Colorectal Cancer Patients with End Stage Renal Disease

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## Key Words

Colorectal cancer;  
Chronic kidney disease;  
End-stage renal disease;  
Clinical outcomes

**Purpose.** Chronic kidney disease is a major health problem affecting populations worldwide, especially end-stage renal disease, may be an obstacle for colorectal cancer patients after surgical resection. The aim of the current study was to evaluate the clinical outcomes of patients with colorectal cancer who have end-stage renal disease following surgical resection.

**Patients and Method.** We retrospectively analyzed 29 colorectal cancer patients with end-stage renal disease who underwent surgical resection between 2008 and 2013, of which the complete medical record of these patients was reviewed.

**Results.** They were predominantly male patients (65%) and the median age was 70 years (range 53-88). The incidence of comorbid illness was relatively high, such as hypertension (72%), diabetes mellitus (45%), and cardiovascular disease (31%). The most frequent location of primary tumor was sigmoid colon. The complication rates were higher in end-stage renal disease group (34%) than non end-stage renal disease group (16%,  $p = 0.008$ ). Postoperative cardiovascular complication in end-stage renal disease group (10.5%) was higher than non end-stage renal disease group (1.8%,  $p = 0.002$ ). The others complications such as anastomotic leakage, surgical wound infection, enterocutaneous fistula, ileus, bleeding and cerebrovascular accident occurred in 3.5% to 7% of studied in end-stage renal disease group. The five-year overall survival demonstrated 1-year was 86%, 2-years was 66%, 3-years was 53%, 4-years was 24% and 5-years was 24%.

**Conclusions.** From the present results, we concluded that colorectal cancer patients with end-stage renal disease who underwent surgical resection must be aware of the significantly high incidence of postoperative adverse events, especially cardiovascular complications, and clinicians should keep this issue in mind.

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Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate. Based

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on guidelines of the National Kidney Foundation, CKD staging system essentially classified patients into 1 of 5 categories (stage 1-5). According to the classification, end-stage renal disease (ESRD) was classified into term of stage 5 (GFR < 15 mL/min per 1.73 m<sup>2</sup>).<sup>1,2</sup> ESRD is associated with higher risks of cardiovascular disease, infection, malignancy, mortality, lower quality of life and increased economic burden.<sup>3</sup> Using the National Health Insurance (NHI) database of all ESRD patients on maintenance dialysis registered from July 1997 to December 2005, we determined the total lifetime cost for peritoneal dialysis patients (US\$ 139,360 ± US\$ 8,336) and hemodialysis patients (US\$ 185,235 ± US\$ 9,623).<sup>4</sup> According to the United States Renal Data System, the incidence of CKD in countries with rising living standards around the world is increasingly high, especially in Taiwan, which has the highest incidence and prevalence rates of ESRD in the world. The prevalence of ESRD reached 2447 per million in 2009 in Taiwan, while rates of 1811 per million has been reported in the United States. Likewise, Hsu et al. reported that the prevalence of CKD stages 3 to 5 in Taiwan was 6.43%, which was significantly higher than the 3.83% to 4.39% determined in the United States.<sup>5</sup>

In Taiwan, malignant neoplasm is the first leading cause of death, of which colorectal cancer (CRC) ranked third. Multiple various comorbidities including ESRD in CRC patients have been reported previously.<sup>6</sup> Nonetheless, there is still a lack of relevant information on the outcomes of CRC patients with ESRD following surgical resection. Therefore, the aim of the current study was to retrospectively investigate surgical morbidity/mortality and clinical outcomes after surgical resection of primary CRC with ESRD.

## Materials and Methods

This is a retrospective descriptive study analyzing data between January 2008 and December 2013. Of these 629 CRC patients, twenty-nine (4.6%) patients were diagnosed as CRC who had ESRD and underwent surgical resection. All patients underwent maintained hemodialysis. We excluded cases with emer-

gency surgery, other coexisting malignancies that were surgically removed simultaneously with colorectal resection. Various parameters analyzed including clinical variables, surgical procedures, postoperative complications, postoperative recurrence, days of intensive care unit and hospitalization after surgery, death and/or the last visit to the hospital were obtained from medical records. The pathological description of CRC was essentially based on the TNM classification.<sup>7</sup>

## Statistical Analysis

All data were analyzed using the Statistical Package for the Social Sciences version 12.0 software (SPSS Inc., Chicago, IL, USA). Descriptive variables of patient characteristics, clinical variables, surgical procedures, postoperative complications, postoperative recurrence, days of intensive care unit and hospitalization after surgery, death and/or the last visit to the hospital were calculated directly from the database. The Chi-Squared test of Fisher's exact test was used to compare complication rates of ESRD group with non-ESRD group in CRC patients. A probability of less than 0.05 was considered statically significant. The overall survival was calculated using the Kaplan-Meier method and compared by Log-rank test.

## Results

The characteristics of these 29 patients are summarized in Table 1. They were predominantly male (65%) and the median age was 70 years (range 53-88). The comorbid illness included hypertension (72%), diabetes mellitus (45%), and cardiovascular disease (31%). The most frequent location of primary tumor was the sigmoid colon (31%). For histological examination, moderated differentiated adenocarcinomas (69%) were the most common histology. The most common involved depth of tumor invasion was T3 (52%) and lymph nodes involvement status was N0 (52%). Only one CRC patient was diagnosed as distant metastasis initially. The most common tumor stage was stage III (45%). According to Table 2, the

right hemicolectomy (28%) was the most common surgical procedure, followed by anterior resection (24%) and low anterior resection (21%). Additionally, three patients (10.3%) had undergone palliative surgical procedure that included the Hartmann procedure and segmental resection due to advanced stage or oc-

curred unstable hemodynamic changes when operation was undergoing.

Table 3 demonstrated details of outcomes in CRC patients with ESRD. Ten of 29 (34%) patients developed postoperative complications. Postoperative complications such as anastomosis leakage, surgical wound infection, enterocutaneous fistula, ileus, cardiovascular complications, bleeding and cerebrovascular accident are described in Table 3. The mean duration of intensive care unit and hospital stay after surgery were 2.25 days and 21.45 days. Fortunately, all patients were discharged uneventfully after surgery. No surgical mortality was noted among these patients during the hospital stay. Only one patient (3.4%) developed local recurrence, and three patients (10.3%) were found to have distant metastasis after primary surgical resection. Fig. 1 demonstrated that overall survival was 86% in 1st year, 66% in second year, 53% in third year, 24% in fourth year and 24% in fifth year. All the included patients received regular follow up till May 2014. The complication rates of ESRD group with

**Table 1.** Clinical and pathologic profile of CRC with ESRD

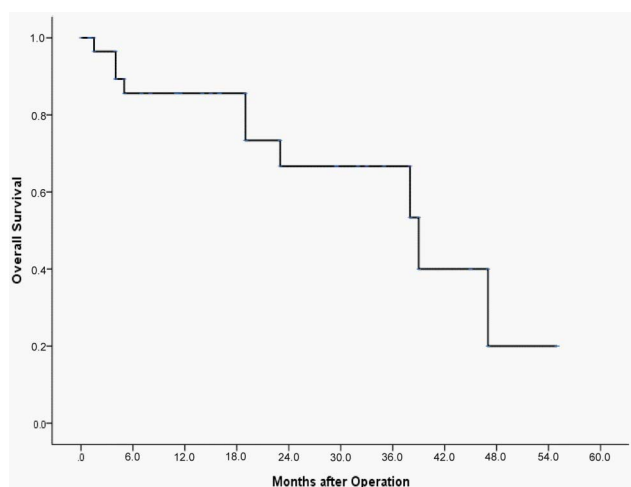
Sex (Male:Female)	16 (65%):13 (35%)
Age, years	70.29
Male	70.44
Female	71.23
Comorbid disease, n (%)	
Hypertension	21 (72)
Diabetes mellitus	13 (45)
Cardiovascular disease	9 (31)
Hepatitis or liver cirrhosis	8 (28)
Peptic ulcer history	6 (21)
Other malignancy	6 (21)
Endocrine disease	2 (7)
Autoimmune disease, such as SLE	2 (7)
Location of primary tumor, n (%)	
Ascending colon	6 (21)
Transverse colon	5 (17)
Descending colon	3 (10)
Sigmoid colon	9 (31)
Rectum	6 (21)
Tumor size, n (%)	
< 5 cm	19 (65)
> 5 cm	10 (35)
Tumor differentiation, n (%)	
Well	6 (21)
Moderated	20 (69)
Poor	3 (10)
Depth, n (%)	
T1	7 (24)
T2	6 (21)
T3	15 (52)
T4	1 (3)
Regional lymph node metastasis, n (%)	
N0	15 (52)
N1	9 (31)
N2	5 (17)
Distant metastasis, n (%)	
M0	28 (97)
M1	1 (3)
Initial TNM stage, n (%)	
I	10 (35)
II	5 (17)
III	13 (45)
IV	1 (3)

**Table 2.** Details of operative procedures, n (%)

Right hemi-colectomy	8 (28)
Anterior resection	7 (24)
Low anterior resection	6 (21)
Left hemi-colectomy	3 (10)
Extended right hemi-colectomy	2 (7)
Hartmann procedure	2 (7)
Segmental resection	1 (3)

**Table 3.** Outcomes of postoperative course of colorectal surgery for patients who had ESRD

Variable	
Complications	10 (34%)
Anastomosis leakage	2 (7%)
Surgical wound infection	1 (3.5%)
Enterocutaneous fistula	1 (3.5%)
Ileus	1 (3.5%)
Cardiovascular complications	3 (10.5%)
Bleeding	1 (3.5%)
Cerebrovascular accident	1 (3.5%)
ICU stay, day	2.25
Hospital stay, day	21.45
30 days Surgery related mortality	0 (0%)
Post operative local recurrence	1 (3.5%)
Post-operative distant metastasis	3 (10.3%)



**Fig. 1.** Overall survival of CRC patient with ESRD after surgical resection.

non-ESRD group in CRC's patients are listed in Table 4. The complication rates of ESRD group (34%) was markedly higher than non-ESRD group (16%) with significant difference between the groups ( $p = 0.008$ ). Among 10 patients with postoperative complications in ESRD group, cardiovascular complications (10.5%) were most commonly encountered in compared with non-ESRD group (1.8%) with significant difference ( $p = 0.002$ ).

## Discussion

ESRD is recognized as a major health problem affecting populations worldwide. Prevalence of ESRD continues to increase, reflecting the continuously growing elderly population and increasing numbers of patients with diabetes and hypertension. Such a phenomenon

was similar to our investigation, as the median age of 70 years was found in our series. As well as this, hypertension, diabetes mellitus and cardiovascular disease were the most common comorbid illnesses in CRC patients. Robert et al. reported ESRD is associated with a number of serious complications, including increased incidence of cardiovascular disease, hyperlipidemia, anemia and metabolic bone disease.<sup>8</sup>

Several studies have revealed maintenance dialysis for ESRD is at a higher risk of postoperative complications after major surgery.<sup>9-13</sup> Additionally, Toh et al. also demonstrated postoperative morbidity and mortality rates were much higher in emergency abdominal surgery than elective operations in patients on hemodialysis.<sup>14</sup> In our series, the overall complications rates was 34% in ESRD group, higher than non ESRD group (16%,  $p = 0.008$ ), similar to a previous study.<sup>15</sup> Cardiovascular complications (10.5%) were most commonly in ESRD group compared with non ESRD group (1.8%) in significant difference ( $p = 0.002$ ). Subsequently, the incidences (3.5% to 7%) of complications were as follows: anastomotic leakage, surgical wound infection, ileus, bleeding, and cerebrovascular accident in ESRD group. Previously Hiroaki et al. reported that perioperative cardiovascular complications were more frequent in the CKD stages 3 to 5 groups (5.3%) than those in the stages 0 to 2 groups (0.8%).<sup>16</sup> But, studies about the relationship between each cardiovascular complication rate and chronic kidney disease stage after abdominal surgery are still lacking. Based on the results of our studies, five-year overall survival of CRC patients with ESRD after surgical resection was poor. This result was also demonstrated in Hiroaki et al. with poorer overall survival in

**Table 4.** Complication rates of ESRD group with non ESRD group in CRC's patients

	ESRD (n = 29)	Non-ESRD (n = 600)	p value
Total complications, n (%)	10 (34%)	96 (16%)	0.008
Anastomosis leak, n (%)	2 (7%)	19 (3.2%)	0.275
Surgical wound infection, n (%)	1 (3.5%)	28 (4.7%)	0.582
Enterocutaneous fistula, n (%)	1 (3.5%)	10 (1.7%)	0.475
Ileus, n (%)	1 (3.5%)	20 (3.3%)	0.973
Cardiovascular complications, n (%)	3 (10.5%)	11 (1.8%)	0.002
Bleeding, n (%)	1 (3.5%)	9 (1.5%)	0.413
Cerebrovascular accident, n (%)	1 (3.5%)	3 (0.5%)	0.051

the chronic kidney disease stage 5 group.<sup>16</sup>

In our current observations, no surgery-related mortality was identified and the patients had favorable recovery and were successfully discharged from hospital. Unfortunately, one patient was found to have local recurrence and he has undergone chemotherapy till the present time. Three patients were found to have distant metastasis (brain, lung and liver) after operation and chemotherapy plus target agent was administered. One of the limitations in this study was the relatively small number of patients in the CRC who had ESRD. Second, this study was a retrospective cohort. Hence, a prospective, large-scale study is warranted on the results.

In conclusion, our present work would demonstrate the high surgical morbidity of primary CRC with ESRD after surgery. Surgeons should keep this in mind while performing resection of tumor for CRC patients and inform patients of the high possibility of postoperative complications.

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原 著

## 原發型大腸直腸癌合併末期腎臟疾病的病人 在手術切除後的臨床結果

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**目的** 慢性腎衰竭是一個影響全世界的主要健康問題，尤其是末期腎臟疾病，對於大腸直腸癌的病人在手術切除以後或許是一個障礙。這個研究的主要目的就是要評估大腸直腸癌合併末期腎臟疾病的病人在手術切除以後的臨床結果。

**病人和方法** 從 2008 至 2013 年間，我們回顧性分析了 29 個經過手術切除的直腸癌合併末期腎臟疾病的病人，這些病人都經過完整的病歷審查。

**結果** 這些病人中，主要是男性病人 (65%)，平均年齡是 70 歲 (範圍 53-88)。合併症的機率相當高，其中高血壓 72%，糖尿病 45% 和心臟血管疾病 31%。最常見的位置是乙狀結腸。發生在大腸直腸癌合併末期腎臟疾病組的術後併發症 (34%) 比非末期腎臟疾病的大腸直腸癌組 (16%， $p = 0.008$ ) 來的高。術後心臟血管疾併發症在大腸直腸癌合併末期腎臟疾病組 (10.5%) 也比非末期腎臟疾病的大腸直腸癌組 (1.8%， $p = 0.002$ ) 來的高。大腸直腸癌合併末期腎臟疾病組的其它併發症如吻合處滲漏，手術傷口感染，腸皮膚瘻管，腸阻塞，出血，腦血管疾病等等，這些併發症佔了 3.5%-7% 的發生率。這些經過手術切除的直腸癌合併末期腎臟疾病的病人，其 5 年存活率分別為第 1 年 (86%)，第 2 年 (66%)，第 3 年 (53%)，第 4 年 (24%) 以及第 5 年 (24%)。

**結論** 從這些結果來看，我們總結了大腸直腸癌合併末期腎臟疾病的病人在經過了手術切除以後，術後併發症的高發生率要有警覺心，外科醫師必須牢記這個議題。

**關鍵詞** 大腸直腸癌、慢性腎衰竭、末期腎臟疾病、臨床結果。