#### **Original** Article

# Mortality Risk and Related Factors of Stage I Colorectal Cancer Patients Death Risk and Related Factors in Stage I Colorectal Cancer Patients: A Nationwide Population-based Study

Ming-Hao Hsieh<sup>1,2</sup> Pei-Tseng Kung<sup>3,4</sup> Wen-Yin Kuo<sup>2</sup> Tao-Wei Ke1 Wen-Chen Tsai<sup>2</sup> <sup>1</sup>Division of Colon & Rectal Surgery, Department of Surgery, China Medical University Hospital, <sup>2</sup>Department of Health Services Administration, China Medical University, <sup>3</sup>Department of Health Administration, Asia University, <sup>4</sup>Department of Medical Research, China Medical University Hospital, China Medical University, Taichung, Taiwan Key Words

Stage I colorectal cancer; Mortality risk; Risk factors **Purpose.** In Taiwan, incidence of colorectal cancer ranks first among the top ten cancers and its mortality ranks third. Probability of post-treatment recurrence or metastasis is low in early-stage colorectal cancer patients. However, clinical observations exhibit an increased mortality risk for some early-stage colorectal cancer patients, possibly owing to lack of follow up by medical units or other risk factors. We aimed to examine the mortality risk and ratio and mortality-related factors in stage I colorectal cancer.

*Methods.* This retrospective study included patients registered at the Taiwan Cancer Registry of the Health Promotion Administration during 2007-2012. The database was linked to the National Health Insurance Research Database; subjects were followed up until the end of 2016. Mortality risk and other related factors in stage I colorectal cancer patients were evaluated using bivariate analysis (log-rank test and Cox proportional hazards model) according to demographic characteristics; economic, environmental, and health factors; treatment modalities and hospitals; and absence/presence of periodic follow up.

**Results.** The 5-year mortality rate of stage I colorectal cancer was 2.54%. Risk factors for stage I colorectal cancer mortality were prevalent in patients aged > 75 years with comorbidity index  $\ge$  2 points and presence of rectal lesions. Conversely, undergoing one or more colonoscopies within 2 years after surgery can reduce stage I colorectal cancer risk.

*Conclusion.* Age, comorbidity index, and tumor site are significantly related to the prognosis of stage I colorectal cancer, and periodic colonoscopy can decrease the mortality risk of stage I colorectal cancer. [*J Soc Colon Rectal Surgeon (Taiwan) 2020;31:168-177*]

The global incidence of colorectal cancer has been increasing year by year. In 2015, the incidence of colorectal cancer ranked third and second in global cancer incidence in males and females, respectively.

Every year, there are 1.65 million newly diagnosed colorectal cancer patients and 830,000 deaths due to colorectal cancer.<sup>1</sup> The incidence of colorectal cancer is higher in developed countries. In Taiwan, diet west-

Received: March 5, 2020. Accepted: April 28, 2020.

Correspondence to: Dr. Ming-Hao Hsieh, No. 49, Ln. 212, Sec. 2, HanXi West Road, Taiping District, Taichung City, Taiwan. Tel: 886-921926401; E-mail: minghao620@gmail.com

ernization, obesity, and lack of exercise have caused the rapid increase of incidence and mortality of colorectal cancer yearly. In Taiwan, the incidence of colorectal cancer ranked first among all cancers. In 2015, 19,226 people developed colorectal cancer (including stage 0). In the same year, 5687 people died due to colorectal cancer, which ranked third among malignancies.<sup>2</sup>

On the other hand, the post-treatment survival rate for colorectal cancer is associated with many risk factors, such as age, comorbidities, socioeconomic status, insurance, and periodic follow up.<sup>3-5</sup>

There are a lot of studies worldwide on survival analysis and mortality risk in early-stage colorectal cancer compared with colorectal cancer at other stages. The aim of this study is to examine the mortality of stage I colorectal cancer, factors related to mortality, and mortality risk. In this study, demographic characteristics, economic factors, health status, treatment modalities, environmental factors, and periodic follow up were examined.

## **Materials and Methods**

#### Data sources and study population

This study employed a retrospective design, and subjects were newly diagnosed stage I colorectal cancer patients from 2007 to 2012. These patients were followed up for at least 4 years until the end of 2016. The exclusion criteria included patients who previously suffered from colorectal cancer, colorectal cancer patients below 20 years old, and patients who suffered from other cancers.

Data for this study were obtained from the National Cancer Registry, Causes of Death File, and National Health Insurance Research Database. To understand the comorbidity severity of the patient, the disease diagnosis code stated in the patient's health insurance was reviewed and used as the baseline comorbidity of the patient one year before a definite diagnosis was obtained. The follow-up period lasted from January 1, 2006 to December 31, 2016.

#### Variable definition

In this study, control variables included gender, age, salary for health insurance premium, level of urbanization of residence, comorbidity index, tumor site, treatment modality, hospital level, type of hospital, and postoperative carcinoembryonic antigen (CEA) tests and colorectal cancer examinations.

For environmental factors, urbanization of residence area was used as a marker, which was divided into seven levels where the highest was level 1 and lowest was level 7.

The tumor site was divided into three groups, namely, the right colon, left colon, and rectum. The right colon includes the cecum (ICD-O3 code, C18.0), ascending colon (C18.2), hepatic flexure of colon (C18.3), transverse colon (C18.4), while the left colon includes the splenic flexure of colon (C18.5), descending colon (C18.6), sigmoid colon (C18.7), and connection between the sigmoid colon and rectum (C19.9). The code for rectum is C20.9.

Treatment modalities include colonoscopic polypectomy, conventional open abdominal resection surgery, and laparoscopic resection surgery. Hospitals were classified as medical centers, metropolitan hospitals, local community hospitals, and clinics. Moreover, hospitals were further classified as public hospitals and private hospitals for hospital attributes. Postoperative follow up was obtained from the health insurance database to determine if the patient underwent colonoscopy test and CEA test. Patients were divided into three groups based on the number of tests (0, 1, and 2 or more).

#### **Outcome measures**

The National Cancer Registry was linked to the Causes of Death File to determine if the patient died during the follow-up period, the survival duration, and whether the cause of death was colorectal cancer.

#### Statistical analysis

This is a retrospective cohort study, and continuous variables (such as age) were divided into groups and presented as ordinal variables. Frequency distribution and percentage were used to describe the distribution of categorical variables and ordinal variables. These variables include gender, age group, and comorbidity index. The percentage of recurrence or death of stage I colorectal cancer patients during the follow-up period was calculated.

The bivariate log-rank test and Cox proportional hazards model were used to examine related factors affecting the mortality risk in stage I colorectal cancer patients during the observation period.

### Results

Our study recorded the number of newly diagnosed colorectal cancer patients from 2007 to 2012 from the National Cancer Registry and followed up on them until the end of 2016. Patients with other comorbid cancers, aged < 20 years, and missing personal data (such as insurance amount and place of insurance) were excluded. A total of 10,250 stage I colorectal cancer patients were included in the study statistics.

The statistical results conveyed that more patients were male (n = 5,952, 58.07%) and aged 61-74 years (n = 4,327, 42.21%). The group with the most people for salary for health insurance premium was the 18,781-28,800 NTD group (n = 4,142, 40.41%) followed by the  $\leq 18,780$  NTD group (n = 2,657, 25.92%). With regard to the level of urbanization, most patients stayed in places with level 1 urbanization (n = 3,091, 30.16%) followed by those who staved in level 2 urbanization (n = 3,068, 29.93%). The group with comorbidity (CCI) score of 0-1 point had the most subjects (n = 5,594, 54.58%), followed by 2-3 points (n = 3,260, 31.80%), and then 4 points and above (n = 1,396, 13.62%). With regard to tumor site, most patients presented with a tumor at the rectum (n = 4, 147, 147)40.46%), followed by the left colon (n = 4,072, 39.73%), and then the right colon (n = 1,915, 18.68%).

With regard to hospital attribute, most patients were from medical centers (n = 5,542, 56.64%) followed by metropolitan hospitals (n = 3,800,38.83%). There were 6,929 patients from private hospitals (68.79%). Most patients received conventional resection surgery (n = 4,565, 44.54%), while others received laparoscopic resection surgery (n = 1,218, 11.88%) and colonoscopic polypectomy (n = 4,467, 43.58%). Most patients underwent a single colonoscopy within two years after definitive diagnosis (n = 3,888, 37.92%), 3,882 patients underwent two or more colonoscopies (37.87%), and 2,480 (24.20%) patients did not undergo colonoscopy at all. Most patients (n = 4,824, 47.06%) did not undergo CEA tests within two years after surgery, while 4,460 (43.51%) underwent two or more tests, and 966 patients (9.42%) underwent one test.

Of the 10,250 stage I colorectal cancer patients, 300 died due to colorectal cancer, and the mean follow-up duration for mortality was  $71.45 \pm 26.33$ months. The mortality rate was 3.52 per 1000 people. The one-year, three-year, and five-year cancer-specific survival rates for stage I colorectal cancer patients were 99.34%, 98.54%, and 97.46%, respectively. Table 1 shows the detailed statistical analysis.

# Related factors affecting stage I colorectal cancer mortality

Bivariate analysis of risk factors for stage I colorectal cancer mortality found statistically significant differences in gender, age, salary for health insurance premium, level of urbanization, comorbidity, tumor site, treatment modality, and postoperative periodic follow up (p < 0.05). The proportion of males who died was higher than females (p < 0.05). With regard to age, the older the patient, the higher the proportion of deaths (p < 0.05). The proportion of deaths was the lowest in the group with a salary for health insurance premium of > 45,801 NTD (p < 0.05). With regard to the level of urbanization, the proportion of deaths was highest for level 4 followed by level 3 (p < 0.001). With regard to comorbidity, the greater the CCI score, the higher the proportion of deaths (p < 0.001). The proportion of deaths was highest when the tumor site was the rectum. With regard to treatment modality, the proportion of deaths was lowest for laparoscopic surgery followed by colonoscopic polypectomy, and the proportion of deaths was highest for open abdominal

	Stage:1 (N = 10,250)	
	n	%
Sex		
Female	4,298	41.93
Male	5,952	58.07
Age (mean $\pm$ SD)	64.68	± 12.23
$\leq 60$	3,513	34.27
61-74	4,327	42.21
≥75	2,410	23.51
Salary for health insurance premium		
≤ 18,780 NTD	2,657	25.92
18,781-28,800 NTD	4,142	40.41
28,801-45,800 NTD	2,071	20.20
≥45,801 NTD	1,380	13.46
Level of urbanization		
Level 1	3,091	30.16
Level 2	3,068	29.93
Level 3	1,558	15.20
Level 4	1,425	13.90
Levels 5-7	1,108	10.81
Comorbidity CCI		
0-1	5,594	
2-3	3,260	31.80
$\geq$ 4	1,396	13.62
Tumor site		
Right colon	1,915	18.68
Left colon	4,072	39.73
Rectum	4,147	40.46
Not specified	116	1.13
Hospital level		
Medical center	5,542	56.64
Metropolitan hospital	3,800	38.83
Local community hospital	443	4.53
Missing values	465	
Nature of hospital		
Private hospital	6,929	68.79
Public hospital	3,143	31.21
Missing values	178	
Type of treatment		
Conventional resection surgery	4,565	44.54
Laparoscopic resection surgery	1,218	11.88
Colonoscopic polypectomy	4,467	43.58
Number of colonoscopies within 2 years	2 490	24.20
0	2,480	24.20
1	3,888	37.93
$\geq 2$	3,882	37.87
Number of carcinoembryonic antigen tests		
within 2 years	4 834	17.00
0	4,824	47.06
1 > 2	966	9.42
	4,460	43.51
Mean follow-up period for mortality (months)		± 26.33
Mortality due to colorectal cancer within 1 year		6%
Mortality due to colorectal cancer within 3 years	1.46% 2.54%	
Mortality due to colorectal cancer within 5 years	2.3	+70

surgery (p < 0.001). The proportion of deaths was lowest for patients who underwent two or more colonoscopies within two years after surgery followed by those who underwent a single colonoscopy, and patients who did not undergo colonoscopy at all had the highest proportion of deaths (p < 0.05). The proportion of patients who underwent two or more CEA tests within two years after surgery had the lowest proportion of deaths (p < 0.05). Table 2 shows the result of bivariate analysis of risk factors.

We further employed Cox proportional hazards model to examine the factors affecting stage I colorectal cancer mortality risk. We found that compared with patients aged < 60 years, the mortality risk for those aged > 75 years was higher (HR, 1.68; 95% CI, 1.23-2.30). Compared with a CCI score of 0-1 point, the mortality risk of patients with a CCI score of 2-3 points was 1.52 (95% CI, 1.17-1.98), and the mortality risk of patients with a CCI score of  $\geq$  4 points was 2.07 (95% CI, 1.49-2.87). In comparison to patients with a tumor site at the right colon, the mortality risk for those with a tumor site at the rectum was higher (HR, 7.08; 95% CI, 4.18-11.99). The mortality risk for males was also higher (HR, 1.25; 95% CI, 0.99-1.59). Furthermore, compared with patients who did not undergo colonoscopy examination within two years after surgery, patients who underwent one colonoscopy (HR, 0.33; 95% CI, 0.25-0.43) or two or more colonoscopies (HR, 0.24; 95% CI, 0.17-0.33) had a significantly lower risk of dying from colorectal cancer. Although bivariate analysis showed that there are differences in the proportion of stage I mortality for treatment modalities, salary for health insurance, and level of urbanization, these differences were not statistically significant in the Cox proportional hazards model. Table 3 shows the result of COX proportional hazards model.

#### Discussion

The subjects of this study were stage I colorectal cancer patients in the National Cancer Registry, and their three-year and five-year cancer-specific survival rates were 98.54% and 97.46%, respectively. In com-

#### 172 Ming-Hao Hsieh, et al.

#### Table 2. Bivariate analysis of mortality in stage I colorectal cancer patients

	Stage: 1				
		n-mortality or mortality not to colon cancer ( $N = 9,950$ )		Mortality due to colon cancer (N = 300)	
	n	%	n	%	
Sex					0.046
Female	4,187	97.42	111	2.58	
Male	5,763	96.82	189	3.18	
Age					< 0.001
$\leq 60$	3,437	97.84	76	2.16	
61-74	4,226	97.67	101	2.33	
≥75	2,287	94.90	123	5.10	
Salary for health insurance premium	,				< 0.001
≤ 18,780 NTD	2,572	96.80	85	3.20	
18,781-28,800 NTD	3,993	96.40	149	3.60	
28,801-45,800 NTD	2,029	97.97	42	2.03	
≥45,801 NTD	1,356	98.26	24	1.74	
Level of urbanization	1,000	90.20	21	1.7 1	0.012
Level 1	3,009	97.35	82	2.65	0.012
Level 2	2,992	97.52	8 <u>2</u> 76	2.48	
Level 3	1,507	96.73	51	3.27	
Level 4	1,365	95.79	60	4.21	
Levels 5-7	1,077	97.20	31	2.80	
Comorbidity CCI	1,077	97.20	51	2.00	< 0.001
0-1	5,474	97.85	120	2.15	< 0.001
2-3	3,141	96.35	120	3.65	
≥-3 ≥4	1,335	95.63	61	4.37	
Tumor site	1,555	95.05	01	<b>H</b> .37	< 0.001
Right colon	1,898	99.11	17	0.89	< 0.001
Left colon	4,032	99.02	40	0.89	
Rectum	4,032 3,904	99.02 94.14	40 243	5.86	
Not specified	3,904 116		243 0		
Hospital level	110	100.00	0	0.00	0.852
Medical center	5,379	97.06	163	2.94	0.852
Metropolitan hospital	3,686	97.00	114	3.00	
Local community hospital	429	96.84	14	3.16	
Missing values	456	98.06	9	1.94	0 102
Nature of hospital	(71)	0( 02	212	2.07	0.193
Private hospital	6,716	96.93	213	3.07	
Public hospital	3,061	97.39	82	2.61	
Missing values	173	97.19	5	2.81	. 0. 0.0.1
Type of treatment	1 2 2 2	0.6.00	1.50		< 0.001
Conventional open abdominal resection surgery	4,393	96.23	172	3.77	
Laparoscopic resection surgery	1,201	98.60	17	1.40	
Colonoscopic polypectomy	4,356	97.52	111	2.48	
Number of colonoscopies within 2 years				,	< 0.001
0	2,315	93.35	165	6.65	
1	3,808	97.94	80	2.06	
≥2	3,827	98.58	55	1.42	
Number of carcinoembryonic antigen tests within 2 years					0.021
0	4,662	96.64	162	3.36	
1	933	96.58	33	3.42	
$\geq 2$	4,355	97.65	105	2.35	

Vol. 31, No. 3

	Mortality due to stage I colon cancer				
-	HR 95% CI			<i>p</i> -value	
Sex					
Female (reference)					
Male	1.25	0.99	1.59	0.066	
Age					
$\leq 60$ (reference)					
61-74	0.96	0.71	1.31	0.797	
≥ 75	1.68	1.23	2.30	0.001	
Salary for health insurance premium					
$\leq$ 18,780 NTD (reference)					
18,781-28,800 NTD	1.10	0.83	1.47	0.511	
28,801-45,800 NTD	0.81	0.55	1.19	0.279	
≥ 45,801 NTD	0.68	0.43	1.08	0.104	
Level of urbanization	0.00	0.15	1.00	0.101	
Level 1 (reference)					
Level 2	0.86	0.63	1.19	0.361	
Level 3	1.07	0.05	1.54	0.709	
Level 5	1.07	0.84	1.74	0.306	
Levels 5-7	0.71	0.84	1.11	0.300	
Comorbidity CCI	0.71	0.45	1.11	0.127	
0-1 (reference)	1.50	1 17	1.09	0.002	
2-3	1.52	1.17	1.98	0.002	
$\geq 4$	2.07	1.49	2.87	< 0.0001	
Tumor site					
Right colon (reference)	1.00	0.67	2.22	0.504	
Left colon	1.23	0.67	2.23	0.504	
Rectum	7.08	4.18	11.99	< 0.0001	
Hospital level					
Medical center (reference)					
Metropolitan hospital	1.01	0.78	1.31	0.924	
Local community hospital	0.77	0.44	1.35	0.363	
Nature of hospital					
Private hospital (reference)					
Public hospital	0.87	0.67	1.14	0.318	
Type of treatment					
Conventional open abdominal resection surgery (reference)					
Laparoscopic resection surgery	0.70	0.42	1.17	0.174	
Colonoscopic polypectomy	0.93	0.73	1.19	0.581	
Number of colonoscopies within 2 years					
0 (reference)					
1	0.33	0.25	0.43	< 0.0001	
$\geq 2$	0.24	0.17	0.33	< 0.0001	
Number of carcinoembryonic antigen (CEA) tests within 2 years					
0 (reference)					
1	1.19	0.80	1.75	0.396	
$\geq 2$	0.86	0.66	1.13	0.283	

Table 3. Related factors to mortality due to stage I colorectal cancer (Cox proportional hazards model)

parison with papers from other countries, a UK study in a single hospital on 63 stage I colorectal cancer patients found that the two-year and five-year overall survival rate after surgery was 93.7% and 92%, respectively.<sup>6</sup> A single study conducted by one South Korean hospital in 860 stage I colorectal cancer patients found that the recurrence rate was 4.1% after a mean follow-up period of 60 months and the five-year recurrence-free survival was 95.7%.<sup>7</sup> This was in contrast to this study in which the five-year cancer-specific survival for stage I colorectal cancer patients was 96.89%. However, cancer-specific survival presented

in this study differs from recurrence-free survival in the aforementioned papers as patients who relapsed but did not die were not included in mortality rate statistics in this study. Papers with large-scale examination of stage I patients for colorectal cancer mortality are not common. However, this study made use of the National Cancer Registry and examined 10,250 stage I colorectal cancer patients. In addition, we simultaneously calculated the mortality rate during the long follow-up period. The statistical results conveyed improvements and popularization of medicine in Taiwan, and related data can be used as a reference for studies in other countries.

From the results of this study, we can see that there are different risk factors influencing the risk of recurrence and mortality in stage I colorectal cancer patients. Age and gender are intimately associated with the incidence of colorectal cancer, and colorectal cancer tends to occur in males aged 50 years and above. However, the association of prognostic factors for colorectal cancer after treatment with gender remains a question. The literature showed that although gender affects incidence, there are no significant differences in prognosis and mortality rate in colorectal cancer patients between genders.<sup>7,8</sup> However, there are studies with different viewpoints: one study found that the prognosis of women with colorectal cancer is significantly better than men.9,10 Our study showed that although there are statistically significant differences in terms of gender in stage I colorectal cancer mortality in the bivariate analysis (poorer for males), these differences were not statistically significant after controlling for other variables in the Cox proportional hazards model.

With regard to the effects of age on colorectal cancer prognosis, many papers showed that age has significant effects on colorectal cancer prognosis.<sup>11,12</sup> However, a study on prognosis after stage I colorectal cancer treatment found that age will not affect recurrence rate after treatment.<sup>7</sup> Our paper only focused on stage I colorectal cancer patients, and results showed that age is a risk factor for stage I colorectal cancer mortality.

Many papers pointed out that comorbidity severity also affects colorectal cancer prognosis.<sup>12,13</sup> The CCI score can clearly affect prognosis: the higher the CCI score, the poorer the prognosis.<sup>4</sup> Our paper also obtained similar results as we found that CCI is a risk factor for stage I colorectal cancer mortality.

In theory, surgery or colonoscopic polypectomy can be used for stage I colorectal cancer. The US Surveillance, Epidemiology, and End Results Program data analysis found that the five-year cancer-free survival rate when colectomy was used in early-stage (stage 0 and 1) colorectal cancer was 96.6%. If only colonoscopic polypectomy was used, the five-year cancer-free survival rate could have been 89.9%.<sup>14</sup> Another study on stage I colorectal cancer patients compared the recurrence rate when colonoscopic polypectomy or surgical resection was performed, and the statistical results showed that the recurrence rate for colonoscopic polypectomy and surgical resection was 6.2% and 3.4%, respectively.<sup>15</sup> However, our study found that in the bivariate mortality rate analysis for stage I colorectal cancer, the mortality rates for conventional open abdominal surgery and colonoscopic polypectomy are higher than that of laparoscopic resection surgery. However, after controlling for relevant variables in the Cox proportional hazards model, it was found that the type of surgery is not related to the mortality risk of stage I colorectal cancer. In addition, many papers found that the mortality risk when the tumor site is at the rectum is higher than those at the colon.<sup>12,16</sup> Similarly, our study found that stage I colorectal cancer has a higher mortality risk compared with colon cancer (HR, 7.08; 95% CI, 4.18-11.99).

In different countries and regions, the outcomes of colorectal cancer treatment are vary: the mean survival rate of colorectal cancer patients in developed countries is significantly higher than those from developing countries. In Asia, the five-year mean survival rates for colorectal cancer in South Korea, mainland China, Thailand, and India are 60%, 44%, 35%, and 28%, respectively. In Europe, these rates are 53.1%, 60.3%, 61.9%, 59.3%, and 32.6% in the UK, France, Germany, Italy, and Poland, respectively.<sup>17,18</sup> Although Taiwan is a developed country, there are large differences between counties and cities as the healthcare level of remote places cannot be compared with those of major cities. Therefore, in this study, villages, town-

ships, and cities in Taiwan were classified by levels of urbanization to compare whether the level of urbanization has any effect on the prognosis of stage I colorectal cancer after treatment. From our study, we found that although there are significant differences in the proportion of deaths in patients from different levels of urbanization, after controlling for related variables in the Cox proportional hazards model, we found that the level of urbanization is not related to mortality risk. This may be because the healthcare level of Taiwan is relatively uniform, and the distance between cities and villages is not far. Patients living in areas with low level of urbanization also have hospitals with suitable healthcare levels, or patients are willing to seek treatment in major cities after diagnosis. Therefore, there is no statistical difference in mortality risk.

Periodic follow up after treatment also affects the prognosis of colorectal cancer patients. The aim of periodic follow up is to discover recurrence or other new tumors as early as possible, thereby, arranging subsequent curative treatment to increase the survival rate of patients.<sup>19</sup> In particular, multiple recurrent or metastatic tumors will not result in many clinical symptoms in patients. Therefore, periodic and close follow up can increase the overall survival of colorectal cancer patients, detect recurrent tumors with no clinical signs, and increase the probability of resecting tumors after recurrence.<sup>20,21</sup>

However, the subjects of most studies on postoperative follow up in colorectal cancer are stages 2 and 3 colorectal cancer patients, and there is no conclusion drawn on stage I colorectal cancer patients at present. Colonoscopy is an important component of post-operative surveillance and allows the detection of relapses with endoluminal lesion, including metachronous adenomas or invasive carcinoma during follow up. Many papers have mentioned that periodic postoperative colonoscopy can reduce the mortality risk of colorectal cancer patients.<sup>22-24</sup> Similar conclusions were obtained in this study: periodic colonoscopy after surgery in stage I colorectal cancer patients can effectively reduce the risk of death from colorectal cancer; a lower mortality risk for stage I colorectal cancer is observed for patients who undergo a single colonoscopy (HR, 0.33; 95% CI, 0.250.43) or two or more colonoscopies (HR, 0.24; 95% CI, 0.17-0.33). Bivariate analysis found that the number of CEA tests establish statistically significant differences in mortality risk in stage I colorectal cancer patients. However, after controlling relevant variables in Cox proportional hazards model analysis, the differences were not statistically significant.

# Conclusion

Our study shows that the five-year mortality rate of stage I colorectal cancer was 2.54%. The risk factors for stage I colorectal cancer mortality were age > 75 years, CCI  $\ge$  2 points, and rectal lesions. Conversely, undergoing one or more colonoscopies within two years after surgery can reduce the risk of colorectal cancer mortality.

# **Financial Support**

N/A.

## References

- Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disabilityadjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the Global Burden of Disease Study. *JAMA Oncol* 2017;3:524-48.
- Health Promotion Administration. Cancer registry annual report, 2015, Taiwan (in Chinese). 2017. Available from: https:// www.hpa.gov.tw/Pages/Detail.aspx?nodeid=269&pid=8084.
- Doubeni CA, Laiyemo AO, Major JM, Schootman M, Lian M, Park Y, et al. Socioeconomic status and the risk of colorectal cancer: an analysis of more than a half million adults in the National Institutes of Health-AARP Diet and Health Study. *Cancer* 2012;118:3636-44.
- Erichsen R, Horváth-Puhó E, Iversen LH, Lash TL, Sørensen HT. Does comorbidity interact with colorectal cancer to increase mortality? A nationwide population-based cohort study. *Br J Cancer* 2013;109:2005-13.
- van Eeghen EE, Bakker SD, van Bochove A, Loffeld RJ. Impact of age and comorbidity on survival in colorectal cancer. *J Gastrointest Oncol* 2015;6:605-12.

- Tarazi M, Guest K, Cook AJ, Balasubramaniam D, Bailey CMH. Two and five year survival for colorectal cancer after resection with curative intent: a retrospective cohort study. *Int J Surg* 2018;55:152-5.
- Lee JH, Lee JL, Park IJ, Lim SB, Yu CS, Kim JC. Identification of recurrence-predictive indicators in stage I colorectal cancer. *World J Surg* 2017;41:1126-33.
- White A, Ironmonger L, Steele RJC, Ormiston-Smith N, Crawford C, Seims A. A review of sex-related differences in colorectal cancer incidence, screening uptake, routes to diagnosis, cancer stage and survival in the UK. *BMC Cancer* 2018;18:906.
- Kotake K, Asano M, Ozawa H, Kobayashi H, Sugihara K. Gender differences in colorectal cancer survival in Japan. *Int J Clin Oncol* 2016;21;194-203.
- Yang Y, Wang G, He J, Ren S, Wu F, Zhang J, Wang F. Gender differences in colorectal cancer survival: a meta-analysis. *Int J Cancer* 2017;141:1942-9.
- Baghestani AR, Daneshvar T, Pourhoseingholi MA, Asadzade H. Survival of colorectal cancer patients in the presence of competing-risk. *Asian Pac J Cancer Prev* 2014;15:6253-5.
- McKay A, Donaleshen J, Helewa RM, Park J, Wirtzfeld D, Hochman D, et al. Does young age influence the prognosis of colorectal cancer: a population-based analysis. *World J Surg Oncol* 2014;12:370.
- Marventano S, Grosso G, Mistretta A, Bogusz-Czerniewicz M, Ferranti R, Nolfo F, et al. Evaluation of four comorbidity indices and Charlson comorbidity index adjustment for colorectal cancer patients. *Int J Colorectal Dis* 2014;29:1159-69.
- Mounzer R, Das A, Yen RD, Rastogi A, Bansal A, Hosford L, et al. Endoscopic and surgical treatment of malignant colorectal polyps: a population-based comparative study. *Gastrointest Endosc* 2015;81:733-40 e2.
- 15. Belderbos TD, van Erning FN, de Hingh IH, van Oijen MG, Lemmens VE, Siersema PD. Long-term recurrence-free survival after standard endoscopic resection versus surgical resection of submucosal invasive colorectal cancer: a popula-

tion-based study. *Clin Gastroenterol Hepatol* 2017;15:403-11 e1.

- Kang SI, Kim DW, Kwak Y, Lee HS, Kim MH, Kim MJ, et al. The prognostic implications of primary tumor location on recurrence in early-stage colorectal cancer with no associated risk factors. *Int J Colorectal Dis* 2018;33:719-26.
- Sankaranarayanan R, Swaminathan R, Brenner H, Chen K, Chia KS, Chen JG, et al. Cancer survival in Africa, Asia, and Central America: a population-based study. *Lancet Oncol* 2010;11:165-73.
- Brenner H, Bouvier AM, Foschi R, Hackl M, Larsen IK, Lemmens V, et al. Progress in colorectal cancer survival in Europe from the late 1980s to the early 21st century: the EUROCARE study. *Int J Cancer* 2012;131:1649-58.
- Ike H, Shimada H, Ohki S, Togo S, Yamaguchi S, Ichikawa Y. Results of aggressive resection of lung metastases from colorectal carcinoma detected by intensive follow-up. *Dis Colon Rectum* 2002;45:468-73; discussion 473-5.
- Pita-Fernández S, Alhayek-Aí M, González-Martín C, López-Calviño B, Seoane-Pillado T, Pértega-Díaz S. Intensive follow-up strategies improve outcomes in nonmetastatic colorectal cancer patients after curative surgery: a systematic review and meta-analysis. *Ann Oncol* 2015;26:644-56.
- Rodrigues RV, Pereira da Silva J, Rosa I, Santos I, Pereira N, Soares C, et al. Intensive follow-up after curative surgery for colorectal cancer. *Acta Med Port* 2017;30:633-41.
- 22. Doubeni CA, Corley DA, Quinn VP, Jensen CD, Zauber AG, Goodman M, et al. Effectiveness of screening colonoscopy in reducing the risk of death from right and left colon cancer: a large community-based study. *Gut* 2018;67:291-8.
- Rulyak SJ, Lieberman DA, Wagner EH, Mandelson MT. Outcome of follow-up colon examination among a populationbased cohort of colorectal cancer patients. *Clin Gastroenterol Hepatol* 2007;5:470-6; quiz 407.
- Fisher DA, Jeffreys A, Grambow SC, Provenzale D. Mortality and follow-up colonoscopy after colorectal cancer. *Am J Gastroenterol* 2003:98:901-6.

謝明皓等

# <u>原 著</u>

# 第一期大腸直腸癌死亡風險及其相關因素

謝明皓<sup>1,2</sup> 龔佩珍<sup>3</sup> 郭娓吟<sup>2</sup> 柯道維<sup>1</sup> 蔡文正<sup>2</sup>

1中國醫學大學附設醫院 大腸直腸外科

2中國醫藥大學 醫務管理學系

3亞洲大學 健康產業管理學院

**目的** 台灣大腸直腸癌發生率在癌症中排行第一,死亡人數占第三位。早期大腸直腸癌 病患經治療後復發或轉移的機會並不高,但在臨床觀察上,仍可發現少數早期病人,可 能因醫療單位及病人過於輕忽而疏於追蹤,或其他危險因子造成死亡風險上升。本研究 欲探討第一期大腸直腸癌病患死亡的風險及比率,及探討其死亡之相關因子。

**方法** 本研究為回朔性研究,以 2007-2012 年,國健署癌症登記檔所登記的第一期大腸 直腸癌為對象,串聯健保資料庫,追蹤至 2016 年底。第一期病患死亡風險的評估將分 別採用雙變項分析 (log-rank test) 及 Cox 比例風險模式 (cox proportional hazard regression),並依照病患之人口學特性、經濟因素、環境因素、健康因素、治療方式和 治療醫院,及有無定期追蹤等來分析相關的危險因子。

**結果** 本研究顯示大腸直腸癌一期病患的五年因大腸直腸癌特定死亡率為 2.54%。死亡 危險因子則分別年紀大於 75 歲、共病指數 2-3 分、共病指數 ≥4 分、直腸病灶。反之, 如果術後兩年內有做一次或兩次以上大腸鏡檢查,可降低第一期大腸直腸癌死亡的風 險。

**結論** 由本研究可知,年紀、共病指數、腫瘤位置、和第一期大腸直腸癌病患預後有明 顯相關,而定期接受大腸鏡檢查,可以降低第一期大腸直腸癌的死亡風險。

關鍵詞 第一期大腸直腸癌、死亡風險、危險因子。