Original Article

Adjuvant Chemotherapy for High-risk Stage II Colon Cancer

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Purpose. Although adjuvant chemotherapy is the standard treatment for stage III colorectal cancer, it is still controversial in patients with stage II disease. This study aimed to evaluate if adjuvant chemotherapy has any survival benefit for stage II colon cancer patients with poor prognostic factors (high-risk stage II).
Methods. A total of 371 patients with stage II colon cancer who underwent curative surgery from January 2003 to December 2012 were enrolled in this study. They were divided into two categories: those with poor prognostic factors and those without. Each category was further divided into two sub-groups according to adjuvant chemotherapy administration. The primary outcome of the analysis was the 5-year overall survival (OS) for patients with poor prognostic factors and chemotherapy administration status.
Results. There were 127 patients with no poor prognostic factors and 244 patients with poor prognostic factors. Poor prognostic factors decreased OS in stage II colon cancer (5-year OS: 78.4% vs. 71.9%, $p = 0.058$), and adjuvant chemotherapy significantly improved the OS (5-year OS: 79.2% vs. 63.1%, $p < 0.001$). Furthermore, patients with poor prognostic factors benefited more from adjuvant chemotherapy than those without poor prognostic factors (5-year OS: 76.3% vs. 62.9%, $p = 0.001$; 5-year OS: 85.5% vs. 61.5%, $p = 0.011$). Three poor prognostic factors had a significant effect on OS in stage II colon cancer. These were the "number of lymph nodes examined, bowel obstruction, and T stage" (hazard ratio 1.75, 95% confidence interval [CI] 1.04-2.95, $p = 0.036$; HR 3.33, 95% CI 1.60-6.96, $p = 0.001$; HR 1.94, 95% CI 1.03-3.62, $p = 0.039$, respectively).
Conclusions. Adjuvant chemotherapy significantly improves OS in patients with stage II colon cancer, especially in high-risk stage II disease. Three poor prognostic factors were independent predictors of OS in stage II colon cancer: "the number of lymph nodes examined, bowel obstruction, and T stage".
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Colorectal cancer has been the most common cancer in Taiwan since 2006. Complete surgical resection is the gold standard treatment for patients with non-metastatic colon cancer. Any additional survival benefit from postoperative adjuvant chemotherapy seems to be stage-specific. Although adjuvant chemo-

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therapy benefits patients with American Joint Committee on Cancer (AJCC) stage III disease,[1] it is still controversial in patients with stage II colon cancer. About 40% of surgically treated patients with colon cancer are identified as AJCC stage II.[2] This cohort has a nearly 20% risk of recurrence, and the use of adjuvant chemotherapy in this setting remains uncertain. No individual clinical trials could prove significant improvements in survival for stage II patients treated with adjuvant 5-fluorouracil (FU)-based regimens; most studies have demonstrated about a 5% improvement in 5-year overall survival (OS), at best.[3] Despite having no definitive impact on survival, adjuvant chemotherapy is routinely administered. In an analysis of the Surveillance Epidemiology and End Results (SEER) data linked with Medicare, Schrag et al.[4] showed that, notwithstanding the uncertainty regarding its efficacy, adjuvant chemotherapy was administered to more than 25% of patients with stage II colon cancer.

According to the AJCC guidelines,[5] there are several clinicopathologic factors in stage II colon cancer that are associated with poor prognosis (high risk stage II). The most robust of these are close or positive surgical margins;[6] diagnosis accompanied by bowel obstruction or perforation;[7,8] high histological grade;[2,9] the number of lymph nodes assessed < 12;[10,11] and lymphatic/vascular invasion.[12,13] The literature suggests that it might be reasonable to consider the administration of adjuvant chemotherapy for patients with these poor prognosis factors. However, although associated with worse outcomes, there is no evidence that these poor prognostic features are predictive of an effective response to adjuvant therapy. The purpose of this study was to evaluate if adjuvant chemotherapy has any survival benefit for patients with AJCC stage II colon cancer with poor prognostic factors (high-risk stage II).

Materials and Methods

Patients and follow-up

From a cohort of 1,953 patients with colon cancer at Tri-Service General Hospital (TSGH) from January 2003 to December 2012, 421 patients who underwent curative resection were diagnosed with stage II disease (T3-T4, N0). The staging of tumors was performed using the international classification for malignant tumors (TNM) from the AJCC, sixth edition. Patients with the following criteria were excluded from the study cohort: synchronous or metachronous colon cancer, R1-R2 resection, a history of other malignancy, incomplete adjuvant chemotherapy, death within the first month after surgery, and a lack of follow-up data. All patients underwent standard curative resection by colorectal surgeons at TSGH, and the clinical, surgical, and pathological data were collected. All patients had a minimum follow-up of 5 years except for those who died or were lost to follow-up within 5 years after the surgery. A total of 371 patients with stage II colon cancer were enrolled in this retrospective study. They were divided into two categories according to whether or not they had poor prognostic factors. According to the American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN) established guidelines, and recently published papers,[6-8] poor prognostic factors include high histological tumor grade, number of lymph nodes examined (< 12), close or positive surgical margins, tumor size (> 5 cm), bowel obstruction or perforation, lymphatic/vascular invasion, and T4 stage. Each category was then divided into two sub-groups according to adjuvant chemotherapy administration. Patients were monitored every 3 months in the first 2 years and every 6 months thereafter, with routine physical examination, serum carcinoembryonic antigen (CEA) measurements, imaging studies, and colonoscopy. The imaging studies included chest radiography, abdominal ultrasonography, and computed tomography, and were performed every 6 months. Follow-up colonoscopy was performed every 6 months to 1 year in the first 2 years, and every 1 to 2 years thereafter. The primary outcome of the analysis was 5-year OS for patients with poor prognostic factors and chemotherapy administration status.

Chemotherapy

According to the status of adjuvant chemotherapy,

the patients were classified as 1) those who did not receive adjuvant chemotherapy and 2) those who received oral chemotherapy (Ufur plus Folina), or intravenous chemotherapy (5-fluorouracil plus leucovorin). Patients were assessed before starting each cycle and chemotherapy was delayed if neutrophils decreased to less than 1500 cells/mm^3, platelets decreased to less than 100,000 cells/mm^3, or when significant toxicity was detected.

Statistical analysis

We described the patient- and disease-related characteristics for each group according chemotherapy administration status, and evaluated the statistical survival differences of poor prognostic factors by the log-rank test. The survival curves were constructed using the Kaplan-Meier method and were used to compare 5-year OS within each group. Multivariate analysis was performed using the Cox proportional hazards regression-based method. All data were analyzed with IBM SPSS statistics software version 22 (IBM R SPSS R statistics 22). The level of statistical significance was set at $p < 0.05$, and all reported p-values were two-tailed.

Results

Patient characteristics

The clinicopathologic characteristics of this cohort of 371 patients with stage II colon cancer are shown in Table 1. All patients underwent complete surgical resection and were stratified into two categories: stage II with no poor prognostic factors (n = 127), and stage II with poor prognostic factors (n = 244). Most of the patients were aged ≥ 65 years (62%) and had moderately differentiated tumors (82%). In the stage II with no poor prognostic features group, 67% of patients received adjuvant chemotherapy compared with 68% of patients in the stage II with poor prognostic features group. When grouped according to poor prognostic factors, patients with no poor prognostic features were predominantly and disproportionately male patients, and their tumors were located more frequently in the sigmoid colon. In contrast, patients with poor prognostic features were disproportionately older and their tumors were located more frequently in the ascending colon. In the stage II with poor prognostic features and chemotherapy subgroup, there were higher proportions of patients with perforation, T4 stage, large tumor size, and poor histology, compared with the no chemotherapy subgroup.

Survival analysis

According to the survival analysis, poor prognostic factors decreased 5-year OS in stage II colon cancer (5-year OS: 78.4% vs. 71.9%, $p = 0.058$) (Fig. 1). When the two experimental cohorts were compared, the administration of adjuvant chemotherapy in patients with no poor prognostic factors was associated with a significant improvement in OS compared to those who did not receive chemotherapy (5-year OS: 85.5% vs. 61.5%, $p = 0.011$). There was also a significant improvement in OS after adjuvant chemotherapy administration in patients with poor prognostic factors compared to those who did not receive chemotherapy (5-year OS: 76.3% vs. 62.9%, $p = 0.001$) (Fig. 2). Furthermore, adjuvant chemotherapy significantly improves OS in stage II disease, regardless of having poor prognostic factors or not (5-year OS: 79.2% vs. 63.1%, $p < 0.001$) (Fig. 3).

Through Cox regression analysis, the clinicopathologic features, including age, gender, tumor location, chemotherapy, and poor prognostic factors (histologic differentiation, number of lymph nodes examined, close or positive margins, tumor size, obstruction, perforation, lymphatic/vascular invasion, and tumor T stage) were analyzed. Multivariate analysis with a log-rank test was performed to identify independent predictors of OS. We observed that age ≥ 65 years (hazard ratio [HR] 2.72, 95% confidence interval [CI] 1.22-6.08, $p = 0.015$) and administration of adjuvant chemotherapy (HR 0.53, 95% CI 0.34-0.84, $p = 0.007$) were significantly associated with OS. Furthermore, 3 poor prognostic factors were also identified as independent predictors of OS in stage II colon cancer. These were the number of nodes examined

Table 1. Characteristics of stage II colon cancer patients receiving curative resection

Patient	Stage II with no poor prognostic factors (n = 127, 34%)			Stage II with any poor prognostic factors (n = 244, 66%)		
Characteristics	No C/T (n = 41)	C/T (n = 86)	*p*	No C/T (n = 77)	C/T (n = 167)	*p*
Age, yrs, (%)			0.008			< 0.001
≤ 50	4 (9.8)	9 (10.5)		2 (2.6)	30 (18)	
51-64	5 (12.2)	32 (37.2)		11 (14.3)	48 (28.7)	
≥ 65	32 (78)	45 (52.3)		64 (83.1)	89 (53.3)	
Sex (%)			0.697			0.684
Men	27 (65.9)	52 (60.5)		43 (55.8)	87 (52.1)	
Women	14 (34.1)	34 (39.5)		34 (44.2)	80 (47.9)	
Tumor location (%)			0.140			0.022
Right colon	14 (34.1)	19 (22.1)		30 (39)	59 (35.3)	
Transverse colon	0	7 (8.1)		12 (15.6)	15 (9)	
Left colon	4 (9.8)	15 (17.4)		4 (5.2)	31 (18.6)	
Sigmoid colon	23 (56.1)	44 (51.2)		26 (33.8)	57 (34.1)	
Unknown	0	1 (1.2)		5 (6.5)	5 (3)	
Poor prognostic factors (%)						
Tumor grade			0.717			0.798
Well	2 (4.9)	7 (8.1)		7 (9.1)	12 (7.2)	
Moderately	39 (95.1)	79 (91.9)		59 (76.6)	127 (76)	
Poorly or undifferentiated	0	0		11 (14.3)	28 (16.8)	
No. of lymph nodes examined			-			0.176
≥ 12	41	86		53 (68.8)	130 (77.8)	
0-11	0	0		24 (31.2)	37 (22.2)	
Close or positive margins			-			1.0
No	41	86		76 (98.7)	165 (98.8)	
Yes	0	0		1 (1.3)	2 (1.2)	
Unknown	0	0		0	0	
Tumor size			-			0.082
≤ 5 cm	41	86		33 (42.9)	51 (30.5)	
> 5 cm	0	0		44 (57.1)	116 (69.5)	
Bowel obstruction			-			0.044
No	41	86		63 (81.8)	153 (91.6)	
Yes	0	0		14 (18.2)	14 (8.4)	
Bowel perforation			-			0.363
No	41	86		73 (94.8)	151 (90.4)	
Yes	0	0		4 (5.2)	16 (9.6)	
Lymphatic/vascular invasion			-			0.266
No	41	86		73 (94.8)	163 (97.6)	
Yes	0	0		4 (5.2)	4 (2.4)	
T stage			-			0.109
T3	41	86		70 (90.9)	137 (82)	
T4	0	0		7 (9.1)	30 (18)	
No. of poor prognostic factors			-			0.883
0	41	86		0	0	
1	0	0		52 (67.5)	105 (62.9)	
2	0	0		20 (26)	48 (28.7)	
3	0	0		3 (3.9)	10 (6)	
≥ 4	0	0		2 (2.6)	4 (2.4)	

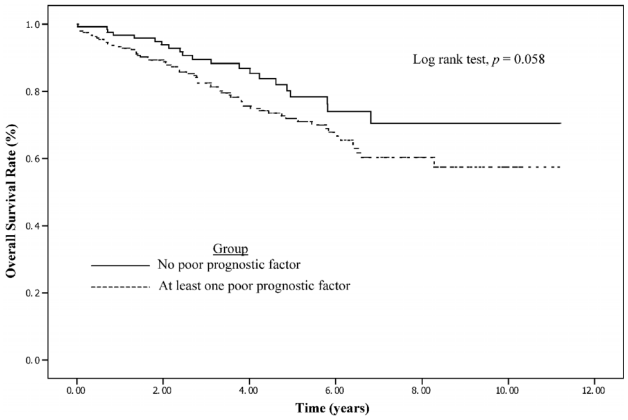

Fig. 1. Comparison of overall survival in stage II colon cancer according to poor prognostic factors.

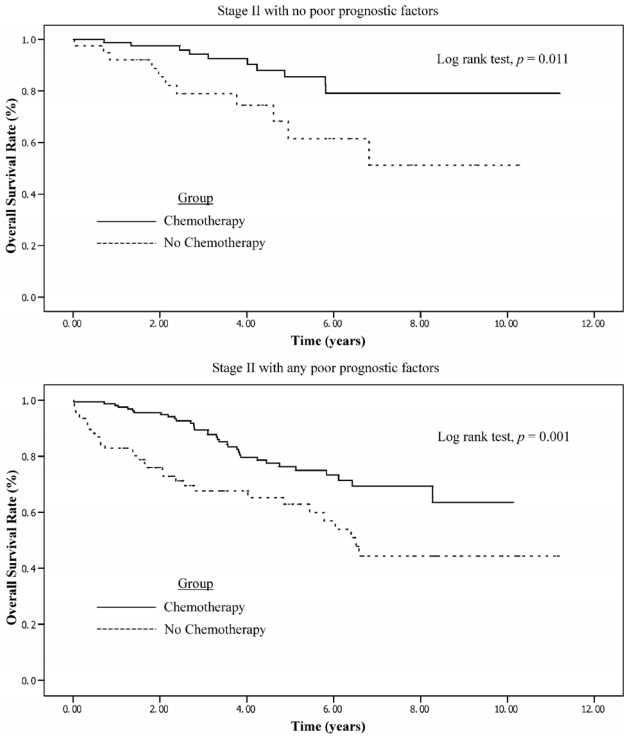

Fig. 2. Comparison of overall survival in stage II colon cancer according to adjuvant chemotherapy and different poor prognostic factors group.

< 12 (HR 1.75, 95% CI 1.04-2.95, $p = 0.036$); bowel obstruction (HR 3.33, 95% CI 1.60-6.96, $p = 0.001$); and T4 stage (HR 1.94, 95% CI 1.03-3.62, $p = 0.039$) (Table 2). Poor prognostic features such as histologic differentiation, close or positive margins, tumor size, perforation, and lymphatic/vascular invasion, were not significant predictors.

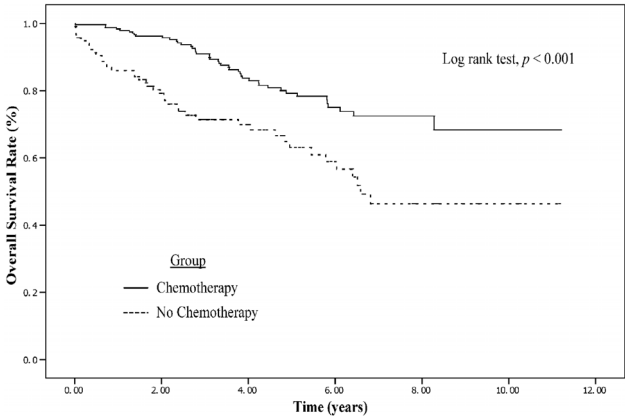

Fig. 3. Comparison of overall survival in stage II colon cancer according to adjuvant chemotherapy.

Discussion

In our study, we observed that patients with poor prognostic factors have significantly reduced OS in stage II colon cancer compared to patients with no poor prognostic factors (5-year OS: 78.4% vs. 71.9%, $p = 0.058$). Adjuvant chemotherapy significantly improves the OS in stage II disease, regardless of whether or not patients have poor prognostic factors (5-year OS: 79.2% vs. 63.1%, $p < 0.001$). Furthermore, patients with poor prognostic factors benefit more from adjuvant chemotherapy than those without poor prognostic factors (5-year OS: 76.3% vs. 62.9%, $p = 0.001$; 5-year OS: 85.5% vs. 61.5%, $p = 0.011$). In addition, 3 poor prognostic factors were significant and independent predictors of OS in stage II colon cancer. These factors were the number of lymph nodes examined, bowel obstruction, and T stage (HR 1.75, 95% CI 1.04-2.95, $p = 0.036$; HR 3.33, 95% CI 1.60-6.96, $p = 0.001$; HR 1.94, 95% CI 1.03-3.62, $p = 0.039$).

Since the National Institutes of Health 1990 consensus conference, the administration of adjuvant 5-fluorouracil (5-FU)-based therapy for patients with stage III colon cancer has become standard therapy and has resulted in a 30-40% decrease in relapse and mortality rates compared with surgery alone.[1] Many large studies have evaluated the potential of adjuvant therapy in stage II colon cancer, and the results show that is has a small benefit. Three large trials specifi-

Table 2. The Cox regression model for overall survival in stage II colon cancer

Variable	Group	Univariate analysis crude HR (95% CI)	*p*	Multivariate adjusted HR (95% CI)	*p*
Age, yrs (%)	≤ 50	1.00 (Ref.)		1.00 (Ref.)	
	51-64	0.56 (0.20-1.60)	0.281	0.70 (0.24-2.04)	0.513
	≥ 65	2.66 (1.22-5.78)	0.014	2.72 (1.22-6.08)	0.015
Sex (%)	Men	1.00 (Ref.)		1.00 (Ref.)	
	Women	0.77 (0.50-1.19)	0.241	0.68 (0.43-1.07)	0.096
Tumor location (%)	Right colon	1.00 (Ref.)		1.00 (Ref.)	
	Transverse colon	1.11 (0.52-2.36)	0.797	0.58 (0.25-1.35)	0.207
	Left colon	0.76 (0.37-1.57)	0.457	0.68 (0.31-1.53)	0.355
	Sigmoid colon	1.10 (0.66-1.82)	0.720	1.18 (0.68-2.05)	0.559
	Unknown	1.35 (0.51-3.53)	0.546	0.88 (0.30-2.61)	0.815
Chemotherapy	No	1.00 (Ref.)		1.00 (Ref.)	
	Yes	0.41 (0.27-0.63)	< 0.001	0.53 (0.34-0.84)	0.007
Poor prognostic factors					
Tumor grade	Well	1.00 (Ref.)		1.00 (Ref.)	
	Moderately	1.42 (0.52-3.88)	0.499	1.34 (0.46-3.90)	0.591
	Poorly or un-differentiated	2.93 (0.95-9.01)	0.061	2.68 (0.80-8.95)	0.110
No. of lymph nodes examined	≥ 12	1.00 (Ref.)		1.00 (Ref.)	
	0-11	2.00 (1.26-3.18)	0.003	1.75 (1.04-2.95)	0.036
Close or positive margins	No	1.00 (Ref.)		1.00 (Ref.)	
	Yes	1.98 (0.27-14.22)	0.499	1.24 (0.16-9.69)	0.839
Tumor size	≤ 5 cm	1.00 (Ref.)		1.00 (Ref.)	
	> 5 cm	0.69 (0.44-1.08)	0.102	0.79 (0.47-1.33)	0.372
Bowel obstruction	No	1.00 (Ref.)		1.00 (Ref.)	
	Yes	2.97 (1.64-5.37)	< 0.001	3.33 (1.60-6.96)	0.001
Bowel perforation	No	1.00 (Ref.)		1.00 (Ref.)	
	Yes	1.37 (0.60-3.15)	0.456	0.78 (0.29-2.05)	0.611
Lymphatic/vascular invasion	No	1.00 (Ref.)		1.00 (Ref.)	
	Yes	1.23 (0.30-4.99)	0.777	1.22 (0.28-5.28)	0.786
T stage	T3	1.00 (Ref.)		1.00 (Ref.)	
	T4	1.64 (0.93-2.91)	0.091	1.94 (1.03-3.62)	0.039

CI, confidence interval; HR, hazard ratio; Ref, reference group.
* $p < 0.05$

cally demonstrate the benefit of 5-FU-based chemotherapy in patients with stage II colon cancer, and show some unequivocal benefit for adjuvant chemotherapy.[14-16] The largest of these, the trial from the Quick and Simple and Reliable (QUASAR) study, randomly assigned 3238 colorectal cancer patients from 150 centers in 17 countries to either adjuvant therapy of 5-FU plus leucovorin, or to observation following resection of colon cancer. Adjuvant chemotherapy was associated with a significant decrease in risk to 22% for disease recurrence and 18% for death, which translates as a 3.6% absolute improvement in 5-year OS.[14] Among patients with stage II colon cancer, this study showed a trend towards better OS (HR 0.86, 95% CI 0.54-1.19, 5-year OS: 83.9% vs. 81.5%). However, the patient population of the QUASAR study included both colon and rectal cancer patients with not only stage II but also stage III colorectal cancer. This is likely to have an impact on the observed OS. Another 2 meta-analyses investigated the benefit of adjuvant chemotherapy in patients with stage II colon cancer. The International Multicenter Pooled Analysis of B2 Colon Cancer Trials (IMPACT B2) included 1025 patients with stage II disease from 5 randomized trials, comparing 5-FU-containing adjuvant chemotherapy with surgery alone. The meta-analysis demonstrated a reduction in the relative risk to 17% recurrence and revealed a 2% absolute improvement

in OS.[15] The Cancer Care Ontario Program included 37 trials and 11 meta-analyses. The study involved a trial of 5-FU plus levamisole and a meta-analysis of 1016 patients with stage II colon cancer, comparing 5-FU with observation only, and it showed a 5-10% absolute improvement in disease-free survival.[16] Therefore, these studies suggest that adjuvant chemotherapy in patients with stage II colon cancer may have some small benefits for patients with stage III disease.

While the 5-year OS after surgery in stage II colorectal cancer is approximately 70-80%, in high-risk stage II disease the clinical outcome is similar to that of patients with stage III disease. The most important prognostic indicator of survival in colon cancer is tumor stage, which is dependent on the depth of tumor invasion through the bowel wall, and the number of lymph nodes involved. Tumors with early penetration through the muscularis propria of the colon wall (T3) have a very favorable prognosis, similar to that of stage I cancer, whereas lesions with transmural extension (T4) generally behave similarly to stage III cancers.[2] High-risk patients are identified by tumors that not only penetrate the bowel wall but also show adhesion to, or direct invasion of, other organs or surrounding structures. However, recent studies using molecular markers, such as loss of heterozygosity of 18q or evidence of microsatellite stable tumors, have identified a subgroup of patients with both stage II and stage III colorectal cancer who have a much worse prognosis. The administration of adjuvant chemotherapy may be beneficial for these patients.[17-20]

The ASCO and the NCCN guidelines are both against the routine use of chemotherapy for patients with stage II colon cancer.[3,21] Nevertheless, there are no data correlating risk features in high-risk stage II colon cancer, and both the ASCO and NCCN suggest that high-risk patients be considered for adjuvant chemotherapy. The poor prognostic features described in the published guidelines represent an ineffective clinical mechanism for identifying patients with high-risk stage II colon cancer. More importantly, recently high-frequency microsatellite instability from DNA mismatch repair defects has become an important predictor of better prognosis, as well as resistance to fluorouracil therapy.[3,19,22] Furthermore, the ASCO and NCCN guidelines define high-risk features as bowel obstruction, perforation, lymphovascular invasion, poor differentiation, perineural invasion, close or positive margins, and < 12 lymph nodes examined. These guidelines, however, do not incorporate other prognostic factors, such as T4 disease, tumor size, tumor location, or carcinoembryonic antigen.[7,9,13,23-25]

Because there were so many poor prognostic factors in the established guidelines, we tried to determine the importance of each poor prognostic factor in the OS of patients with stage II colon cancer. We identified 3 factors as independent predictors of OS in stage II colon cancer. These factors were the number of lymph nodes examined, bowel obstruction, and T stage (HR 1.75, 95% CI 1.04-2.95, $p = 0.036$; HR 3.33, 95% CI 1.60-6.96, $p = 0.001$; HR 1.94, 95% CI 1.03-3.62, $p = 0.039$). Their statistical significance shows that these factors play a much more important role in OS compared to other poor prognostic factors. Our analysis supports the use of adjuvant chemotherapy in patients with stage II disease regardless of high-risk characteristics. The population-based study has the major strength of investigating a sufficient number of patients over a 10-year period to perform this analysis adequately.

This study has the limitation of any retrospective analysis, which is susceptible to selection bias. For example, there were differences between patients who received adjuvant chemotherapy and those who did not, particularly in age, suggesting that patients with better performance status were offered chemotherapy. In addition, the primary outcome of this study was 5-year OS instead of disease-free survival, so survival bias would arise if patients died of other diseases. Furthermore, there was no detailed information of comorbidity and the performance status of the patients. Therefore, when assigning patients to adjuvant chemotherapy, selection bias could occur.

Conclusions

This study has highlighted the significant OS benefit of adjuvant chemotherapy in patients with stage II colon cancer, especially in high-risk stage II dis-

ease. Furthermore, we also identified 3 independent predictors of OS (number of lymph nodes examined, bowel obstruction, and T stage) in stage II disease by multivariate analysis, showing that they play a more important role in OS of patients with resected stage II colon cancer compared to other poor prognostic factors. They not only improve outcome predictions for patients with stage II colon cancer, but also help clinicians decide upon administration of adjuvant chemotherapy. Large, multicenter, randomized controlled trials with adequate follow-up are still required to evaluate the benefit of adjuvant chemotherapy in patients with stage II disease.

Disclaimers

The authors declare no conflicts of interest.

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原　著

輔助性化學治療在高風險第二期大腸癌病患之分析

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目的　輔助性化學治療在術後第三期大腸癌病患已是標準治療，但對於高危險第二期大腸癌的病患是否有助益、仍令人存疑；這項研究在評估輔助性化學治療在高危險第二期大腸癌病患的存活效益。

方法　從 2003 年 1 月至 2012 年 12 月，共 371 位接受過治癒性手術的第二期大腸癌病患。先將病患依照有無「高危險因子」分成兩大組，每一大組再依照有無接受「輔助性化學治療」分成兩小組，進而去比較每一個組別之間五年整體存活率的差異性。

結果　共計 127 位病患無高危險因子，以及 244 位病患有任何一項高危險因子。就整體第二期大腸癌病患來說，高危險因子確實會降低五年整體存活率 (78.4% vs. 71.9%, p = 0.058)，輔助性化學治療可明顯增加第二期大腸癌病患的五年整體存活率 (79.2% vs. 63.1%, p < 0.001)。比起無高危險因子的病患，輔助性化學治療對高危險病患而言，提昇五年整體存活率效果尤其顯著 (76.3% vs. 62.9%, p = 0.001; 85.5% vs. 61.5%, p = 0.011)！經由統計分析，三個高危險因素被視為能明顯影響第二期大腸癌病患五年整體存活率的獨立預測因子:「術後淋巴結摘取數」、「腸阻塞症狀」和「癌症 T 分期」(HR 1.75, 95% CI 1.04-2.95, p = 0.036; HR 3.33, 95% CI 1.60-6.96, p = 0.001; HR 1.94, 95% CI 1.03-3.62, p = 0.039)。

結論　輔助性化學治療可明顯增加第二期大腸癌病患的五年整體存活率，高危險的病患尤其效果顯著；此外，「術後淋巴結摘取數」、「腸阻塞症狀」和「癌症 T 分期」這三個高危險因素，被視為能顯著影響第二期大腸癌病患五年整體存活率存活率的獨立預測因子。

關鍵詞　輔助性化學治療、高危險、第二期大腸癌。