Original Article

Adjuvant Chemotherapy Duration in Colon Cancer with Solitary Tumor Deposits: A Retrospective Analysis of Survival Outcomes

Wei-Yuan Chen[1,2]
Chia-Lin Chou[1]
Feng-Fan Chiang[2]
Chih-An Lin[2]
Ming-Cheng Chen[2]
Chun-Yu Lin[2]
[1]*Division of Colon and Rectal Surgery, Department of Surgery, Chi Mei Medical Center, Tainan,*
[2]*Division of Colorectal Surgery, Department of Surgery, Taichung Veterans General Hospital, Taichung, Taiwan*

Key Words
Colorectal cancer;
Adjuvant chemotherapy;
Tumor deposits

Introduction. Colorectal cancer (CRC) is a leading cause of cancer-related morbidity and mortality worldwide. Although treatments have improved, outcomes still depend on tumor features. The TNM staging system is important for prognosis but does not fully account for factors like tumor deposits (TDs), which are linked to worse outcomes, especially in patients without lymph node metastasis. For patients with solitary TDs in the TanyN1cM0 stage, the best chemotherapy regimen and duration are still unclear. This retrospective study, conducted at two medical centers in Taiwan, examines how the length of adjuvant chemotherapy affects progression-free survival (PFS) and overall survival (OS) in these patients.
Materials & Methods. This retrospective study analyzed patients with TanyN1cM0 CRC who underwent curative colorectal surgery at Taichung Veterans General Hospital and Chi Mei Medical Center between January 1, 2013, and December 31, 2022. A total of 61 patients were included, with 43 receiving adjuvant chemotherapy for 6 cycles or fewer, and 18 receiving more than 6 cycles. The primary outcomes were PFS and OS. After 1:2 propensity score matching, 23 patients were selected for analysis. Kaplan-Meier survival curves were generated, and Cox regression models were used to identify prognostic factors.
Results. After 1:2 propensity score matching, the five-year OS rate for patients receiving chemotherapy for 6 cycles or fewer was 67.7%, while it was 87.5% for those receiving more than 6 cycles of chemotherapy. Similarly, the five-year PFS rate was 64.3% for the 6 cycles or fewer group and 87.5% for the more than 6 cycles group. However, there were no statistically significant differences in either PFS or OS between the two groups. Univariable and multivariable Cox regression analyses identified pathological margin involvement as a significant predictor of poorer OS.
Conclusion. This study provides valuable insights into the role of adjuvant chemotherapy duration in TanyN1cM0 CRC with solitary TDs. While we observed no significant difference in survival outcomes between chemotherapy durations, further research with larger cohorts and extended follow-up is necessary to establish the optimal chemotherapy regimen and duration for these patients. Personalized treatment approaches that consider individual patient factors are crucial for improving outcomes in this subgroup of CRC patients.

[*J Soc Colon Rectal Surgeon* (*Taiwan*) *2026;37:52-60*]

Received: April 8, 2025. Accepted: June 18, 2025.
Correspondence to: Dr. Chih-An Lin, Division of Colorectal Surgery, Department of Surgery, Taichung Veterans General Hospital, No. 1650, Sect. 4, Taiwan Boulevard, Taichung 407219, Taiwan. Tel: 886-4-2359-2525 ext. 61606; E-mail: waterdrophead@gmail.com

Colorectal cancer (CRC) is the third most commonly diagnosed and third leading cause of cancer death worldwide, with over 1.9 million new cases in 2022.[1,2] In the U.S., 153,020 cases were expected in 2023, including nearly 20,000 in individuals under 50.[3] By 2025, more than 150,000 new cases of colon and rectal cancer are expected.

The TNM staging system guides prognosis based on tumor size, nodal status, and metastasis but does not account for other key pathological features. In its seventh edition, pericolonic tumor deposits (TDs) without lymph node involvement were reclassified as stage III (N1c).[4]

TDs are found in approximately 20% of CRC cases and are linked to poor prognosis and recurrence, especially in rectal cancer.[5-8] Although adjuvant chemotherapy is standard for N1c patients, data on its benefit in solitary TDs are limited. A 2022 national study showed chemotherapy improved overall and cancer-specific survival in such patients.[9] Conversely, a Korean study found no benefit in those with solitary lymph node metastasis.[10]

FOLFOX and CAPOX are common adjuvant regimens, but the optimal duration for TanyN1cM0 cases is unknown. This study compares outcomes between short (≤ 6 cycles) and long (> 6 cycles) duration of chemotherapy to determine whether prolonged treatment improves survival or a shorter course is sufficient for this high-risk subgroup.

Materials & Methods

Study population

Patients with stage TanyN1cM0 colon cancer are a relatively small population. In this study, we utilized databases from Taichung Veterans General Hospital (TCVGH) and Chi Mei Medical Center (CMMC) to retrospectively include patients who underwent radical colorectal surgery and had pathological reports indicating the presence of tumor deposits (TDs) between January 1, 2013, and December 31, 2022. Patients who had multiple comorbidities or expired during hospitalization were excluded from the study. Additionally, we excluded patients who underwent surgery at other hospitals without available pathological reports, as well as those with distant organ metastasis or additional lymph node metastasis.

All patients were recommended to receive an oxaliplatin-based doublet chemotherapy regimen as adjuvant treatment, consistent with standard care for stage III colon cancer during the study period. The specific regimens used were either FOLFOX or CAPOX (XELOX). The choice of FOLFOX vs. CAPOX was at the treating oncologist's discretion and often based on patient factors and preference. For the purposes of this study, we did not stratify outcomes by regimen, as both are considered equivalent in efficacy; instead, we focused on the overall duration of chemotherapy.

For patients in the ≤ 6-cycles cohort, early discontinuation most commonly resulted from cumulative neuropathy, gastrointestinal adverse events, or patient preference after achieving adequate tolerability; no protocol-mandated stop was applied.

Statistical analysis

The primary outcomes of this study were progression-free survival (PFS) and overall survival (OS). PFS was defined as the time from cancer diagnosis to recurrence, while OS was defined as the time from cancer diagnosis to death from any cause.

Demographic and clinicopathological characteristics of the patients were analyzed, including age at diagnosis, gender, BMI, ECOG performance status, tumor location, staging, surgical approach, initial CEA level, Charlson-Deyo comorbidity index, lymph node harvest, margin involvement, perineural invasion, angiolymphatic invasion, and neoadjuvant radiotherapy.

To assess the differences in the distribution of variables between patients, Pearson's chi-square test or Mann-Whitney U test were employed, depending on the data type. The Kaplan-Meier method was used to estimate PFS and OS, and the log-rank test was performed to evaluate whether the differences in survival rates between subgroups were statistically significant.

Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox regression models to

assess the prognostic value of various demographic and clinicopathological factors. A *p*-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) software 30.0 (IBM Corporation, Chicago, IL, USA).

Results

Patients

In our retrospective study, 72 patients who underwent colorectal surgery between January 1, 2013, and December 31, 2022, with clinicopathologic TanyN1cM0 were included (Fig. 1). Patients with recurrence, R2 resection, those who expired during hospitalization, and those without available pathological reports were excluded. After exclusions, 61 patients remained for analysis.

Of these 61 patients, 43 received adjuvant chemotherapy with FOLFOX or CAPOX for 6 cycles or fewer, while 18 patients received more than 6 cycles of FOLFOX or CAPOX (Table 1).

The initial analysis revealed that patients receiving 6 cycles or fewer of chemotherapy had lower initial CEA levels, and this group had a higher proportion of female patients. There were no significant differences between the groups regarding age, tumor location, surgical approach, comorbidities, neoadjuvant radiotherapy, or pathological results. In the univariable and multivariable Cox regression analysis, older age and pathologic margin involvement were associated with a higher hazard ratio (HR) for overall survival (OS).

Due to the imbalance in sample sizes between the two groups, the statistical analysis revealed no significant differences in OS or PFS. To address this, we performed 1:2 propensity score matching (PSM), resulting in the selection of 23 patients.

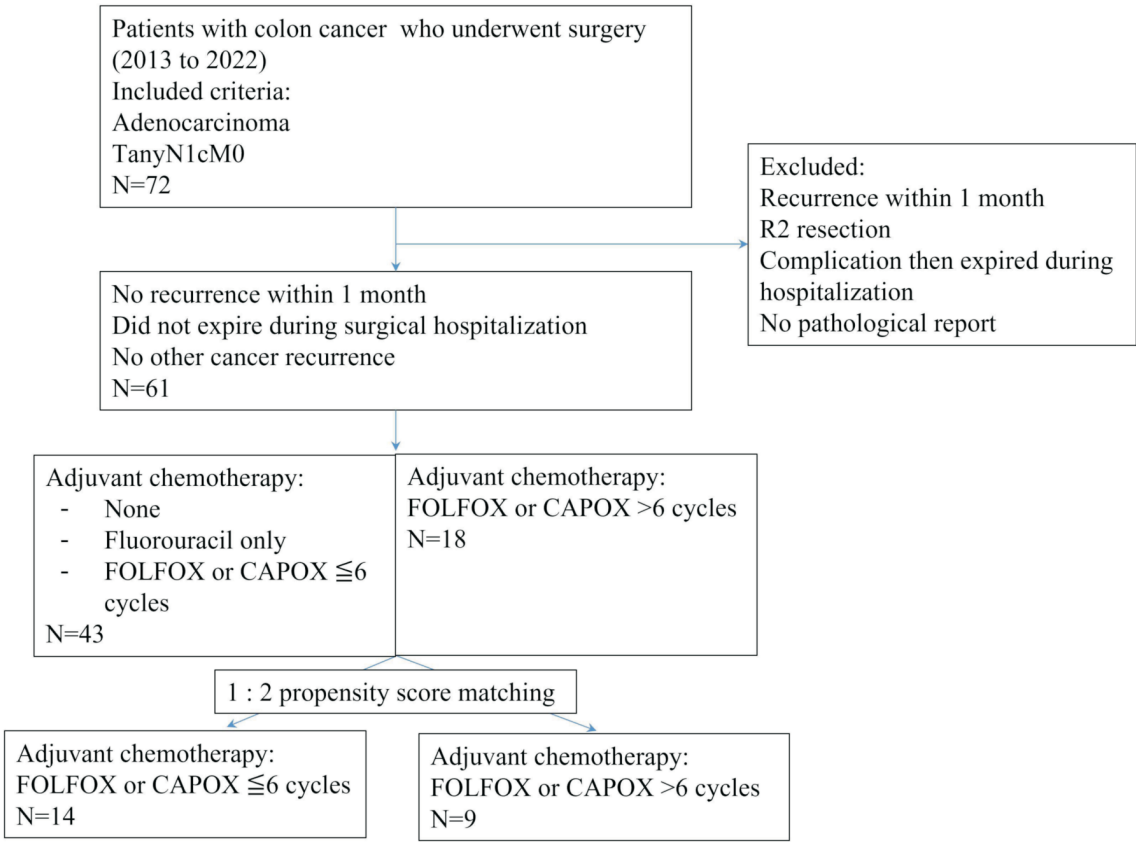

Fig. 1. Flow chart.

The median and maximum follow up periods in the ≤ 6-cycles group were 42.0 months and 71.1 months, respectively. The median and maximum follow up periods in the > 6 cycles group were 46.5 months and 74.0 months, respectively.

As shown in Table 1, after PSM, there were no significant differences between the groups in basic patient characteristics. In the univariable and multivariable Cox regression analysis, pathologic margin involvement was associated with higher hazard ratio for overall survival (Table 2).

Recurrence and survival

After PSM, the five-year overall survival (OS) rates were 67.7% in the 6 cycles or fewer chemotherapy group and 87.5% in the group that received more than 6 cycles of chemotherapy (Fig. 2a). The five-year progression-free survival (PFS) rates were 64.3% for the 6 cycles or fewer group and 87.5% for the more than 6-cycles group (Fig. 2b). However, there were no statistically significant differences in either PFS or OS between the two groups.

Table 1. Patient demographics & tumor characteristics (N = 23)

	Adjuvant FOLFOX		*p* value
	≤ 6 cycles (n = 14)	> 6 cycles (n = 9)	
Age (y)	65.5 (45.8-81.5)	64.0 (56.0-68.0)	0.850
Gender			0.505
Female	5 (35.7%)	4 (44.4%)	
Male	9 (64.3%)	5 (55.6%)	
BMI (kg/m^2)	23 (20.5-27.2)	24.4 (20.9-26.0)	0.950
ECOG			0.650
0	6 (42.9%)	5 (55.6%)	
1	7 (50.0%)	4 (44.4%)	
2-3	1 (7.1%)	0 (0.0%)	
Lesion site			0.517
Left	12 (85.7%)	7 (77.8%)	
Right	2 (14.3%)	2 (22.2%)	
Pathologic T			0.666
1	1 (7.1%)	1 (11.1%)	
2	1 (7.1%)	1 (11.1%)	
3	11 (78.6%)	5 (55.6%)	
4	1 (7.1%)	2 (22.2%)	
Surgical approach			0.681
Open	7 (50.0%)	4 (44.4%)	
Laparoscopic	4 (28.6%)	4 (44.4%)	
Robotic	3 (21.4%)	1 (11.1%)	
Log initial CEA (ng/ml)	1.5 (1.0-2.8)	1.3 (1.0-2.3)	0.659
Charlson-Deyo comorbidity			0.567
Minor	7 (50.0%)	4 (44.4%)	
Major	7 (50.0%)	5 (55.6%)	
Lymph node harvest			0.609
< 12	1 (7.1%)	0 (0.0%)	
12+	13 (92.9%)	9 (100%)	
Margin involved	1 (7.1%)	1 (11.1%)	0.640
Perineural invasion	3 (21.4%)	2 (22.2%)	0.673
Angiolymphatic invasion	3 (21.4%)	1 (11.1%)	0.483
Neoadjuvant RT	1 (7.1%)	1 (11.1%)	0.640
Follow-up period (month)	42.0 (20.6-71.1)	46.5 (40.2-74.0)	0.450

Chi-square test or Mann-Whitney U test. Median (IQR) * $p < 0.05$, ** $p < 0.01$.

Table 2. Cox regression — OS (N = 23)

	Univariate			Multivariable		
	Hazard ratio	95% CI	*p* value	Hazard ratio	95% CI	*p* value
Age (y)	1.11	(1.02-1.22)	0.023*	1.13	(1.00-1.27)	0.055
Gender						
Female	Reference					
Male	0.73	(0.12-4.36)	0.727			
BMI (kg/m^2)	1.00	(0.83-1.21)	0.995			
ECOG						
0	Reference					
1	1.00	(0.17-6.06)	1.000			
2-3	1.00	(0.00-10292.00)	1.000			
Lesion site						
Left	Reference					
Right	0.04	(0.00-627.55)	0.505			
Pathologic T						
1-2	Reference					
3	0.75	(0.78-7.23)	0.804			
4	1.35	(0.08-21.63)	0.833			
Surgical approach						
Open	Reference					
Lapa	0.27	(0.03-2.44)	0.754			
Robot	0.00	(0.00-.	0.977			
Log initial CEA (ng/ml)	1.77	(0.77-4.10)	0.179			
Charlson-Deyo comorbidity						
Minor	Reference					
Major	4.67	(0.52-42.01)	0.169			
Lymph node harvest						
< 12	Reference					
12+	0.11	(0.10-1.19)	0.069			
Margin involved	7.30	(1.20-44.42)	0.031*	16.46	(1.40-193.93)	0.026*
Perineural invasion	0.75	(0.84-6.71)	0.796			
Angiolymphatic invasion	1.03	(0.12-9.23)	0.979			
Neoadjuvant RT	2.70	(0.30-24.43)	0.378			
Adjuvant FOLFOX						
≤ 6 cycles	Reference			Reference		
> 6 cycles	0.32	(0.04-2.85)	0.305	0.20	(0.01-2.92)	0.241

Cox proportional hazard regression. * $p < 0.05$, ** $p < 0.01$.

Discussion

Colorectal cancer (CRC) remains a significant global health concern, being the third most common cancer worldwide, with over 1.9 million cases diagnosed in 2022. Despite advances in early detection and treatment, the prognosis for CRC patients still varies considerably, particularly among those with stage TanyN1cM0 disease. The presence of tumor deposits (TDs) in these patients has been shown to correlate with worse outcomes, including higher local recurrence and reduced survival rates. In this study, we aimed to evaluate the impact of adjuvant chemotherapy duration on progression-free survival (PFS) and overall survival (OS) in patients diagnosed with solitary TDs.

Lin et al.[9] analyzed 877 SEER database patients and found that any adjuvant chemotherapy significantly improved overall and cancer-specific survival. However, our study focused on treatment duration.

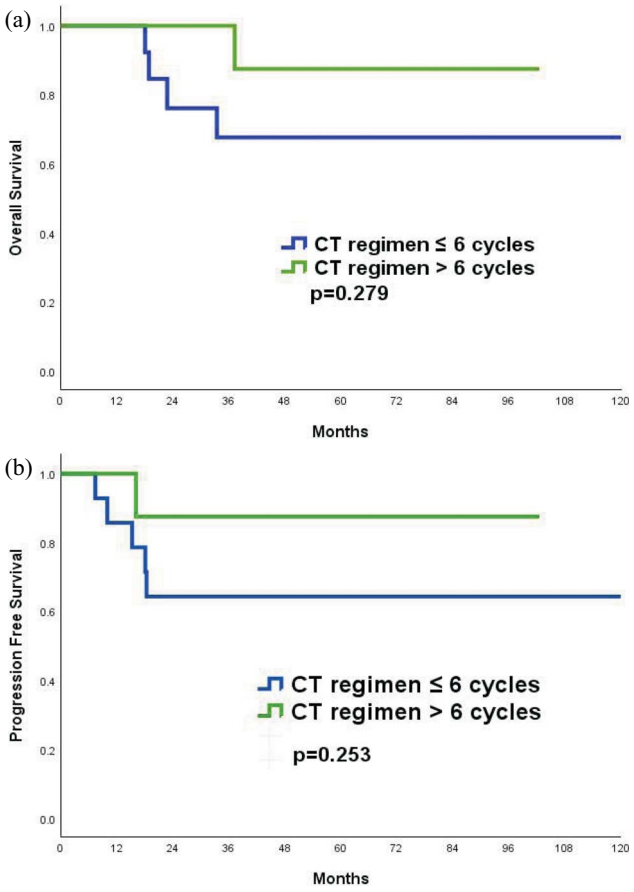

Fig. 2. (a) Overall survival curve and (b) Progression-free survival curve with ≤ 6 cycles versus > 6 cycles of adjuvant chemotherapy.

Importantly, the study by Lin et al. may have included heterogeneous N1c definitions based on registry data, whereas our cohort was strictly limited to pathologically confirmed solitary TDs without lymph node involvement. Moreover, Lin's study did not assess chemotherapy cycles.

In contrast to the study by Lin et al., our study did not show a clear benefit from intensifying treatment once chemotherapy had been initiated, suggesting that prolonged duration may not be necessary for all N1c patients. However, selection bias and lack of randomization remain limitations. Additionally, neither study assessed treatment-related toxicities or quality of life, which are critical when evaluating prolonged therapy.

The IDEA pooled analysis[11] showed that, for low-risk stage III disease, 3 months of CAPOX was non-inferior to 6 months, whereas high-risk patients derived incremental benefit from the longer course.

In our study, the cutoff for grouping was set at 6 cycles of chemotherapy, which corresponds to approximately 3 months of a FOLFOX regimen. Our data suggest that within the biologically distinct N1c population, extending therapy beyond approximately three months did not result in additional OS or PFS benefits, although the limited statistical power precludes a definitive conclusion. Due to the relatively small sample size, we did not stratify patients into CAPOX and FOLFOX subgroups.

Furthermore, there were no significant differences in baseline patient characteristics between the groups. Both univariate and multivariate Cox regression analyses demonstrated that pathologic margin involvement was associated with an increased risk of mortality.

This lack of difference in outcomes could be attributed to several factors. One potential reason was the relatively small sample size, which limited the power of the study to detect meaningful differences between groups. Furthermore, a significant proportion of patients may have been lost to follow-up, further reducing the ability to observe long-term survival outcomes accurately. The small sample size and the possibility of loss to follow-up could have obscured any potential survival benefit of extended chemotherapy. With a relatively small sample size (N = 61) and an imbalanced distribution between treatment groups (43 vs. 18), we conducted post hoc power analysis based on OS. The power was 0.57, below the commonly accepted threshold of 0.8, which indicated that the non-significant results of OS may be attributed to insufficient statistical power, suggesting a potential risk of a type II error.

Another consideration is patient selection and tolerance for therapy. Because this was not a randomized trial, the decision to give cycles of chemotherapy was individualized. Based on patients' medical records, physicians suggested older patients and those with more comorbidities receive chemotherapy for 6 cycles or fewer, whereas for those who were fitter or deemed to be at higher risk were recommended to receive more than 6 cycles. The initial suggestion for those with high risk was 12 cycles of chemotherapy. However, the treatment course was discontinued in

most cases due to adverse side effects. The initial patient selection resulted in 43 vs. 18 for the ≤ 6 cycles and > 6 cycles groups, respectively. To manage the imbalanced distribution between the groups, we conducted 1:2 propensity score matching (PSM). After PSM, the baseline patient characteristics were similar between the groups. In the Cox regression analysis, pathologic margin involvement was associated with higher HR. There were still no significant differences in OS and PFS between the groups.

Our study has limitations that warrant discussion. The retrospective design of the study meant we could not confirm the accuracy of medical records and had no control over treatment assignments. There may have been unknown confounders influencing who got 6 cycles of therapy or fewer. The sample size was small, due to the rarity of N1c classification. We attempted to compensate by using PSM, but the results still revealed no significance between groups. Because of the small cohort, we did not perform extensive subset analyses (for example, separating patients by T stage in the outcome analysis) to avoid statistically spurious findings. Additionally, we focused on survival endpoints; we did not systematically assess chemotherapy-related toxicities or quality of life, which are important considerations when comparing shorter versus longer treatment.

The optimal chemotherapy regimen and duration for patients with TanyN1cM0 remain uncertain, although FOLFOX and CAPOX are the most commonly used regimens. To our knowledge, this is the first study exploring duration of oxaliplatin-based adjuvant chemotherapy specifically in N1c colon cancer with solitary tumor deposits.

Our findings suggest that further research is needed to determine whether a longer duration of chemotherapy offers significant benefits for these patients, especially considering the potential for treatment-related toxicities and the lack of clear survival advantages.

Conclusions

In conclusion, our study provides important insights into the role of adjuvant chemotherapy in patients with staging of TanyN1cM0 in colorectal cancer. While we observed no significant difference in progression-free survival or overall survival between patients receiving 6 or fewer cycles of chemotherapy versus more than 6 cycles, the lack of statistical significance may be due to the small sample size and potential loss to follow-up. These factors should be considered when interpreting the results. Despite these limitations, our study underscores the need for further research to establish the optimal chemotherapy duration and regimen for patients with TanyN1cM0 colorectal cancer with tumor deposits.

Personalized treatment approaches, taking into account factors such as tumor characteristics, patient age, and comorbidities, are critical in improving survival outcomes for these patients. Future studies with larger sample sizes and more rigorous follow-up are necessary to clarify the role of chemotherapy duration in this patient subgroup and to develop evidence-based treatment guidelines for managing CRC with tumor deposits.

Acknowledgements

We thank the patients participating in this study and all staff at the hospitals for their contributions to this study.

Conflict of Interest Statement

The authors declare no conflict of interest in this study.

Role of Any Funding Source

The authors declare there was no role of funding in the study.

References

1. Morgan E, Arnold M, Gini A, et al. Global burden of colo-

rectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut* 2023;72(2):338-44. doi:10.1136/gutjnl-2022-327736
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71(3):209-49. doi:10.3322/caac.21660
3. Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2023. *CA Cancer J Clin* 2023;73(3):233-54. doi:10.3322/caac.21772
4. Sobin LH, Gospodarowicz MK, Wittekind C. TNM Classification of Malignant Tumours (7th Edn). Chichester: Wiley-Blackwell; 2009., n.d.
5. Nagtegaal ID, Knijn N, Hugen N, et al. Tumor deposits in colorectal cancer: improving the value of modern staging-a systematic review and meta-analysis. *J Clin Oncol* 2017;35(10):1119-27. doi:10.1200/JCO.2016.68.9091
6. Delattre JF, Selcen Oguz Erdogan A, Cohen R, et al. A comprehensive overview of tumour deposits in colorectal cancer: towards a next TNM classification. *Cancer Treat Rev* 2022;103:102325. doi:10.1016/j.ctrv.2021.102325
7. Bouquot M, Creavin B, Goasguen N, et al. Prognostic value and characteristics of N1c colorectal cancer. *Colorectal Dis* 2018;20(9):O248-55. doi:10.1111/codi.14289
8. Jörgren F, Agger E, Lydrup ML, Buchwald P. Tumour deposits in colon cancer predict recurrence and reduced survival in a nationwide population-based study. *BJS Open* 2023;7(6):zrad122. doi:10.1093/bjsopen/zrad122
9. Lin Q, Zhou H, Shi S, Lin J, Yan W. The prognostic value of adjuvant chemotherapy in colon cancer with solitary tumor deposit. *Front Oncol* 2022;12:916091. Published 2022 Jul 13. doi:10.3389/fonc.2022.916091
10. Yeom SS, Lee SY, Kim CH, Kim HR, Kim YJ. The prognostic effect of adjuvant chemotherapy in the colon cancer patients with solitary lymph node metastasis. *Int J Colorectal Dis* 2019;34(8):1483-90. doi:10.1007/s00384-019-03346-7
11. André T, Vernerey D, Mineur L, et al. Three versus 6 months of oxaliplatin-based adjuvant chemotherapy for patients with stage III colon cancer: disease-free survival results from a randomized, open-label, international duration evaluation of adjuvant (IDEA) France, phase III trial. *J Clin Oncol* 2018;36(15):1469-77. doi:10.1200/JCO.2017.76.0355

原　著

結直腸癌伴孤立腫瘤沉積物的輔助化療療程：生存結果的回顧性分析

陳威遠[1,2]　周家麟[1]　蔣鋒帆[2]　林志安[2]　陳明正[2]　林俊余[2]

[1]奇美醫學中心　外科部　大腸直腸外科

[2]台中榮民總醫院　外科部　大腸直腸外科

目的　結直腸癌 (CRC) 是全球癌症相關發生和死亡的主要原因之一。儘管治療上已有進展，但結直腸癌患者的預後仍根據腫瘤特徵而異。TNM 分期系統在預測預後中扮演著重要角色，但無法全面考量到腫瘤沉積物 (tumor deposits) 等因素，而這些因素與較差預後相關，尤其在沒有淋巴結轉移的患者中。對 TanyN1cM0 階段僅有腫瘤沉積物的患者，目前仍不清楚最佳的化學治療方案與療程。本回顧性研究於台灣兩家醫學中心進行，探討術後輔助化療療程長短對這類患者之無病進展生存期 (PFS) 與總存活期 (OS) 的影響。

材料與方法　本研究進行了一項回顧性分析，對 2013 年 1 月 1 日至 2022 年 12 月 31 日期間在台中榮民總醫院和奇美醫學中心接受根治性結直腸手術的 TanyN1cM0 結直腸癌患者進行分析。共有 61 名患者納入分析，其中 43 名患者接受了 6 次以下的術後輔助化療，18 名患者接受了超過 6 次的化療。研究的主要結果是 PFS 和 OS。通過 1 比 2 的 propensity score matching 篩選出 23 位病人，以 Kaplan-Meier 生存曲線生成，並使用 Cox 回歸模型來分析預後因素。

結果　經 1 比 2 傾向分數配對後，接受 6 次以下化療的患者五年總生存率為 67.7%，而接受超過 6 次化療的患者為 87.5%。6 次以下組的五年無病進展生存率為 64.3%，而超過 6 次組為 87.5%。然而，兩組之間在 PFS 和 OS 上均未顯示出統計學上的顯著差異。單變量和多變量 Cox 回歸分析顯示病理標本邊緣受腫瘤侵犯是總生存期較差的重要預測因子。

結論　本研究提供了有關輔助化療療程在 TanyN1cM0 階段的結直腸癌患者中的作用的意見。儘管我們在化療療程長短上未觀察到顯著的生存結果差異，但需要進一步的研究，包括蒐集更大規模的患者群體和更長時間的追蹤，以確立這些患者的最佳化療療程。針對個別病患條件制定個人化治療策略，對於改善此類大腸直腸癌患者的治療成果至關重要。

關鍵詞　大腸直腸癌、輔助化學治療、腫瘤沉積物。