Original Article

Comparable Treatment Results of Localized Colon Cancer with Fast-track Pre-operative Survey — Single Institute Experience

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Key Words
Colon cancer;
Pre-operative survey;
Complication rates;
Recurrence rate

Background. This study aimed to evaluate whether fast-track preoperative surveys conducted in a relatively abundant medical resource region can confirm the efficacy of treatment for localized colon cancer.
Materials and Methods. The patients who underwent curative resection for stage I-III colonic adenocarcinoma between 2014 and 2018 were enrolled. The patients were divided into two groups ("within 2 weeks" group and "2 weeks later" group) based on the timing of curative surgery from the initial diagnosis. Retrospective study with propensity score matching was used to compare the outcomes included postoperative complications and 2-year recurrence rate between the two groups.
Results. Exactly 224 patients were enrolled in the analysis. Of the total patients, 122 were men and 102 were women, with a median age of 67 years (range: 29-91). The lesion frequently developed in the sigmoid colon (37%) and subsequently in the ascending colon (27%). One hundred sixteen patients were included in the "within 2 weeks" group, while the rest were included in the "2 weeks later" group. No significant difference was found in the outcomes (e.g., postoperative complications and 2-year recurrence rate) between the two groups. To reduce disparities, these two groups were adjusted by performing propensity score matching in a 1:1 ratio. Each group comprised 85 patients, and the results (such as the 2-year recurrence rate) was similar between the two groups (12.9 vs. 10.6, p = 0.63).
Conclusion. Localized colon cancer patients who participated in the fast-track preoperative survey and underwent radical resection had equivalent results compared with those who participated in the preoperative survey in a leisurely manner. These results were associated with the aggressive coordination between the multidisciplinary facilities in the hospital, which not only provided equal oncological treatment results but also had advantage to alleviating the anxiety of the patients and their family members who really concern delay treatment of cancer.

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Colorectal cancer is one of the most common malignancy and the third leading cause of mortality in Taiwan.[1] Delay in the diagnosis of colon cancer is common owing to its asymptomatic or non-specific

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presentation. Hence, the tumor is usually diagnosed at a later stage and the prognosis is poor.[2-5] However, in the past decade, public health policy held the wide screening of fecal immunochemical testing in Taiwan has improved the detection rate of stage 0 to I colorectal cancer.

Radical resection of localized colon cancer is the standard therapy,[6,7] and most patients with colon cancer undergo elective surgery except those whose develop complications such as obstruction or perforation.[6,8-10] Based on this scenario, the best timing for curative surgery remains controversial and needs to be elucidated further.[6,7] Some previous studies[11,12] reported that a delay in curative surgery of over 12 weeks was associated with increased cancer mortality, while other observational studies did not show any difference. Therefore, it is important to evaluate the effects of the interval from initial diagnosis to radical resection of localized colon cancer.

In 2020, Kucejko et al. reported that the best timing for a colon cancer patient to undergo radical resection is 3-4 weeks after initial diagnosis. Patients whose treatment period was less than two weeks (14 days) owing to the noncompletion of all stages of the studies and lack of preoperative surveys conducted in the United States (US) had higher risk of mortality and recurrence.[13] This problem was due to the limited medical resources in the US; however, this was not the case in Taiwan due to the wide coverage of their national medical insurance.

Thus, the present study aimed to evaluate whether shorter preoperative surveys at relatively abundant medical resource area can confirm the efficacy of treatment for localized colon cancer.

Materials and Methods

This single-center retrospective study reviewed the data of consecutive patients with colon cancer who were admitted in Chang Gung Memorial Hospital (CGMH), Keelung branch, between January 2014 and December 2018. This study was approved by the institutional review board (IRB) of Chang Gung Memorial Hospital, Taiwan (IRB no.201800424B0).

Patients who were pathologically diagnosed with colon cancer or whose diagnosis was made by colonoscopy, abdominal computerized tomography (CT) scan, magnetic resonance imaging (MRI) scan, or lower gastrointestinal series were included in this study. Patients with rectal cancer, with stage 0 or IV colon cancer, who underwent emergent surgery due to bowel obstruction or perforation, or who received neoadjuvant chemotherapy were excluded. The demographic data, timing from diagnosis to elective radical resection, pathological results, short-term results including length of hospital stay, and postoperative complications were obtained retrospectively from the electronic medical records and analyzed. The 2-year cumulative recurrence rate was set as the primary endpoint.

All patients were followed for at least two years postoperatively, with the longest follow-up of up to 7 years. The participants were divided into two groups based on the treatment interval from initial diagnosis to elective radical resection which was defined as duration of pre-operative survey. The primary endpoint was 2-year recurrence rate, while the secondary point was length of hospital stay, surgical quality, and postoperative complications. X^2 test was used for univariate analyses, while log-rank test was performed to compare the two-year recurrence rate between the two study groups. To reduce the disparities between the two groups, propensity score matching was performed in a 1:1 ratio to determine the possible confounding factors such as age, Charlson Comorbidity Index, American Joint Committee on Cancer (AJCC) stage, and surgical approach. All statistical analyses were performed using SPSS statistical software (version 25, IBM Inc.). A p value of < 0.05 was considered significant.

Results

A total of 706 patients were diagnosed with colorectal cancer (CRC) during our study period. Among them, 482 patients who developed a tumor in the rectum (238), with stage IV and 0 colon cancer (128 and 26, respectively), who underwent emergent surgery (47), and with missing data (43) were excluded. Hence,

only 224 patients were included in our study. The flow chart of the patient selection process is shown in Fig. 1.

Of the 224 patients, 122 were men and 102 were women, with a median age of 67 years (range: 29-91). The colon tumor was most observed in the loci of the sigmoid colon (37%) and subsequent was ascending colon (27%). The splenic flexure is the least location of tumor, accounting for 2% of our cases. The demographic and clinical data of patients are shown in Table 1. The patients were regularly followed up based on the CGMH CRC consensus follow-up guidelines. Carcinoembryonic antigen testing was performed every 3 months, while complete colonoscopy and CT scan of the abdomen were performed annually or if tumor recurrence was suspected. The least follow-up duration was 24 months with a median of 53 months (24-84 months).

All 224 patients were divided into two groups based on the treatment interval between the diagnosis of colon cancer and the date of elective radical surgical intervention. A total of 116 patients were included in the "within 2 weeks" group, while the rest were included in the longer than 2 weeks group. No significant differences were between the two groups in terms of age, gender, tumor location, American Society of Anesthesia (ASA) score, and Charlson Comorbidity Index. Patients with more advanced-stage colon can-

Table 1. Participants' baseline data

Total	224
Mean age, y	66.6
Sex, no. (%)	
Male	122 (54.5)
Female	102 (45.5)
Tumor	
Location, no.	
Ascending	62
Hepatic flexure	17
Transverse	29
Splenic flexure	5
Descending	28
Sigmoid	83
Charlson Comorbidity Index, no. (%)	
0	106 (47.3)
1	72 (32.1)
≥ 2	46 (20.5)
ASA score, no. (%)	
≤ II	95 (42.4)
III	117 (52.2)
≥ IV	12 (5.3)
Surgical approach, no. (%)	
Laparoscopic	101 (45.1)
Laparotomy	123 (55.0)
Outcome	
Mean length of hospital stay after tumor resection, d	13.8
Clavien-Dindo classification, no. (%)	
I	185 (82.6)
II	18 (14.7)
≥ III	6 (2.7)
Two-year recurrence rate, % (no.)	10.3% (23)

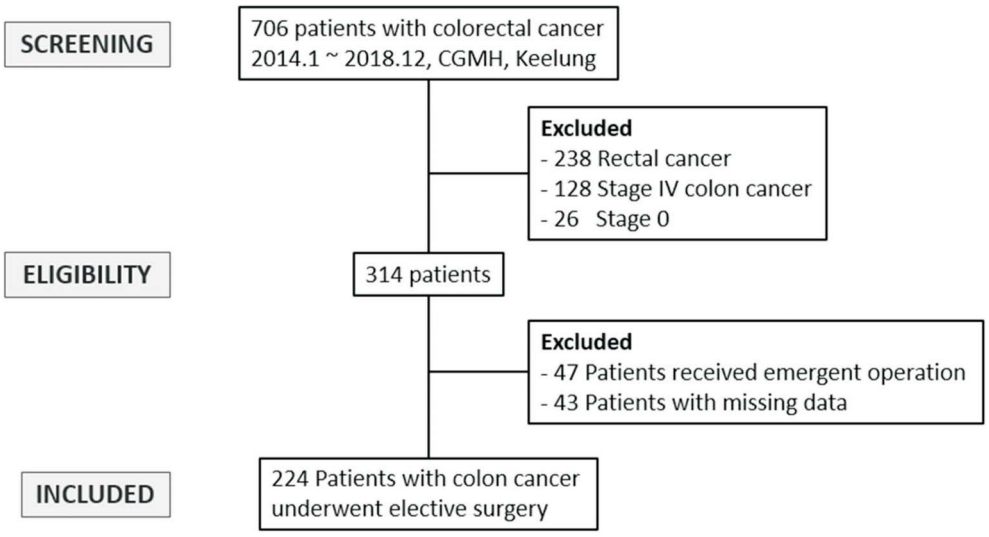

Fig. 1. A total of 706 patients were diagnosed with colorectal cancer between 2013 and 2017. After adjustment based on the exclusion and inclusion criteria, 224 patients with stage I-III colon cancer were included in the study.

cer (AJCC stage III, 50.9% vs. 35.2%, $p = 0.004$) who underwent laparotomy (62% vs. 47.2%, $p = 0.026$) were stratified in the short treatment interval group. The number of lymph nodes harvested during surgery (33.2 vs. 23.9, $p < 0.001$) showed a significant difference, while the mean length of hospital stay after tumor resection (14.9 days vs. 12.7 days, $p = 0.07$) showed a marginal difference in the short treatment interval group. Meanwhile, no significant difference was observed in the short-term outcomes such as post-operative complications and long-term outcome such as 2-year recurrence rate between the two groups (Table 2 & Fig. 2).

After adjusting for covariates through propensity score matching in a 1:1 ratio, each group comprised 85 patients. Accordingly, no significant differences were found between the two groups in terms of age, gender, tumor location, AJCC stage, ASA score,

Table 2. Data of the participants

Duration of pre-operative survey, d	Unadjusted			Adjusted		
	≤ 14 days	> 14 days	*p* value	≤ 14 days	> 14 days	*p* value
Total	116	108		85	85	
Mean age, y	65.6	67.75	0.210	67.0	67.5	0.760
Sex, no. (%)			0.656			0.539
Male	61 (52.5)	61 (56.4)		46 (54.1)	42 (49.4)	
Female	55 (47.4)	47 (43.5)		39 (45.9)	43 (50.6)	
Tumor, location, no.			0.570			0.154
Ascending	28	34		22	37	
Hepatic flexure	10	7		9	7	
Transverse	19	10		12	9	
Splenic flexure	3	2		2	0	
Descending	14	14		8	9	
Sigmoid	42	41		32	33	
AJCC stage, no. (%)			0.004			0.767
I	16 (13.7)	34 (31.5)		15 (17.6)	18 (21.2)	
II	41 (35.3)	36 (33.3)		35 (41.2)	31 (36.5)	
III	59 (50.9)	38 (35.2)		35 (41.2)	36 (42.4)	
Mean size, cm	3.44	4.24	0.002	4.16	3.71	0.142
Charlson Comorbidity Index, no. (%)			0.398			0.801
0	52 (44.8)	54 (50.0)		40 (43.9)	43 (50.0)	
1	42 (36.2)	30 (27.7)		28 (39.0)	24 (30.5)	
≥ 2	22 (18.9)	24 (22.2)		17 (17.1)	18 (20.0)	
ASA score, no. (%)			0.458			0.210
≤ II	46 (39.7)	49 (45.4)		31 (36.5)	39 (45.9)	
III	62 (53.4)	55 (50.9)		48 (56.5)	44 (51.8)	
≥ IV	8 (6.9)	4 (3.7)		6 (7.1)	2 (2.4)	
Surgical approach, no. (%)			0.026			0.441
Laparoscopic	44 (37.9)	57 (52.7)		41 (48.2)	36 (42.4)	
Laparotomy	72 (62.0)	51 (47.2)		44 (51.8)	49 (57.6)	
Outcome						
Mean length of hospital stay after tumor resection, d	14.9	12.7	0.070	15.4	12.7	0.069
Clavien-Dindo classification, no. (%)			0.299			0.446
I	93 (80.2)	92 (85.2)		69 (81.2)	70 (82.4)	
II	18 (15.5)	15 (13.9)		12 (14.1)	14 (16.5)	
≥ III	5 (4.3)	1 (0.9)		4 (4.7)	1 (1.2)	
Mean number of nodes resected (positive)	33.20 (1.85)	23.88 (1.58)	< 0.001	31.6 (1.38)	25.6 (1.99)	0.008
Two-year recurrence rate, % (no.)	12.1% (14)	8.3% (9)	0.357	12.9% (11)	10.6% (9)	0.634

Charlson Comorbidity Index, and surgical approach. No significant difference was observed in the short-term outcomes (e.g., postoperative complications) between the two groups, but a marginal significance was observed in terms of length of hospital stay. Moreover, no significant difference was found in the 2-year recurrence rate between the two groups (12.9 vs. 10.6, p = 0.63). After PSM, a significant difference was found between the two groups in terms of the number of lymph nodes harvested during radical resection (31.6 vs. 25.6, P = 0.008), which may attributed to the similar quality of surgical treatment performed in these two groups (Table 2 & Fig. 3).

Discussion

Optimization of treatment for localized colon cancer requires timely preparation and intervention. Delay in treatment could worsen the prognosis of patients with localized colon cancer. Hence, financial penalty would be imposed if the recommended 2-week urgent referral system in the United Kingdom is not met.[14,15] However, the treatment guidelines for localized colon cancer worldwide did not strictly define the specific treatment interval between diagnosis and radical resection. The standard treatment interval should be within 6 weeks in order to allow comprehensive preoperative preparation included staging survey, curtailing of comorbidities and associated risks, and optimization of aerobic exercise as part of routine rehabilitation. However, informing patients regarding their cancer diagnosis induces anxiety, which requires timely management. Hence, the influence of timely treatment should be elucidated further without compromising the preoperative preparation in this group of patients.

In our study, no significant difference was observed in the short-term (length of hospital stay, postoperative complications and 2-year recurrence rate) outcomes between the two groups. In other words, fast-track preoperative survey and surgical intervention within 2 weeks after colon cancer diagnosis had similar results compared with the ordinary treatment interval, mostly within 3-6 weeks after diagnosis. Another reason for the need to perform a fast-track surgical intervention is the higher proportion of advanced-stage colon cancer patient, which may present with more aggressive symptoms and signs that require urgent manipulation. The proportion of patients with more advanced-stage colon cancer could also explain the high rate of laparotomy procedures compared with the rate of minimal invasive procedures in the fast-track group. It also could explain the marginal significance of longer hospital stay in this group of patients.

Patients who were diagnosed with colon cancer underwent complete pretreatment tumor survey, which included CT scan, MRI scan, echocardiography, pulmonary function test, and anesthesia risk evaluation before receiving the recommended treatment. All of these procedures required scheduling to determine the time that they can be performed and were time consuming, taking longer than 4 weeks to complete. Hence,

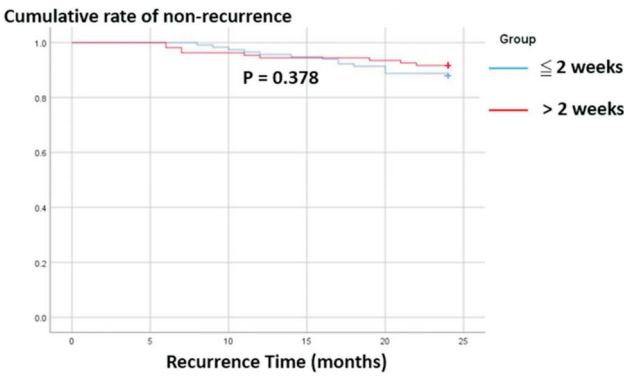

Fig. 2. Log-rank test of two non-adjusted groups showed no significant difference in the 2-year recurrence rate.

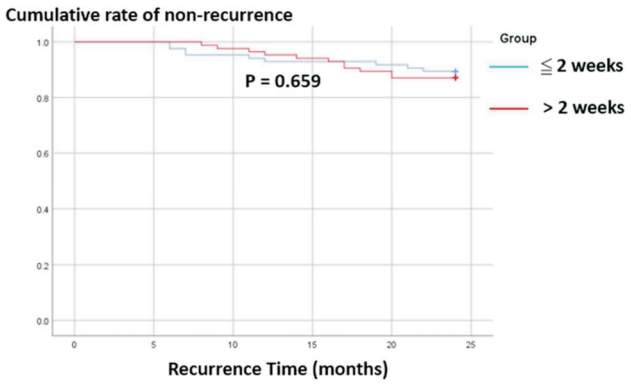

Fig. 3. Log-rank test of two post-PSM adjusted groups showed no significant difference in the 2-year recurrence rate.

the index study[13] reported the hazard effect of radical resection when performed within 2 weeks after the initial diagnosis due to the incompleteness of the preoperative survey. However, in our hospital, most of the patients (> 50%) underwent complete preoperative survey within 2 weeks after their colon cancer diagnosis. This is due to the fact that the national health insurance system in Taiwan has a wide coverage, thus leading to the high accessibility of medical resource.

In our adjusted data, no significant difference was observed in the nutrition status (evaluated based on the patients' body mass index and albumin level) between the two groups. Most of our patients were diagnosed by colonoscopy with tumor biopsy, whose results were obtained after an average of 4.7 days (range: 1-14 days). Patients in the shorter interval group underwent preoperative CT scan for tumor staging within a mean of 3.4 days after the initial diagnosis, while those in long time interval group underwent the procedure within a mean of 12.2 days. A total of 35 patients underwent preoperative two-dimensional (2D) echocardiography within an average of 12.6 days after colon cancer diagnosis. Twelve participants who required pulmonary function test prior to surgery underwent this procedure within two weeks after diagnosis (Table 3). Based on the data above, the delay in surgical treatment was due to the longer time frame for scheduled preoperative studies like CT scan, 2D echocardiography, and pulmonary function test. Delays in the performance of these imaging studies can be prevented through active communication and discussion with the patient and healthcare team. Accordingly, informing patients regarding their cancer diagnosis will induce anxiety, depression, or feelings of hopelessness. These events can lead to emotional instability and further affect the treatment results. Some studies emphasized on the provision of early intensive care, which is thought to be important for alleviating psychological stress in patients and families.[16]

Since 2010, our institute established a multidisciplinary treatment committee that attends to the needs of CRC patients. This committee comprised colorectal surgeons, hepatobiliary surgeons, chest surgeons, oncologists, radio-oncologists, radiologists, and nuclear medicine specialists. Case managers and cancer registry members were also enrolled, who played significant roles in coordinating the patients' treatment. All CRC patients were scheduled for pre-treatment survey, which included CT scan of the trunk (from the lower neck to the upper thigh). MRI or positron emission tomography scan for evaluation of specific foci were scheduled per patients' request or as suggested by the committee. The cases of all patients who were scheduled to undergo surgical intervention were discussed by the members of the committee to achieve treatment consensus. In our study, all patients in the fast-track and delayed treatment groups underwent complete preoperative survey prior to surgery. Completion of preoperative survey possibly caused the similarity in short-term results (such as postoperative complications). Interestingly, the fast-track treatment group had higher number of lymph nodes harvested compared with the delayed treatment group. However, the number of retrieved specimens in all patients was more than 12 lymph nodes. The higher number of harvested lymph nodes in the fast-track group indicated that surgical quality was not compromised in this treatment group.

Table 3. Preoperative evaluation and nutrition status (adjusted)

Duration of pre-operative survey, d	≤ 14 days	> 14 days	*p* value
Total	85	85	
Nutrition status			
Mean BMI, kg/m^2	23.8	25.0	0.124
Mean albumin [no. (%)]	3.96 [81, (95.3)]	4.06 [83, (97.7)]	0.224
Preoperative exam, days [no. (%)]			
Colonoscopy tumor biopsy pathology	4.7 [60, (70.1)]	4.6 [70, (82.4)]	0.691
CT (chest to pelvic) [days, no. (%)]	3.4 [85, (100)]	12.2 [85, (100)]	< 0.000
Echocardiography	5.8 [17, (20.0)]	19.2 [18, (21.2)]	< 0.000
Pulmonary function test	4.3 [7, (8.2)]	9.8 [5, (5.9)]	0.002

The other factors associated with incomplete preoperative preparation that influenced the patient's outcomes were malnutrition and less aerobic exercise; therefore, intensive nutritional support and rehabilitation were suggested. These factors had significant impact on patient's short-term outcome and long-term outcome. Several previous studies[6,17-21] pointed out the influence of these factors on the interval from diagnosis to treatment. These factors were also the primary cause of delay in achieving a better preoperative preparation prior to surgery, thus affecting the patient's outcomes and causing tension while waiting for their surgical oncologist. During the coronavirus disease 2019 pandemic, these results were explained to the CRC patient and their family members. It was also emphasized that delays in treatment did not further affect the oncological result; instead, the patients' condition still improved due to the provision of preoperative nutritional support and rehabilitation. However, as effective prevention strategies were implemented in our country, shortage in medical resources did not occur during the pandemic; adequate medical supply and timely treatment were provided.

Our study has several limitations. First, this study was retrospective in nature. Second, the follow-up period was relatively short (median: 53 months), making it difficult to obtain the 5-year survival data. Third, it was not clearly determined whether the type of recurrence was local or distant, which could have helped estimate the effect of preoperative survey completeness. Overall, the personalized treatment strategy with shared decision making influenced the treatment interval, and further randomized study is warranted to address these limitations.

Conclusion

In terms of interval from diagnosis to resection of localized colon cancer, the "within 2 weeks" group had equal short-term outcomes compared with the "longer than 2 weeks" group. These results could be related to the aggressive treatment and cooperation of the multidisciplinary team which provide efficient and comprehensive preoperative survey within short time period. In our clinical observation, this scenario not only provided equal oncological treatment results but also potentially alleviated the anxiety of the most patients and their family members who really concern delay treatment of cancer.

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原　著

局部大腸癌經快速術前準備之治療的短期與長期預後分析 — 單一機構經驗

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目的　本篇研究探討局部病灶之大腸癌患者經快速的術前準備而後接受手術時，與經較長期術前準備之族群比較。

方法　收集 2014~2018 年診斷局部病灶之大腸癌病人，依術前準備時間 (診斷至開刀)，分成“大於兩週”以及“小於兩週”兩組。透過傾向評分校正和回溯分析短期及長期預後。

結果　總共收錄 224 位患者，其中 116 位屬於“小於兩週”，另 108 位為“大於兩週”的組別，經傾向評分和統計分析，兩組預後並無顯著差異。

結論　兩組預後並無顯著差異，其關鍵應為“積極”、“多學科參與”引入的醫療資源導致的結果，其優勢在於擁有相同治療預後下，快速且提早的介入可以減少病人及家屬面對重大疾病時的焦慮。

關鍵詞　大腸癌、術前準備、併發症機率、復發率。