Left colon as a novel high-risk factor for postoperative recurrence of stage II colon cancer

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Abstract

Background: It is not clear whether stage II colon and rectal cancer have the same risk factors for recurrence. Thus, the purpose of this study was to identify the risk factors for postoperative recurrence in stage II colorectal cancer.

Patients and methods: We retrospectively analyzed the data of 990 patients who had undergone radical surgery for stage II colorectal cancer. Patients' pathological features and characteristics including age, sex, family history, body mass index, tumor diameter, gross type of tumor, infiltration degree (T3/T4), tumor grade, perineural invasion, vascular invasion, lymphatic invasion, pathologic examination of lymph node number, and preoperative carcinoembryonic assay (CEA) level was compared between patients with and without recurrence. Finally, the prediction of the left and right colons was analyzed.

Results: The mean ages of the colon cancer and rectal cancer patients were 69.5 years and 66.4 years, respectively. In total, 508 (82.1%) and 285 (76.8%) patients were treated laparoscopically for colon cancer and rectal cancer, respectively, with median follow-up periods of 42.2 months and 41.8 months, respectively. Forty-four recurrences occurred in both the colon cancer (7.1%) and rectal cancer (11.9%) groups. The preoperative serum CEA level and T4 infiltration were significantly higher in recurrent colorectal cancer patients. The postoperative recurrence rate of left colon cancer (descending colon, sigmoid colon) was higher than that of right colon cancer (cecum, ascending colon, transverse colon) (OR 2.191, 95% CI 1.091–4.400, \( P = 0.027 \)). In COX survival factor analysis of colon cancer, the left colon is one of the independent risk factors (risk ratio 5.377, 95% CI 0.216–0.88, \( P = 0.02 \)). In disease-free survival (DFS), the left colon has a relatively poor prognosis (\( P = 0.05 \)). However, in the COX analysis and prognosis analysis of OS, no difference was found between the left colon and the right colon.

Conclusion: Preoperative CEA and depth of infiltration (T4) are high-risk factors associated with recurrence and are prognostic factors in stage II colorectal cancer. Left colon is also a risk factor for postoperative recurrence of stage II colon cancer.

Keywords: Colorectal cancer, Carcinoembryonic antigen, Stage II, Left colon cancer
identify the risk factors for postoperative recurrence in stage II colorectal cancer.

**Patients and methods**

We retrospectively analyzed the clinical data of 990 patients with stage II CRC in the Division of Gastroenterological Surgery of Saitama Medical University from 2007 to 2016. The surgery was considered therapeutic when there was no macroscopic or microscopic residual cancer after surgery. There were 579 men and 411 women, comprising 619 patients with colon cancer and 371 patients with rectal cancer. Patients receiving preoperative treatment or presenting with intestinal obstruction or perforation were excluded from the analysis.

Peripheral blood samples were collected before surgery. The serum CEA level was determined by radioimmunoassay. The CEA level was considered high at \( \geq 5 \text{ ng/ml} \). The resected specimens were pathologically classified according to the 7th edition of the Union for International Cancer Control TNM classification of malignant tumors.

| Clinicopathological Parameters | Rectal cancer | Colon cancer | \( P \) value |
|-------------------------------|--------------|--------------|------------|
| Gender (Total n=)             | 371 (100.00%)| 619 (100.00%)|            |
| Male                          | 245 (66.04%) | 334 (53.96%) | <0.01      |
| Female                        | 126 (33.96%) | 285 (46.04%) |            |
| Age (year)                    | 66.4±0.55    | 69.5±0.42    | <0.01      |
| Post Operation Recurrence     |              |              |            |
| No                            | 327 (88.14%) | 574 (92.73%) | 0.011      |
| Yes                           | 44 (11.86%)  | 44 (7.11%)   |            |
| Open or Laparoscopic          |              |              | 0.059      |
| Open                          | 86 (23.18%)  | 113 (18.26%) |            |
| Laparoscopic                  | 285 (76.82%) | 508 (82.07%) |            |
| Gross Type                    |              |              | 0.105      |
| Protruding                    | 18 (4.85%)   | 56 (9.05%)   | 0.015      |
| Ulcerative & Infiltratie      | 353 (95.15%) | 563 (90.95%) |            |
| Diameter (cm)                 | 5.44±0.11    | 5.24±0.10    |            |
| Differentiation               |              |              | 0.37       |
| Well & Moderate               | 354 (95.42%) | 581 (93.86%) |            |
| Poor & Mucinous               | 17 (4.58%)   | 38 (6.14%)   |            |
| T                             |              |              | 0.324      |
| T3                            | 329 (89.64%) | 536 (87.39%) |            |
| T4                            | 39 (10.51%)  | 78 (12.60%)  |            |
| CEA (ng/mL)                   |              |              | <0.01      |
| <5                            | 192 (51.75%) | 400 (64.62%) |            |
| \( \geq 5 \)                 | 179 (48.25%) | 219 (35.38%) |            |
| Number of dissected lymph nodes|            |              | 0.05       |
| <12                           | 59 (15.90%)  | 71 (11.47%)  |            |
| \( \geq 12 \)                | 312 (84.10%) | 548 (88.53%) |            |
| Perineural Invasion           |              |              | 0.77       |
| No                            | 316 (85.18%) | 523 (84.49%) |            |
| Yes                           | 55 (14.82%)  | 96 (15.51%)  |            |
| Vascular Invasion             |              |              | <0.01      |
| No                            | 318 (85.71%) | 263 (42.49%) |            |
| Yes                           | 53 (14.29%)  | 356 (57.51%) |            |
| Infiltration lymphatic vessels|              |              | 0.24       |
| No                            | 312 (84.10%) | 501 (80.94%) |            |
| Yes                           | 59 (15.90%)  | 118 (19.06%) |            |
| Clinicopathological Parameters | Rectal Non-Recurrence | Rectal Recurrence | P value |
|-------------------------------|------------------------|-------------------|---------|
| Gender (Total n=)             | 327 (100.00%)          | 44 (100.00%)      |         |
| Male                          | 216 (66.06%)           | 29 (65.91%)       | 0.88    |
| Female                        | 111 (33.94%)           | 15 (34.09%)       |         |
| Age (year)                    | 66.35±1.32             | 65.7±0.55         | 0.30    |
| Cancer Family History         |                        |                   |         |
| None                          | 140 (42.81%)           | 22 (50.00%)       |         |
| Yes                           | 187 (57.19%)           | 22 (50.00%)       |         |
| BMI                           |                        |                   |         |
| <25                           | 309 (94.50%)           | 34 (77.27%)       |         |
| ≥25                           | 18 (5.50%)             | 10 (22.73%)       | 0.0001  |
| Duplicate Cancer              |                        |                   |         |
| None                          | 298 (91.13%)           | 38 (86.36%)       |         |
| Yes                           | 29 (8.87%)             | 6 (13.64%)        | 0.45    |
| Multiple Cancer               |                        |                   |         |
| None                          | 308 (94.19%)           | 38 (86.36%)       |         |
| Yes                           | 19 (5.81%)             | 6 (13.64%)        | 0.104   |
| Post Appendectomy             |                        |                   |         |
| None                          | 266 (81.35%)           | 37 (84.09%)       |         |
| Yes                           | 61 (18.65%)            | 7 (15.91%)        | 0.81    |
| Gross Type                    |                        |                   |         |
| Protruding                    | 20 (6.12%)             | 2 (4.55%)         | 0.49    |
| Ulcerative & Infiltrative     | 307 (93.88%)           | 42 (95.45%)       | 0.94    |
| Diameter (cm)                 | 5.42±0.11              | 6.00±0.34         | 0.045   |
| Differentiation               |                        |                   |         |
| Well & Moderate               | 316 (96.64%)           | 38 (86.36%)       |         |
| Poor & Mucinous               | 11 (3.36%)             | 6 (13.64%)        | 0.007   |
| T                             |                        |                   |         |
| T3                            | 298 (91.15%)           | 30 (68.17%)       |         |
| T4                            | 29 (8.85%)             | 14 (31.82%)       | 0.005   |
| CEA (ng/mL)                   |                        |                   |         |
| <5                            | 187 (57.19%)           | 14 (31.82%)       |         |
| ≥5                            | 140 (42.81%)           | 30 (68.18%)       | 0.002   |
| Number of dissected lymph nodes|                      |                   |         |
| <12                           | 54 (16.51%)            | 6 (13.64%)        | 0.78    |
| ≥12                           | 273 (83.49%)           | 38 (86.36%)       |         |
| Perineural Invasion           |                        |                   |         |
| No                            | 49 (14.98%)            | 37 (84.09%)       | <0.001  |
| Yes                           | 278 (85.02%)           | 7 (15.91%)        |         |
| Vascular Invasion             |                        |                   |         |
| No                            | 118 (36.09%)           | 8 (18.18%)        |         |
| Yes                           | 209 (63.91%)           | 36 (81.82%)       | 0.028   |
| Infiltration lymphatic vessels|                        |                   |         |
| No                            | 291 (88.99%)           | 29 (65.91%)       | <0.001  |
| Yes                           | 36 (11.01%)            | 15 (34.09%)       |         |
### Table 3: Clinicopathological parameters for colon cancer recurrence and non-recurrence

| Clinicopathological Parameters | Colon Non-Recurrence | Colon Recurrence | P value |
|--------------------------------|-----------------------|------------------|---------|
| Gender (Total n=)              |                       |                  |         |
| Male                           | 309 (53.74%)          | 24 (54.55%)      | 0.95    |
| Female                         | 266 (46.26%)          | 20 (45.45%)      |         |
| Age (year)                     | 69.7±0.43             | 70.3±1.73        | 0.35    |
| Cancer Family History          |                       |                  |         |
| None                           | 272 (47.30%)          | 19 (43.18%)      | 0.71    |
| Yes                            | 303 (52.70%)          | 25 (56.82%)      |         |
| BMI                            |                       |                  |         |
| <25                            | 448 (77.91%)          | 36 (81.82%)      | 0.67    |
| ≥25                            | 127 (22.09%)          | 8 (18.18%)       |         |
| Duplicate cancer               |                       |                  |         |
| None                           | 493 (85.74%)          | 40 (90.91%)      | 0.46    |
| Yes                            | 82 (14.26%)           | 4 (9.09%)        |         |
| Multiple Cancer                |                       |                  |         |
| None                           | 543 (94.43%)          | 42 (95.45%)      | 0.95    |
| Yes                            | 32 (5.57%)            | 2 (4.55%)        |         |
| Tumor location                 |                       |                  |         |
| Left colon                     | 278 (48.34%)          | 27 (61.37%)      | 0.09    |
| Right colon                    | 297 (51.65%)          | 17 (38.63%)      |         |
| Gross Type                     |                       |                  |         |
| Protruding                     | 51 (8.87%)            | 1 (2.27%)        | 0.21    |
| Ulcerative & Infiltratie       | 524 (91.13%)          | 43 (97.73%)      |         |
| Diameter (cm)                  | 5.2±0.10              | 5.45±0.48        | 0.25    |
| Differentiation                |                       |                  |         |
| Well & Moderate                | 527 (91.65%)          | 37 (84.09%)      | 0.15    |
| Poor & Mucinous                | 48 (8.35%)            | 7 (15.91%)       |         |
| T                              |                       |                  |         |
| T3                             | 511 (88.8%)           | 30 (68.18%)      | <0.0001 |
| T4                             | 64 (11.2%)            | 14 (31.82%)      |         |
| CEA (ng/mL)                    |                       |                  |         |
| <5                             | 380 (66.09%)          | 20 (45.45%)      | 0.009   |
| ≥5                             | 195 (33.91%)          | 24 (54.55%)      |         |
| Number of dissected lymph nodes|                       |                  |         |
| <12                            | 68 (11.83%)           | 4 (9.09%)        | 0.76    |
| ≥12                            | 507 (88.17%)          | 40 (90.91%)      |         |
| Perineural Invasion            | (0.00%)               |                  |         |
| No                             | 494 (85.91%)          | 40 (90.91%)      | 0.48    |
| Yes                            | 81 (14.09%)           | 4 (9.09%)        |         |
| Vascular Invasion              |                       |                  |         |
| No                             | 250 (43.48%)          | 13 (29.55%)      | 0.1     |
| Yes                            | 325 (56.52%)          | 31 (70.45%)      |         |
| Infiltration lymphatic vessels |                       |                  |         |
| No                             | 469 (81.57%)          | 35 (79.55%)      | 0.89    |
| Yes                            | 106 (18.43%)          | 9 (20.45%)       |         |
All patients underwent follow up with regular physical and blood examinations, colonoscopy, and computed tomography. All statistical analyses were performed using the SPSS software package version 22.0 for Macintosh (IBM Japan, Tokyo, Japan). The significance of the correlations between the preoperative CEA level and the pathological features was analyzed using the chi-squared test for independence according to each parameter. In order to control for confounding factors, binary logistic regression was used. Wald test was used to evaluate the significance of the association. Survival curves were plotted with the Kaplan–Meier method and analyzed with a log-rank test. \( P < 0.05 \) was considered statistically significant.

### Results

#### Clinical characteristics of CRCs

As shown in Table 1, a total of 990 CRC patients were included, comprising 371 with rectal cancer and 619 with colon cancer. The mean ages of colon cancer and rectal cancer patients were 69.5 years and 66.4 years, respectively. Of these, 508 (82.1%) of the colon cancer patients and 285 (76.8%) of the rectal cancer patients were treated laparoscopically. The median follow-up periods were 42.2 months for colon cancer and 41.8 months for rectal cancer. Forty-four recurrences occurred in both the colon cancer (7.1%) and rectal cancer (11.9%) groups. We observed significant differences between the colon and rectal cancer patients regarding sex, average age, and body mass index (BMI).

#### Table 4 Correlations between the preoperative CEA levels and the site of recurrence in stage II rectal cancer and colon cancer

|                      | Rectal Cancer CEA (ng/ml) | Colon Cancer CEA (ng/ml) |
|----------------------|---------------------------|--------------------------|
|                      | CEA < 5                   | CEA \( \geq 5 \)          | \( p \)-Value | CEA < 5                   | CEA \( \geq 5 \)          | \( p \)-Value |
|                      | \( n = 191 \)             | \( n = 170 \)             | \            | \( n = 389 \)             | \( n = 219 \)             | \            |
| Liver metastasis     |                           |                          | \            |                           |                          | \            |
| Negative             | 187 (97.91%)              | 161 (94.71%)             | 0.10        | 381 (97.94%)              | 209 (95.43%)              | 0.07        |
| Positive             | 4 (2.09%)                 | 9 (5.29%)                |             | 8 (2.06%)                 | 10 (4.57%)                |             |
| Lung metastasis      |                           |                          | \            |                           |                          | \            |
| Negative             | 187 (97.91%)              | 163 (95.88%)             | 0.26        | 384 (98.71%)              | 214 (97.72%)              | 0.35        |
| Positive             | 4 (2.09%)                 | 7 (4.12%)                |             | 5 (1.29%)                 | 5 (2.28%)                 |             |
| Local recurrence     |                           |                          | \            |                           |                          | \            |
| Negative             | 185 (96.08%)              | 157 (92.35%)             | 0.028       | 384 (98.71%)              | 213 (97.26%)              | 0.96        |
| Positive             | 6 (3.92%)                 | 13 (7.65%)               |             | 5 (1.29%)                 | 6 (2.74%)                 |             |
| Peritoneal dissemination |                       |                          | \            |                           |                          | \            |
| Negative             | 190 (99.48%)              | 169 (99.41%)             | 0.93        | 386 (99.23%)              | 213 (97.26%)              | 0.053       |
| Positive             | 1 (0.52%)                 | 1 (0.59%)                |             | 3 (0.77%)                 | 6 (2.74%)                 |             |

#### Table 5 Correlations between the depth of infiltration and the site of recurrence in stage II rectal cancer and colon cancer

|                      | Rectal Cancer |                   | Colon Cancer |                   | \( p \)-Value |
|----------------------|---------------|-------------------|--------------|-------------------|---------------|
|                      | T3            | T4                | \( p \)-Value | T3                | T4            | \( p \)-Value |
| Liver metastasis     |               |                   |              |                   |               |             |
| Negative             | 320 (96.39%)  | 38 (97.44%)       | 0.735        | 526 (97.05%)      | 74 (96.10%)   | 0.651        |
| Positive             | 12 (3.61%)    | 1 (2.56%)         |              | 16 (2.95%)        | 3 (3.90%)     |              |
| Lung metastasis      |               |                   |              |                   |               |             |
| Negative             | 325 (97.89%)  | 35 (89.74%)       | 0.004        | 535 (98.71%)      | 74 (96.10%)   | 0.089        |
| Positive             | 7 (2.11%)     | 4 (10.26%)        |              | 7 (1.29%)         | 3 (3.90%)     |              |
| Local recurrence     |               |                   |              |                   |               |             |
| Negative             | 318 (95.78%)  | 34 (87.18%)       |              | 534 (98.52%)      | 70 (90.91%)   | <0.001       |
| Positive             | 14 (4.22%)    | 5 (12.82%)        |              | 8 (1.48%)         | 7 (9.09%)     |              |
| Peritoneal dissemination |           |                   |              |                   |               |             |
| Negative             | 331 (99.70%)  | 38 (97.44%)       | 0.067        | 538 (99.26%)      | 74 (96.10%)   | 0.014        |
| Positive             | 1 (0.30%)     | 1 (2.56%)         |              | 4 (0.74%)         | 3 (3.90%)     |              |
age, postoperative recurrence rate, gross type, serum CEA levels, and vascular invasion (all \( P < 0.05 \)). Other features were not significantly different, including open or laparoscopic methods, differentiation, invasion depth (T), perineural invasion, cancer diameter, and infiltration of lymphatic vessels.

Comparisons of clinicopathological parameters between CRC recurrence and non-recurrence

Rectal cancer recurrence was associated with a body mass index greater than 25 kg/m\(^2\) (\( P = 0.0001 \)), a larger tumor size (6.00 ± 0.34; \( P < 0.001 \)), advanced T stage (\( P < 0.005 \)), higher serum CEA levels (\( P < 0.002 \)), poor differentiation or mucinous histology (\( P < 0.007 \)), perineural invasion (\( P <

### Table 6 Multivariate logistic regression analysis evaluating possible risk factors associated with recurrence

|                | Rectal Cancer |                | Colon Cancer |                |
|----------------|---------------|----------------|--------------|----------------|
|                | Odds ratio    | 95% CI         | \( p \)      | Odds ratio     | 95% CI         | \( p \)      |
| Gender         | 1.259         | 0.587-2.70     | 0.554        | 0.879          | 0.453-1.704    | 0.702        |
| Age, year      | 0.983         | 0.953-1.014    | 0.270        | 1.017          | 0.985-1.050    | 0.300        |
| T4 vs T3       | 3.867         | 1.547-9.663    | 0.004        | 3.222          | 1.238-8.390    | 0.017        |
| CEA (ng/mL)    | 1.011         | 1.000-1.021    | 0.048        | 1.010          | 1.003-1.017    | 0.004        |
| Tumor location | Rb vs Ra, RS  | 0.825          | 0.411-1.651  | 0.589          | 2.191          | 1.091-4.400  | 0.027        |
|                | Left colon vs Right colon |          |              |                |

Tumor location*: Rectal cancer (Rb & Ra, RS). Rb rectum above the peritoneal reflection, Ra rectum below the peritoneal reflection, RS rectosigmoid. Colon cancer: Left colon (Descending colon, sigmoid colon) & Right colon( Cecum, ascending colon, transverse colon)

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**Fig. 1** Survival outcomes for colorectal cancer patients with CEA ≥ 5 vs. CEA < 5

**Fig. 2** Survival outcomes for colorectal cancer patients with T3 vs. T4
< 0.001), vascular invasion \((P = 0.028)\), and infiltration of lymphatic vessels \((P < 0.001)\) (Table 2).

Compared with rectal cancer, colon cancer recurrence was associated with just an advanced T stage \((P < 0.0001)\) and higher serum CEA levels \((P = 0.009)\) (Table 3).

**Correlations between the preoperative CEA levels and the site of recurrence**

Local recurrences were significantly more common for rectal cancers with a higher CEA level than for those with a lower CEA level \((P < 0.05)\). However, there was no significant difference in liver metastasis, lung metastasis, or peritoneal spread between the two groups (Table 4).

Although the patients with higher CEA levels were more likely to develop colon cancer recurrence, there was no significant difference in the site of recurrence (Table 4).

**Correlations between the depth of infiltration and the site of recurrence**

Local recurrences were significantly more common for colorectal cancers with T4 infiltration than for those with T3 infiltration (both \(P < 0.05\)) (Table 5). There was a higher rate of lung metastasis recurrence in patients with T4 rectal cancer compared with T3 \((P = 0.004)\). In patients with T4 colon cancer, there was a higher rate of peritoneal metastasis \((P = 0.014)\).

In multivariate analysis, a higher CEA level was associated with a higher chance of recurrence of both rectal cancer (odds ratio [OR] 1.011, 95% confidence interval [95% CI] 1.00–1.021, \(P = 0.048\)) and colon cancer (OR 1.010 95% CI 1.003–1.017, \(P = 0.004\)). In addition, T4 cancer had a higher chance of recurrence in both rectal cancer (OR 3.867, 95% CI 1.547–9.663, \(P = 0.004\)) and colon cancer (OR 3.222, 95% CI 1.238–8.390, \(P = 0.017\)) (Table 6). In colon cancer, the postoperative recurrence rate of left colon cancer (descending colon, sigmoid...
colon) was higher than that of right colon cancer (cecum, ascending colon, transverse colon) (OR 2.191, 95% CI 1.091–4.400, \( P = 0.027 \)). However, there was no significant difference between low rectal cancer and upper rectal cancer.

**Correlations of the preoperative CEA levels and depth of infiltration with the survival rate**

The overall survival rate was significantly lower in both colon and rectal cancer patients with high levels of CEA and in T4 patients (\( P = 0.005, 0.006, 0.0044, \) and 0.006, respectively) (Figs. 1a, b and 2a, b). High levels of serum CEA and T4 reduced the disease-free survival (\( P = 0.005, 0.001, 0.000, \) and 0.000) (Figs. 3a, b and 4a, b).

**Prognostic differences between the left colon and the right colon**

To compare the prognosis of histological parameters determined in univariate analysis, Cox’s proportional hazard regression model was applied. For DFS, left colon, vascular invasion, infiltrating pattern, and T4 were all shown to be independent risk factors. For OS, signet ring cell carcinoma, mucinous carcinoma, poorly differentiated carcinoma, vascular invasion, infiltrating pattern etc. were shown to be independent risk factors (Table 7). For the DFS Kaplan–Meier survival curve, the left colon also has a relatively poor prognosis. However, in the OS curve, there is no difference between the left colon and the right colon (Fig. 5a, b). There is no statistical difference in the ratio of T4:T3 (\( P = 0.337 \)) and CEA \( \geq 5 \) ng/mL (\( P = 0.32 \)) in left colon cancer and right colon cancer (detailed data not shown).

**Discussion**

The question of whether colon and rectal cancer should be treated as a single entity or as two separate entities remains controversial [8]. The treatment of stage II CRCs has also been extensively debated [7, 9]. Our findings indicate that these two groups show considerable differences in many clinicopathological characteristics. Significant differences were seen between the two groups in sex, average age, postoperative recurrence, gross type, surgical procedure (open/laparoscopic), serum CEA level, and vascular invasion. Therefore, our results showed that, in stage II CRC, the characteristics of colon

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**Table 7** Cox proportional hazard regression model comparing the effects of different parameters on the prognosis of patients with stage II Colon cancer

|                | Disease free survival rates | Overall survival rates |
|----------------|-----------------------------|------------------------|
|                | Risk ratio 95% CI P-value   | Risk ratio 95% CI P-value |
| Left colon vs. Right colon CEA (ng/mL) | 5.377 0.216-0.88 0.02 | 0.001 0.587-1.734 0.974 |
| MUC,SRC,Poor vs. ADC | 6.177 0.191-0.822 0.013 | 6.294 0.267-0.85 0.012 |
| Vascular invasion, Yes vs. No | 1.126 0.212-1.587 0.289 | 4.975 0.199-0.901 0.026 |
| INF b,c vs. INFa | 6.365 1.523-28.485 0.012 | 5.228 1.288-26.994 0.022 |
| T4 vs T3 | 11.147 0.126-0.583 0.001 | 1.444 0.291-1.345 0.23 |

ADC adenocarcinoma, CEA carcinoembryonic antigen, CI confidence interval, SRC signet ring cell carcinoma, HR hazard ratio, Poor poorly differentiated adenocarcinoma, INF Infiltrating pattern of invasion, INFa Swelling proliferation, INF c Invasive proliferation, INF b between a and c. vs. versus, Left colon (Descending colon, sigmoid colon); Right colon (Cecum, ascending colon, transverse colon)
cancer and rectal cancer were different, which is why they should be considered two separate entities.

Out of 4,244 primary CRC patients, 990 cases (23.3%) of stage II CRC were found in our hospital in the past 10 years. In view of the different characteristics of rectal cancer and colon cancer, we independently analyzed their relapse characteristics. The depth of infiltration and level of the preoperative tumor marker CEA were directly related to recurrence in the colon cancer recurrence group compared with the non-recurrence group. This is consistent with the results of another study [10]. However, rectal cancer recurrence is much more complicated. It was not only related to the serum CEA level and depth of infiltration, but also obesity, tumor size, tumor type, and postoperative pathological lymphatic infiltration and perineural invasion. Therefore, CEA level and depth of infiltration are the common factors for the recurrence of the stage II CRC. These results are largely consistent with those of another study that also found that CEA and CA19-9 were factors associated with recurrence [11, 12].

We then looked at whether CEA was associated with the site of tumor recurrence. Although CEA is a complex glycoprotein that is the most commonly used tumor marker for CRC, it is highly nonspecific. In colon cancer, we did not find any relationship between CEA and the location of tumor recurrence but it was significantly associated with the local recurrence of rectal cancer. Local recurrence of rectal cancer involves lymph nodes near the sacrum, lymph nodes around the great arteries, and lateral lymph nodes. In this study, the preoperative CEA level and depth of infiltration (T4) were risk factors and prognostic factors for recurrence of stage II colon cancer. The different biological characteristics between rectal cancer and colon cancer lead to diverse recurrence factors and prognostic factors.

We found that the incidence of postoperative recurrence for left colon cancer was higher than that of right, and left colon is one of the independent risk factors of poorer DFS, which was consistent with some reports [13, 14]. The majority of the literature differs, reporting that there is no difference [15] or that the right colon has a relatively poor prognosis [16–19]. The inclusion of the rectum in the left colon is the biggest difference between these reports. This study also shows that many biological characteristics of the colon and rectum are different. The distinction between the descending colon and the sigmoid colon from the rectum may be more conducive to future treatment.

But more surprisingly, there was no difference in OS between the left colon and the right colon. This may be because the left colon, when compared with the right colon, even though RAS/BRAF are wild-type, has more advantages in the choice of chemotherapy drugs cetuximab or panitumumab [20]. It is important to recognize the limitations of this study. The chemotherapy effect of CRC is closely related to KRAS and BRAF gene mutations or microsatellite instability (MSI) [21]. In future analysis, research on genetic components needs to be strengthened. Second, this study is a single-center retrospective study with a relatively small sample size, and we look forward to future multi-center clinical studies.

**Conclusion**

Our results indicate that the preoperative CEA level and depth of infiltration (T4) are high-risk factors associated with recurrence and are prognostic factors in stage II colorectal cancer. Left colon is also a risk factor for the postoperative recurrence of stage II colon cancer, and special attention should be paid during follow-up.

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LMW and YH drafted the manuscript and provided the original pictures. TI, HK, KH, NO, and SY reviewed the manuscript. All authors read and approved the final manuscript.

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**Ethics approval and consent to participate**

All the study participants provided their informed consent. The study design was approved by the Ethics Committee of the Saitama Medical University International Medical Center (Number: 18-274).

**Consent for publication**

All patients have agreed to use their personal medical data for research and publication. Please refer to the attached file for details.

**Competing interests**

The authors declare that they have no competing interests.

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