Propensity Score Analysis in the Comparison of Long−Term Outcomes for Locally Advanced Colon Cancer Between Laparoscopic Colectomy and Open Colectomy

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Objective: It is difficult to conduct a randomised control trial in a single institution because of the small number of cases. The current study was conducted to investigate if there is any difference in long−term outcome between laparoscopic surgery (LAC) and open surgery (OC) using propensity−score matching analysis based on prognostic factors.

Materials: Two hundred and sixteen patients with locally−advanced colon cancer who underwent surgery with curative intent at our department between 2002 and 2010 were enrolled in the current study.

Methods: Propensity score matching analysis and Inverse Probability Weighting (IPW) estimator were used to adjust for differences in the clinicopathological severity between LAC and OC.

Results: Before propensity score matching analysis recurrence−free survival in LAC was statistically better than that in OC (Hazard ratio= 0.59, 95% CI 0.35−0.98, p=0.04), and no statistically significant difference was recognized for cancer−specific survival (Hazard ratio=0.63, 95% CI 0.27−1.37, p=0.25). After propensity score matching analysis there were no statistically significant differences for recurrence−free (Hazard ratio=0.91, 95% CI 0.41−2.01, p=0.81) or cancer−specific survival (Hazard ratio=1.38, 95% CI 0.41−4.82, p=0.59). In addition, the IPW estimator revealed that the difference for recurrence−free survival was not significant between the two groups.

Conclusion: The one−to−one pair propensity score matching successfully balanced the clinicopathological factors between LAC and OC. The propensity score matching analysis demonstrated no significant difference between LAC and OC.

Key words: colon cancer, laparoscopic colectomy, long−term outcome, open colectomy, propensity score matching analysis

Introduction

Colon cancer is one of the most common causes of cancer death in the United States and Japan, and its incidence in Japan is increasing rapidly[1,2]. Surgery is the mainstay of treatment, providing definitive management and potential cure in early cases, and effective palliation in advanced cases[3]. Laparoscopic colectomy (LAC) results in several benefits during the immediate postoperative period compared with open colectomy (OC)[4]. LAC has been proven to be safe and feasible[5,6]. In randomised trials there was no difference between LAC and OC with regard to long−term outcome[7−9]. However, it...
is difficult to conduct a randomised control trial in a single institution because of the small number of cases. Thus, the current study was conducted to investigate if there is any difference in long-term outcome between LAC and OC using propensity-score matching analysis to eliminate selection bias due to nonrandom treatment assignment.

### Materials and Methods

#### 1. Patient selection

Two hundred and sixteen patients with locally-advanced colon cancer (TNM classification 7th edition\(^{10}\): Stage II/III) who underwent surgery with curative intent at our department between 2002 and 2010 were enrolled in the current study. Cases with transverse or descending colon cancer or conversion or emergency operation, due to perforation and ileus, were excluded from this investigation. We retrospectively reviewed the database and medical records.

#### 2. Colectomy

We essentially performed complete mesocolic excision and D3 lymph node dissection for locally advanced colon cancer according to the Japanese Classification of Colorectal Carcinoma, Second English Edition\(^{11}\). In LAC, pneumoperitoneal and intracorporeal approaches were used to explore the abdomen, mobilize the colon, identify critical structures and ligate the vascular pedicle\(^{12}\). Resection of the colon, ligation of the vascular pedicle and reconstruction were performed by the pneumoperitoneal approach or the intracorporeal approach via a small incision (<8.0 cm)\(^{12}\).

#### 3. Clinicopathological analysis

Clinicopathological factors, i.e., year of surgery (2002 - 2006 / 2007 - 2010), age (<70/≥70), gender (male/female), body mass index (BMI) (<25/≥25), American Society of Anesthesiologists (ASA) score (1, 2/3), previous laparotomy (absent/present), location (cecum, ascending colon/sigmoid, rectosigmoid colon), preoperative serum CEA (normal/elevated), maximal tumor size (<50 mm/≥50 mm), differentiation (well- or moderately- differentiated adenocarcinoma/Poorly-differentiated or mucinous adenocarcinoma or signet ring cell carcinoma), invasion depth (TNM classification 7th edition\(^{10}\): T1-3/T4), lymphatic invasion (Japanese Classification of Colorectal Carcinoma, Second English Edition\(^{11}\): none-mild/moderate-severe), venous invasion (Japanese Classification of Colorectal Carcinoma, Second English Edition\(^{11}\): none-mild/moderate-severe), the number of dissected lymph nodes (<12/≥12), stage (TNM classification 7th edition\(^{10}\): II/III) and survival data were analyzed in the current study.

#### 4. Pathological examination

All specimens were examined in the following manner\(^{13}\): After resection of the primary tumor, the excised specimen was opened on the antimesenteric side by the surgeon. The surgeon identified the lymph nodes, isolated them, and recorded both their number and distribution\(^{13}\). After fixation in formalin, the specimen and lymph nodes were also examined by the pathologist\(^{13}\).

#### 5. Follow-up program

During the first 3 years, patients were followed through clinical assessment and measurement of serum carcinoembryonic antigen every 3 months, and with chest X-ray and abdominal ultrasonography or computed tomography every 3-6 months\(^{13}\). For the remaining 2 years, all tests were performed every 6 months\(^{13}\). Colonoscopy was performed 1 year after the operation and every 2 years, thereafter, for the next 4 years\(^{13}\).

#### 6. Propensity score matching analysis

Propensity score matching analysis was used to adjust for differences in the clinicopathological severity between LAC and OC. First, the propensity score was estimated. The log-odds ratio of the probability that a patient had OC was modeled for potential confounders: i.e., year of surgery, age, location, invasion depth, American Society of Anesthesiologists (ASA) score and the diameter of the primary tumor. We used postoperative findings in terms of invasion depth and the diameter of the primary tumor because preoperative findings about those factors were not available in the current study. The reason we selected these clinicopathological factors as confounders for propensity score matching analysis was because the procedure recommended to the patients was based primarily on these factors. The discrimination of the propensity model was assessed with calculation of the
c-statistic. One-to-one pair matching was performed without replacement, and propensity scores were matched with calipers < 0.1. Propensity score matching analysis was performed using SPSS Statistics version 22 (IBM Corporation, Somers, NY, USA). We also compared the two groups using the Inverse Probability Weighting (IPW) estimator.

7. Statistical analysis

Recurrence-free and cancer-specific survival were calculated using the Kaplan-Meier method and univariate analyses were performed using the log-rank test. Discrete variables were compared using Fisher's exact probability test and continuous variables were compared using the Mann-Whitney U-test. The Cox proportional-hazard model was used to determine Hazard ratios and 95% confidence intervals. Data were analyzed statistically using JMP 9.0.2 software (SAS Institute Inc., Cary, NC, USA). Differences were considered statistically significant at \( p < 0.05 \). Values are expressed as the median (min.-max.).

Results

1. Comparisons of recurrence-free and cancer-specific survival according to the clinicopathological factors among the entire cohort

The median observation period was 58.0 months (range: 1.2–110.8 months). Significant differences in recurrence-free survival were recognized with respect to location \( (p = 0.03) \), preoperative CEA \( (p = 0.008) \), invasion depth \( (p < 0.0001) \), lymphatic invasion \( (p < 0.0001) \), venous invasion \( (p = 0.0001) \) and stage \( (p = 0.009) \) (Table-1). There were no significant differences with respect to the other clinicopathological factors. Significant differences in cancer-specific survival were subsequently recognized with respect to preoperative CEA \( (p = 0.003) \), invasion depth \( (p < 0.0001) \), lymphatic invasion \( (p < 0.0001) \), venous invasion \( (p = 0.001) \) and stage \( (p < 0.0001) \). There were no significant differences with respect to the other clinicopathological factors.

2. Comparisons of recurrence-free and cancer-specific survival according to the procedure among the entire cohort

Comparisons of recurrence-free and cancer-specific survival according to the procedure among the entire cohort are shown in Figure-1A, B. Recurrence-free survival in LAC was statistically better than that in OC (Hazard ratio = 0.59, 95% CI 0.35–0.98, \( p = 0.04 \)). However, no statistically significant difference was recognized for cancer-specific survival (Hazard ratio = 0.63, 95% CI 0.27–1.37, \( p = 0.25 \)).

3. Comparison of the clinicopathological factors between LAC and OC among the entire cohort

In univariate analysis, there were significant differences for the year of surgery \( (p < 0.0001) \), age \( (p = 0.002) \), ASA score \( (p = 0.005) \), location \( (p = 0.03) \), preoperative CEA \( (p < 0.0001) \), maximal tumor size \( (p < 0.0001) \), invasion depth \( (p < 0.0001) \), lymphatic invasion \( (p = 0.002) \) and venous invasion \( (p = 0.004) \) between LAC and OC. Specifically, LAC was more often performed in the latter period, among younger patients with an ASA score of 1 or 2, Sigmoid and Rectosigmoid colon, with lower preoperative CEA, smaller tumor, invasion depth of T1–3 and patients with less lymphatic and venous invasion compared with OC (Table-2). There were no significant differences between the two groups with respect to the other clinicopathological factors.

4. Comparisons of recurrence-free and cancer-specific survival according to the procedure in the propensity matched cohort

The median propensity scores were 0.31 (0.09–0.93) and 0.82 (0.08–0.99), respectively, in the patients with LAC vs. the patients with OC \( (p < 0.0001) \). The c-statistic was 0.85, indicating satisfactory discrimination. After propensity score-matching analysis, in univariate analysis, there were no significant differences with respect to the clinicopathological factors between LAC and OC (Table-3). Comparisons of recurrence-free and cancer-specific survival in propensity score-matched patients according to the procedure are shown in Figure-1C, D. There were no statistically significant differences for recurrence-free (Hazard ratio = 0.91, 95% CI 0.41–2.01, \( p = 0.81 \)) or cancer-specific survival (Hazard ratio = 1.38, 95% CI 0.41–4.82, \( p = 0.59 \)).
5. Comparisons of recurrence-free and cancer-specific survival according to the procedure using IPW estimator

As noted above, recurrence-free survival in LAC was statistically better than that in OC (Hazard ratio = 0.59, 95% CI 0.35–0.98, p = 0.04). However, the IPW estimator revealed that the difference for recurrence-free survival was not significant between the two groups (Hazard ratio = 0.90, 95% CI 0.41–2.00, p = 0.80). Also, in terms of cancer-specific survival, IPW estimator revealed that there was no statistically significant difference between the two groups (Hazard ratio = 1.37, 95% CI 0.41–4.79, p = 0.60).

Discussion

Laparoscopic surgery has been widely accepted because of the excellent results in the treatment of benign digestive disease, such as cholecystectomy. In colorectal cancer, this technique

Table 1. Comparisons of recurrence-free and cancer-specific survival according to the clinicopathological factors among the entire cohort

| Clinicopathological factors | Variables | n   | RFS<sup>a</sup> 5y (%) | p-value | CSS<sup>b</sup> 5y (%) | p-value |
|-----------------------------|-----------|-----|-------------------------|---------|-------------------------|---------|
| Year of surgery             |           |     |                         |         |                         |         |
| 2002 - 2006                 |           | 107 | 72.0                    | 0.70    | 83.3                    | 0.48    |
| 2007 - 2010                 |           | 119 | 76.7                    |         | 86.9                    |         |
| Age                         |           |     |                         |         |                         |         |
| <70                         |           | 130 | 78.5                    | 0.43    | 87.3                    | 0.60    |
| ≥70                         |           | 96  | 68.9                    |         | 82.5                    |         |
| Gender                      |           |     |                         |         |                         |         |
| Male                        |           | 126 | 75.2                    | 0.86    | 87.3                    | 0.31    |
| Female                      |           | 100 | 74.1                    |         | 83.2                    |         |
| Body mass index (BMI)       |           |     |                         |         |                         |         |
| <25                         |           | 177 | 69.8                    | 0.68    | 86.4                    | 0.76    |
| ≥25                         |           | 49  | 67.9                    |         | 82.5                    |         |
| ASA score<sup>c</sup>       |           |     |                         |         |                         |         |
| 1, 2                        |           | 178 | 75.0                    | 0.58    | 85.5                    | 0.86    |
| ≥3                          |           | 48  | 72.4                    |         | 84.8                    |         |
| Previous laparotomy         |           |     |                         |         |                         |         |
| Absent                      |           | 146 | 74.4                    | 0.73    | 86.8                    | 0.41    |
| Present                     |           | 80  | 75.3                    |         | 82.9                    |         |
| Location                    |           |     |                         |         |                         |         |
| Proximal<sup>d</sup>        |           | 71  | 66.9                    | 0.03    | 82.8                    | 0.52    |
| Distal<sup>e</sup>          |           | 155 | 78.5                    |         | 86.7                    |         |
| Preoperative CEA            |           |     |                         |         |                         |         |
| Normal                      |           | 92  | 83.9                    | 0.008   | 94.4                    | 0.003   |
| Elevated<sup>f</sup>        |           | 134 | 68.7                    |         | 79.5                    |         |
| Maximal tumor size          |           |     |                         |         |                         |         |
| <50 mm                      |           | 140 | 78.0                    | 0.74    | 87.7                    | 0.27    |
| ≥50 mm                      |           | 86  | 69.7                    |         | 81.9                    |         |
| Differentiation             |           |     |                         |         |                         |         |
| Low grade<sup>g</sup>       |           | 209 | 84.3                    | 0.0001  | 85.7                    | 0.001   |
| High grade<sup>h</sup>      |           | 17  | 70.6                    |         | 82.4                    |         |
| Invasion depth              |           |     |                         |         |                         |         |
| T1–3                        |           | 170 | 84.4                    | <0.0001 | 93.3                    | <0.0001 |
| T4                          |           | 56  | 46.0                    |         | 60.0                    |         |
| Lymphatic invasion          |           |     |                         |         |                         |         |
| None–mild                   |           | 173 | 82.2                    | <0.0001 | 91.9                    | <0.0001 |
| Moderate–severe             |           | 53  | 53.3                    |         | 65.8                    |         |
| Venous invasion             |           |     |                         |         |                         |         |
| None–mild                   |           | 167 | 82.3                    | 0.0001  | 91.0                    | 0.001   |
| Moderate–severe             |           | 59  | 55.1                    |         | 70.1                    |         |
| No. of dissected lymph nodes|           |     |                         |         |                         |         |
| ≥12                         |           | 199 | 72.8                    | 0.10    | 84.6                    | 0.34    |
| <12                         |           | 27  | 87.8                    |         | 91.3                    |         |
| Stage                       |           |     |                         |         |                         |         |
| II                          |           | 101 | 84.6                    | 0.009   | 96.7                    | <0.0001 |
| III                         |           | 125 | 66.8                    |         | 76.6                    |         |

<sup>a</sup> Recurrence-free survival  <sup>b</sup> Cancer-specific survival  <sup>c</sup> American Society of Anesthesiologists score  
<sup>d</sup> Cecum or ascending colon  <sup>e</sup> Sigmoid colon or rectosigmoid colon  
<sup>f</sup> CEA ≥3.1 ng/ml  <sup>g</sup> Well- and moderately-differentiated adenocarcinoma  
<sup>h</sup> Poorly-differentiated or mucinous adenocarcinoma or signet ring cell carcinoma
has been applied to early stage disease. Since then, a large number of controlled studies and meta-analyses have shown that LAC is associated with short-term outcomes, such as lesser pain, earlier recovery of bowel movement and shorter hospital stay, compared with OC. The impact of LAC on long-term outcomes for locally advanced colon cancer has been the subject of controversy for many years, especially because of port-site metastasis and concerns regarding the lower number of lymph nodes retrieved. However, some prospective randomised multicenter trials have reported no differences in oncological outcomes between LAC and OC. These clinical trials were conducted...

Figure 1  Recurrence-free and cancer-specific survival according to the procedure
A: Recurrence-free survival among the entire cohort. B: Cancer-specific survival among the entire cohort. C: Recurrence-free survival in the propensity matched cohort. D: Cancer-specific survival in the propensity matched cohort.
### Table 2: Comparison of the clinicopathological factors between LAC and OC among the entire cohort

| Clinicopathological factors | Variables | Laparoscopic colectomy (LAC) (n=98) | Open colectomy (OC) (n=128) | p-value |
|-----------------------------|-----------|-------------------------------------|-----------------------------|---------|
| Year of surgery             |           |                                     |                             |         |
| 2002 - 2006                 | 22        | 85                                  |                             | <0.0001 |
| 2007 - 2010                 | 76        | 43                                  |                             |         |
| Age                         |           | 65 (35 - 86)                        | 69 (32 - 89)                | 0.002   |
| Gender                      |           |                                     |                             |         |
| Male                        | 54        | 72                                  |                             | 0.89    |
| Female                      | 44        | 56                                  |                             |         |
| Body mass index (BMI)       |           | 22.8 (14.4 - 30.2)                  | 22.8 (16.0 - 32.6)          | 0.96    |
| ASA score<sup>a</sup>       |           |                                     |                             |         |
| 1, 2                        | 88        | 90                                  |                             | 0.0005  |
| ≥3                          | 10        | 38                                  |                             |         |
| Previous laparotomy         |           |                                     |                             |         |
| Absent                      | 66        | 80                                  |                             | 0.48    |
| Present                     | 32        | 48                                  |                             |         |
| Location                    |           |                                     |                             |         |
| Proximal<sup>b</sup>        | 23        | 48                                  |                             | 0.03    |
| Distal<sup>c</sup>          | 75        | 80                                  |                             |         |
| Preoperative CEA (ng/ml)    |           | 2.8 (0.0 - 120.5)                   | 4.6 (0.6 - 155.5)          | 0.0001  |
| Maximal tumor size (mm)     |           | 35 (9 - 80)                         | 50 (15 - 110)               | <0.0001 |
| Differentiation             |           |                                     |                             |         |
| Low grade<sup>d</sup>       | 94        | 115                                 |                             | 0.13    |
| High grade<sup>e</sup>      | 4         | 13                                  |                             |         |
| Invasion depth              |           |                                     |                             |         |
| T1-3                        | 87        | 83                                  |                             | <0.0001 |
| T4                          | 11        | 45                                  |                             |         |
| Lymphatic invasion          |           |                                     |                             |         |
| None-mild                   | 85        | 88                                  |                             | 0.002   |
| Moderate-severe             | 13        | 40                                  |                             |         |
| Venous invasion             |           |                                     |                             |         |
| None-mild                   | 82        | 85                                  |                             | 0.004   |
| Moderate-severe             | 16        | 43                                  |                             |         |
| No. of dissected lymph nodes|           |                                     |                             |         |
| ≥12                         | 87        | 112                                 |                             | 0.84    |
| <12                         | 11        | 16                                  |                             |         |
| Stage                       |           |                                     |                             |         |
| II                          | 40        | 61                                  |                             | 0.35    |
| III                         | 58        | 67                                  |                             |         |

<sup>a</sup> American Society of Anesthesiologists score  
<sup>b</sup> Cecum or ascending colon  
<sup>c</sup> Sigmoid colon or rectosigmoid colon  
<sup>d</sup> Well- and moderately-differentiated adenocarcinoma  
<sup>e</sup> Poorly-differentiated or mucinous adenocarcinoma or signet ring cell carcinoma

### Table 3: Comparisons of the clinicopathological factors between LAC and OC in the propensity matched cohort

| Clinicopathological factors | Variables | Laparoscopic colectomy (LAC) (n=44) | Open colectomy (OC) (n=44) | p-value |
|-----------------------------|-----------|-------------------------------------|-----------------------------|---------|
| Year of surgery             |           |                                     |                             |         |
| 2002 - 2006                 | 21        | 22                                  |                             | 1.00    |
| 2007 - 2010                 | 23        | 22                                  |                             |         |
| Age                         |           | 69 (35 - 86)                        | 66 (32 - 82)                | 0.25    |
| ASA score<sup>a</sup>       |           |                                     |                             |         |
| 1, 2                        | 38        | 39                                  |                             | 1.00    |
| ≥3                          | 6         | 5                                   |                             |         |
| Location                    |           |                                     |                             |         |
| Proximal<sup>b</sup>        | 9         | 10                                  |                             | 1.00    |
| Distal<sup>c</sup>          | 35        | 34                                  |                             |         |
| Maximal tumor size          |           |                                     |                             |         |
| <50 mm                      | 30        | 31                                  |                             | 1.00    |
| ≥50 mm                      | 14        | 13                                  |                             |         |
| Invasion depth              |           |                                     |                             |         |
| T3                          | 36        | 35                                  |                             | 1.00    |
| T4                          | 8         | 9                                   |                             |         |

<sup>a</sup> American Society of Anesthesiologists score  
<sup>b</sup> Cecum or ascending colon  
<sup>c</sup> Sigmoid colon or rectosigmoid colon
in multi-centers. Therefore, it is necessary to investigate these outcomes in our institution in order to determine whether or not we can apply the conclusions from these trials to our institution. However, it is impractical for a single institution to conduct a prospective randomised controlled study due to the small number of such cases. In the current study, propensity score matching analysis was performed to investigate whether or not LAC for colon cancer exhibits an equivalent long-term oncological outcome compared with OC.

The propensity score is the probability of treatment assignment conditional on measured baseline covariates\(^2\). Propensity score methods are increasingly used to reduce or minimize the confounding that occurs frequently in observational studies of the effect of treatment on outcomes\(^3\). In clinical practice, there are significant differences between patients who undergo LAC vs. OC, particularly with regard to age and clinicopathological factors. Therefore, in the current study we used propensity score matching analysis techniques to address selection bias due to nonrandom treatment assignment. As a result, although analysis of baseline clinicopathological factors for the entire cohort indicated more active indication of OC among the patients with more severe clinicopathological factors, the one-to-one pair matching successfully balanced the clinicopathological factors between the patients with LAC and OC. To our knowledge, there have been only three reports to date regarding long-term outcomes in colon cancer using propensity score matching analysis. Cummins and colleagues\(^2\) used propensity score matching analysis to achieve reliable evaluation of long-term outcomes in the Surveillance, Epidemiology, and End Results-Medicare (SEER) database. They reported that there was no significant difference in the long-term outcomes for the propensity-matched patients with colon cancer. Although the study includes cases with distant metastases, this result is similar to that of the current study. Hasegawa and colleagues\(^3\) also performed propensity score analysis in patients with Stage I – III colon cancer. They only used the propensity score for adjustment in order to avoid reduction in study size. The score was subsequently incorporated as a covariate in a proportional hazards model. Consequently, they concluded that there was no significant difference in the long-term disease-free survival between LAC and OC. Similarly, we compared the two groups using an Inverse Probability Weighting (IPW) estimator for adjustment because we were concerned that one-to-one pair matching might reduce the number of matched cases in each group. Our results also revealed that there was no statistically significant difference between the two groups. Numata and colleagues\(^4\) examined the long-term outcomes in patients with Stage I/II colon cancer. They also reported that there was no statistically significant difference between the two groups, although the study was relatively small. While the results may vary depending upon the confounders that are used in the propensity score matching analysis, these reports and our study were consistent with previous studies\(^5\)-\(^9\) that demonstrated no significant difference in long-term survivals.

Finally, there are several limitations in the current study that should be considered, which are inherent to retrospective studies and the non-randomized design that should be considered. Firstly, this data was collected and examined at a single institute, and only a small number of patients were enrolled. Secondly, the regimens of oral postoperative adjuvant chemotherapy were not fixed throughout the duration of investigation. In addition, the current study includes both Stage II and III colon cancer, for which the indications of postoperative adjuvant chemotherapy are different. Third, the results in the propensity score analysis depend on establishing a manner to divide the clinicopathological factors as confounders into two groups. We followed the Japanese Classification of Colorectal Carcinoma, Second English Edition\(^1\). In particular, the differences in the location of the tumor, such as the scope of lymph node dissection, could influence the long-term outcome in the current study. Finally, the historical transitions in the indication of LAC for locally-advanced colon cancer should be taken into account because we had been expanding the indication of LAC with the progress of our skills, especially since 2007.

A recent multi-institutional, randomized controlled trial (Japan Clinical Oncology Study; JCOG 0404) revealed that there were no statistically significant differences in either the 5-year overall survival or 5-year recurrence-free survival in the
patients with Stage II/III colon cancer. In that study, cases with transverse or descending colon cancer were excluded due to technical difficulties with the procedure. LAC for transverse or descending colon cancer has been questioned on the basis of the technical challenges. In Japan, LAC for sigmoid colon or rectosigmoid colon cancer has been developed and standardized in relation to the Practice Guidelines on Endoscopic Surgery for qualified surgeons by the Endoscopic Surgical Skill Qualification System. In future, standardization of the procedure for LAC in transverse or descending colon cancer is anticipated in a similar manner.

Conclusions

The one-to-one pair propensity score matching successfully balanced the clinicopathological factors between LAC and OC. The propensity score analysis with both one-to-one pair matching and Inverse Probability Weighting (IPW) estimator demonstrated no significant difference in long-term outcomes among patients with Stage II/III colon cancer.

Conflict of interest

The authors declare that they have no conflict of interest.

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