D3 lymph node dissection with versus without left colic artery preservation in single-incision laparoscopic surgery for sigmoid and rectosigmoid cancer: A propensity score-matched analysis

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Abstract

Purpose: In surgery for colorectal cancer, dissection of the lymph nodes and fatty tissue around the root of the inferior mesenteric artery is important from an oncologic point of view. However, it is debatable whether it is better to preserve or remove the left colic artery (LCA). This study aimed to compare D3 lymphadenectomy with versus without LCA preservation in single-incision laparoscopic surgery for sigmoid and rectosigmoid cancer.

Methods: A total of 1138 patients underwent surgery for colorectal cancer between April 2011 and December 2018 at Fukui Prefectural Hospital. This propensity score-matched retrospective study analyzed the data of 163 patients: 42 patients with LCA preservation (group A) and 129 without LCA preservation (group B). Clinical and oncological outcomes were compared between the two groups.

Results: There were no significant differences between groups A and B in patient characteristics, surgical outcomes, including the 5-year overall survival rate (75% vs. 64.2%, hazard ratio [HR] 1.34, 95% confidence interval [CI] 0.37–4.30), 5-year disease-free survival rate (85.7% vs. 85.7%, HR 0.99, 95% CI 0.24–4.22), and 5-year cancer-specific survival rate (92.8% vs. 89.3%, HR 1.50, 95% CI 0.25–11.4).

Conclusion: There were no significant differences in the short- and long-term outcomes of patients who underwent single-incision laparoscopic surgery with D3 lymphadenectomy with versus without LCA preservation. This suggests that LCA preservation is safe and feasible in single-incision laparoscopic surgery for sigmoid and rectosigmoid colon cancer.

Keywords
colon cancer, left colic artery, single-incision laparoscopic surgery
In colorectal cancer, the number and status of lymph nodes are important prognostic factors. For pT3/T4 sigmoid colon cancer, the reported prevalence of metastasis to the lymph nodes at the root of the inferior mesenteric artery (IMA) is 3.6%.

Therefore, dissection of the lymph nodes and fatty tissue around the IMA root is important from an oncologic point of view. However, dissection of the lymph nodes at the root of the inferior mesenteric artery (IMA) is 3.6%.

Therefore, dissection of the lymph nodes and fatty tissue around the IMA root is important from an oncologic point of view. However, dissection of the lymph nodes at the IMA root disrupts the blood flow from the IMA to the left colic artery (LCA). This means that blood flow to the anastomosis is dependent on the mesocolonic system, which may not only reduce the blood flow, but may also significantly impact the selection of surgical treatment if colorectal cancer recurs in the same region.

It is debatable whether it is beneficial to preserve the LCA during lymph node dissection. Several previous studies have found no significant differences in the long-term results of lymphadenectomy with versus without LCA preservation. The JCOG0404 randomized controlled trial conducted by the Colorectal Cancer Study Group of the Japan Clinical Oncology Group confirmed the noninferiority of laparoscopic surgery compared with open surgery for Stage II/III colon cancer in terms of overall survival (OS).

Furthermore, the short- and long-term outcomes reportedly tend to be better after D3 lymphadenectomy with LCA preservation than D3 lymphadenectomy without LCA preservation, indicating that it may be optimal to preserve the LCA.

Some studies report that laparoscopic lymph node resection with LCA preservation and skeletonization at the IMA root is effective and safe in selected patients. However, no study has evaluated the feasibility and safety of LCA preservation in single-incision laparoscopic surgery (SILS) for sigmoid cancer. This study aimed to compare D3 lymphadenectomy with versus without LCA preservation in SILS for sigmoid and rectosigmoid cancer.

This was a retrospective propensity score-matched study. Among 1138 consecutive patients who underwent surgery for colorectal cancer between April 2011 and December 2018 at Fukui Prefectural Hospital, 217 underwent SILS for sigmoid or rectosigmoid cancer.

Inclusion criteria were: diagnosis of adenocarcinoma confirmed by colon biopsy, age >18 years, sigmoid or rectosigmoid cancer diagnosed as T2 or higher preoperatively, and necessity of D3 lymphadenectomy. Exclusion criteria were: emergency surgery, Stage IV cancer, synchronous cancer, or conversion to laparotomy. The final study cohort comprised 163 patients, including 42 with LCA preservation (group A) and 129 without LCA preservation (group B). Data were extracted from the electronic medical records. The main outcome measures were intra- and postoperative complications, OS, disease-free survival (DFS), and cancer-specific survival (CSS). Patient age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, medical comorbidities, and tumor-nodes-metastasis stage were also analyzed. Postoperative morbidity and mortality were defined as complications and death, respectively, occurring within 30 days of surgery. Postoperative complications were defined as those classified as Clavien–Dindo grade two or above.

OS was defined as the length of time from surgery to the date of death from any cause or final follow-up. DFS was defined as the length of time from surgery to the date of recurrence or death from any cause or final follow-up. CSS was defined as the length of time from surgery to the date of death in the absence of other causes of death. Propensity matching score for short- and long-term endpoint analyses was conducted, and after matching 30 pairs of patients were respectively analyzed for the long- and short-term endpoints.

The study protocol was approved by the Ethics Committee of Fukui Prefectural Hospital and conforms to the provisions of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board for the Use of Human Subjects of our institution, and written informed consent was obtained from all patients prior to study inclusion.

2.1 | Surgical technique

All surgeries were performed by surgeons who were qualified based on the endoscopic surgical skill qualification system of the Japan Society for Endoscopic Surgery.

2.1.1 | Patient position and access

Under general anesthesia, the patient was placed in the modified lithotomy position. A lap protector (Hakko Shoji, Tokyo, Japan) was inserted through a 2.5-cm transumbilical incision to protect the wound. An EZ-access (Hakko Shoji) was attached to the lap protector, and three ports were created on the EZ-access. Almost all procedures were performed using standard laparoscopic instruments, and the surgical technique was similar to standard laparoscopic colorectal resection using a flexible scope.
2.1.2 | Sparing the LCA and dissecting the lymph nodes around the IMA root

The root of the IMA was exposed and the vascular sheath of the IMA was dissected to expose the outer membrane of the IMA. Once the loose layer between the vascular sheath and the adventitia was accessed, the vascular sheath and lymph nodes were easily detached from the IMA. The vascular sheath was detached to the junction of the LCA and the superior rectal artery, and the dissection was extended directly toward the LCA. From the intersection of the LCA and the inferior mesenteric vein (IMV), the dissection proceeded along the IMV to the level of the IMA root. The sigmoid mesentery was incised from the root of the IMA to the IMV to complete the en bloc dissection of the lymph nodes around the IMA. After lymph node dissection, the root of the superior rectal artery was ligated and the IMV was ligated just distal to the LCA (Figure 2).
2.2 | Follow-up

All patients were followed up for survival. Recurrence and distant metastases were diagnosed on the basis of blood tests (including tumor markers), CT, endoscopy, MRI, and positron emission tomography-CT. Blood testing was performed every 3 months for 3 years postoperatively. Endoscopy was performed annually for 5 years postoperatively. Patients with pathological Stage III cancer consulted oncologists for chemotherapy.

2.3 | Statistical analysis

Statistical analyses were performed using JMP Pro 10 software (SAS Institute, Cary, NC, USA). Continuous variables are summarized as means and standard deviations, or medians and ranges; categorical variables are summarized as numbers and frequencies. Median and mean values were compared between groups using the Mann–Whitney test or the Chi-squared test. Postoperative complications were analyzed using binary logistic regression. OS, DFS, and CSS rates were analyzed using the Kaplan–Meier method and Cox’s proportional hazards model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). \( p < 0.05 \) was considered to indicate significant differences.

2.4 | Propensity score matching (PSM)

PSM was conducted to minimize the effects of intergroup differences. Propensity scores were calculated for each patient with bivariate logistic regression on the basis of

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**Table 1** Characteristics before and after propensity score matching

| Overall                        | After                        | \( p < 0.05^a \) | \( p < 0.05^a \) |
|-------------------------------|-----------------------------|------------------|------------------|
| Group A (n = 42) | Group B (n = 129) | \( p < 0.05^a \) | Group A (n = 28) | Group B (n = 28) | \( p < 0.05^a \) |
| ---                          | ---                          | ---              | ---              | ---              | ---              |
| Age 64 (34–92)                | 71 (37–88)                  | 0.0012           | 66.5 (37–92)     | 72.5 (55–88)     | 0.56             |
| Sex                           |                             |                 |                 |                 |                 |
| male 22 (52.4%)               | 72 (55.8%)                  | 0.698\(^b\)     | 15 (53%)         | 15 (53%)         | 1\(^b\)          |
| female 20 (47.6%)             | 57 (44.2%)                  |                 | 13 (46%)         | 13 (46%)         |                 |
| BMI 0.001                     |                             |                 | 23.9 (13.5–29)  | 23.4 (16.2–29)  | 0.65             |
| ASA                           |                             | 0.048\(^b\)     | 23.4 (16.2–29)  | 23.4 (16.2–29)  | 0.65             |
| 1 8 (19%)                     | 18 (14.2%)                  | 0.048\(^b\)     | 6 (14.3%)        | 6 (14.3%)        | 0.68\(^b\)       |
| 2 28 (66.7%)                  | 67 (52.8%)                  |                 | 18 (64.3%)       | 15 (53.6%)       |                 |
| 3 6 (14.3%)                   | 42 (33.0%)                  |                 | 6 (21.4%)        | 7 (25%)          |                 |
| CEA                           |                             | 0.81             | 2.8 (0.6–21.7)  | 3.6 (1.2–16.6)  | 0.79             |
| CA19-9                        |                             | 0.34             | 9.5 (3–70)       | 8.5 (2–88.5)     | 0.23             |
| T 0.46\(^b\)                 |                             |                 | 1 (3.57%)        | 3 (10.7%)        | 0.54\(^b\)       |
| 1 2 (4.76%)                   | 8 (6.2%)                    |                 | 7 (25%)          | 4 (14.3%)        |                 |
| 2 10 (23.8%)                  | 20 (15.5%)                  |                 | 10 (35.7%)       | 9 (32%)          |                 |
| 3 16 (38%)                    | 43 (33.3%)                  |                 | 10 (35.7%)       | 12 (42.8%)       |                 |
| 4 14 (33.3%)                  | 58 (44.9%)                  |                 |                 |                 |                 |
| N 0.23\(^b\)                 |                             |                 | 17 (60.7%)       | 16 (57.1%)       | 0.78\(^b\)       |
| 0 24 (57%)                    | 60 (46.5%)                  |                 | 11 (39.3%)       | 12 (42.8%)       |                 |
| 1 18 (42%)                    | 69 (53.5%)                  |                 |                 |                 |                 |
| stage 0.09\(^b\)              |                             |                 | 10 (23.8%)       | 6 (21.4%)        | 1\(^b\)          |
| 1 10 (23.8%)                  | 26 (20%)                    |                 | 6 (21.4%)        | 6 (21.4%)        |                 |
| 2 7 (16.7%)                   | 43 (33.3%)                  |                 | 6 (21.4%)        | 6 (21.4%)        |                 |
| 3 25 (59.5%)                  | 60 (46.5%)                  |                 | 16 (57.1%)       | 16 (57.1%)       |                 |

Note: Values are given as median (range) or n (%). A group: preservation of LCA. B group: without preservation of LCA.
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; LCA, left colic artery.
\(^a\) \( p \) values calculated using Fisher's exact test.
\(^b\) \( p \) values calculated using the \( \Pi^2 \) test.
**Table 2** Surgical outcomes

|                               | Group A (n = 28) | Group B (n = 28) | p < 0.05<sup>a</sup> |
|-------------------------------|------------------|------------------|----------------------|
| Operative time, min           | 199 (123–429)<sup>b</sup> | 175 (65–279)<sup>b</sup> | 0.02<sup>c</sup> |
| Bleeding volume, ml           | 23 (0–300)<sup>b</sup> | 5 (1–60)<sup>b</sup> | 0.09<sup>c</sup> |
| Intraoperative complications  | 0                | 0                | 0                    |
| Postoperative complications   |                  |                  |                      |
| Anastomotic leakage           | 0                | 0                | 0                    |
| Ileus                         | 0                | 0                | 0                    |
| Abscess                       | 0                | 0                | 0                    |
| SSI                           |                  |                  |                      |
| Transfusion Yes/No            | 0                | 0                | 0                    |
| Mortality                     | 0                | 0                | 0                    |
| Adjuvant chemotherapy Yes/No  | 13 (46.4%)       | 14 (50%)         | 0.78                 |
| Postoperative stay            | 10 (7–33)<sup>b</sup> | 10 (8–17)<sup>b</sup> | 0.23                 |
| Incision of length            | 2.5 (2.5–5)<sup>b</sup> | 2.5 (2.5–4)<sup>b</sup> | 0.76                 |

Note: Data are shown as n (%) unless otherwise indicated. A group: preservation of LCA; B group: without preservation of LCA.

*a* p values calculated using Fisher’s exact test.

*b* Data shown as median (range).

*c* p values calculated using the Mann–Whitney U test.

**Table 3** Pathological findings

|                               | Group A (n = 28) | Group B (n = 28) | p < 0.05<sup>a</sup> |
|-------------------------------|------------------|------------------|----------------------|
| Tumor location                |                  |                  | 0.78                 |
| Rs                            | 11 (39.3%)       | 12 (42.9%)       |                      |
| S                             | 17 (60.7%)       | 16 (57.1%)       |                      |
| Tumor size (mm)               | 39.5 (10–90)<sup>b</sup> | 42 (10–76)<sup>b</sup> | 0.79<sup>c</sup> |
| Harvested lymph nodes         | 21.5 (10–40)<sup>b</sup> | 20 (10–41)<sup>b</sup> | 0.62<sup>c</sup> |
| Histological type             |                  |                  | 0.09                 |
| tub1                          | 12 (42.9%)       | 16 (57%)         |                      |
| tub2                          | 7 (25%)          | 11 (39%)         |                      |
| muc                           | 1 (3.5%)         | 0 (0%)           |                      |
| por1                          | 2 (7.1%)         | 0 (0%)           |                      |
| pap                           | 6 (21.4%)        | 1 (3.57%)        |                      |
| Ly                            |                  |                  | 0.4                  |
| –                             | 4 (14.3%)        | 8 (28.6%)        |                      |
| +                             | 24 (85.7%)       | 22 (71.4%)       |                      |
| v                             |                  |                  | 0.67                 |
| –                             | 4 (14.3%)        | 5 (18.5%)        |                      |
| +                             | 24 (85.7%)       | 23 (81.5%)       |                      |
| Recurrence                    |                  |                  | 0.83                 |
| Local                         | 1 (3.57%)        | 2 (7.14%)        |                      |
| distance                      | 2 (7.14%)        | 2 (7.14%)        |                      |

Note: Data are shown as n (%) unless otherwise indicated. A group: preservation of LCA; B group: without preservation of LCA.

*a* p values calculated using Fisher’s exact test; data shown as median (range).

*b* p values calculated using the Mann–Whitney U test.

*c* p values calculated using the $Q^2$ test.
the following covariates: sex, age, BMI, ASA score, and the T, N, and pathological stage. These propensity scores were used to match patients in group A in a 1:1 ratio with patients in group B. We used the nearest-available Mahalanobis metric-matching distance with calipers, defined by the propensity score (caliper = 0.02).

3 | RESULTS

3.1 | Characteristics before and after PSM

Before PSM, there were significant differences between the two groups in age \((p = 0.0012)\), BMI \((p = 0.001)\), and ASA score \((p = 0.048)\). After PSM, each group included 28 patients and did not differ significantly in age, sex, BMI, ASA, tumor markers, T, N, or pathological stage (Table 1).

3.2 | Peri- and postoperative outcomes after PSM

The perioperative outcomes after PSM are summarized in Table 2. The two groups did not significantly differ regarding the incidences of intra- and postoperative complications, use of adjuvant chemotherapy, mortality, median operative time, intraoperative blood loss volume, incision length, or duration of postoperative hospitalization. There was no conversion to laparotomy or additional port placement in either group.

3.3 | Pathological findings after PSM

The pathological and oncological outcomes after PSM are summarized in Table 3. There were no significant differences between groups regarding the median number of harvested lymph nodes, tumor size, degree of differentiation, depth of invasion, lymphatic invasion, venous invasion, or lymph node classification. The two groups had similar local and distance recurrence rates (Table 3).

3.4 | Oncological outcomes after PSM

After PSM, the median follow-up duration was 115 months (range, 11–120 months) in group A and 72.5 months (range, 4–120 months) in group B. There were no significant differences between groups A and B in the 5-year OS rate (75% vs. 64.2%, hazard ratio...
[HR] 1.34, 95% confidence interval [CI] 0.37–4.30, \( p = 0.24 \), 5-year DFS rate (78.5% vs. 85.7%, HR 0.99, 95% CI 0.24–4.22, \( p = 0.99 \), and 5-year CSS rate (92.8% vs. 89.3%, HR 1.50, CI 0.25–11.4, \( p = 0.64 \)) (Figure 3).

4 | DISCUSSION

The present study compared the short- and long-term outcomes of SILS for sigmoid and rectosigmoid cancer with D3 lymphadenectomy with or without LCA preservation using PSM. The two groups had similar OS, DFS, and CSS. Short-term results suggested that the operative time was slightly longer in group A than in group B, but there were no significant differences in complications or blood loss. The present study showed that the CSS rates in groups A and B were 90.4% and 88.4%, respectively, which were comparable to the OS reported in the JCOG0404 trial. The DFS rates in groups A and B were 83.3% and 82%, respectively, which were comparable with the DFS rate of the JCOG0404 trial.

Some previous studies reported that high IMA ligation for rectal cancer does not improve the long-term outcomes compared with low IMA ligation. Other studies reported that LCA preservation in sigmoid colon cancer surgery contributes to a decrease in anastomosis leakage but does not affect the long-term outcomes. LCA preservation maintains adequate blood supply to the colon proximal to the anastomosis, whereas ligation of the IMA root means that vascularization of the distal colon and sigmoid depends completely on the middle colic and marginal arteries. Therefore, if a patient develops transverse colon cancer after undergoing surgery for sigmoid colon and rectal cancer, the blood flow in the distal colon can be expected to be maintained if the LCA is preserved. However, the disadvantage of LCA preservation is the possibility of spillage of micrometastatic cells because of skeletonization of the LCA and the need for a more complicated procedure with a longer operative time than surgery without LCA preservation.

In our study, although the operative time was 30 min longer in group A than in group B, the two groups had a similar number of lymph nodes removed, blood loss volume, and incidences of intra- and postoperative complications; these findings suggest that D3 lymphadenectomy with LCA preservation is a safe surgical procedure. Therefore, we would recommend D3 dissection with LCA preservation unless the patient is an older adult, in which case we would recommend D3 dissection with LCA preservation.

SILS for colorectal diseases was reported in 2008, and the short-term results are reportedly similar to single-incision laparoscopic colectomy and conventional laparoscopic colectomy. A recent randomized controlled trial showed that SILS achieves similar long-term outcomes to conventional laparoscopic surgery. Furthermore, SILS reportedly achieves a better cosmetic effect and less postoperative pain than conventional multipoort laparoscopic surgery for ascending colon cancer, sigmoid colon cancer, and rectosigmoid cancer. Although right hemicolectomy requires a lot of vascular treatment, SILS reportedly has a shorter operative time than conventional laparoscopic surgery. Therefore, it seems that even complicated procedures such as LCA preservation can be performed via SILS.

The present study has some limitations. First, this was a retrospective single-center study with a small sample size. Second, the learning curve of surgical techniques was not considered. Third, there was bias in the indication for SILS. Group A tended to include younger patients than group B owing to the increased likelihood of new colorectal cancer after surgery in younger patients. Group A was significantly younger before PSM, and the ASA score was significantly higher in group A than in group B even after PSM. Group A also tended to have a higher rate of postoperative adjuvant chemotherapy than group B (56.7% vs. 40%), although this difference was not statistically significant. These intergroup differences may have affected the long-term outcomes.

In conclusion, LCA preservation is safe and feasible in SILS for sigmoid colon and rectosigmoid cancer, with a slight increase in operative time in group A than in group B, but no significant intergroup differences in short- and long-term outcomes.

AUTHOR CONTRIBUTIONS

Y.I., C.H., and Y.H. designed the study and performed the experiments; H.Y., M.H., K.D., and Y.I. performed the experiments, analyzed the data, and wrote the article.

ACKNOWLEDGMENTS

We thank Kelly Zammit, BVSc, from Edanz (https://jp.edanz.com/ac) for editing a draft of this article.

CONFLICT OF INTEREST

The authors declare no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to restrictions (e.g., containing information that could compromise the privacy of research participants).

ETHICS STATEMENT

The study protocol was approved by the Ethics Committee of Fukui Prefectural Hospital and conforms to the
provisions of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board for the Use of Human Subjects of Fukui Prefectural Hospital.

INFORMED CONSENT
Written informed consent was obtained from all patients prior to study inclusion.

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How to cite this article: Hiranuma C, Ishiyama Y, Hirano Y, Hattori M, Douden K. D3 lymph node dissection with versus without left colic artery preservation in single-incision laparoscopic surgery for sigmoid and rectosigmoid cancer: A propensity score-matched analysis. Asian J Endosc Surg. 2023;16(2):233-240. doi:10.1111/ases.13145