Short- and long-term outcomes of preservation of the superior rectal artery versus ligation of the inferior mesenteric artery in laparoscopic D3 lymph node dissection for descending colon cancer: a propensity score-matched analysis

Aya Sato
Hakodate Municipal Hospital

Ken Imaizumi (imaken1983@gmail.com)
Hakodate Municipal Hospital

Hiroyuki Kasajima
Hakodate Municipal Hospital

Kentaro Ichimura
Hakodate Municipal Hospital

Kentaro Sato
Hakodate Municipal Hospital

Daisuke Yamana
Hakodate Municipal Hospital

Yosuke Tsuruga
Hakodate Municipal Hospital

Minoru Umehara
Hakodate Municipal Hospital

Michihiro Kurushima
Hakodate Municipal Hospital

Kazuaki Nakanishi
Hakodate Municipal Hospital

Research Article

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Abstract

Purpose

This study aimed to compare the short- and long-term outcomes of laparoscopic D3 lymph node (LN) dissection between ligation of the inferior mesenteric artery (IMA) (LIMA) and preservation of the superior rectal artery (SRA) (PSRA) for descending colon cancer using propensity score-matched analysis.

Methods

This retrospective study included 101 patients with stage I-III descending colon cancer who underwent laparoscopic D3 LN dissection with LIMA (n = 60) or PSRA (n = 41) at a single center between January 2005 and March 2022. After propensity score matching, 64 patients (LIMA, n = 32; PSRA, n = 32) were included in the analysis. The primary endpoint was the long-term outcomes, and the secondary endpoint was the surgical outcomes.

Results

In the matched cohort, no significant difference was noted in surgical outcomes, included the operative time, estimated blood loss, number of harvested LNs, number of harvested LN 253, and complication rate. The long-term outcomes were also not significantly different between the LIMA and PSRA groups (3-year recurrence-free survival: 78.7% vs. 88.9%, \( P = 0.335 \); 5-year overall survival: 69.8% vs. 63.4%, \( P = 0.888 \); 5-year cancer-specific survival: 84.2% vs. 82.8%, \( P = 0.607 \)). No recurrence of LN metastasis was observed around the IMA root.

Conclusion

Laparoscopic D3 dissection in PSRA was comparable to that in LIMA regarding both short- and long-term outcomes. The optimal LN dissection for descending colon cancer should be investigated in future large-scale studies.

Introduction

Colorectal cancer (CRC) represents one of the most common malignancies worldwide. Over the past several decades, the operative method for CRC has been updated. Some studies have recently shown that complete mesocolic excision (CME) with central vascular ligation (CVL) has prognostic importance in localized colon cancer [1–3]. According to West et al., D3 lymph node (LN) dissection and CME with CVL were based on similar oncologic principles and improved the CRC outcomes [1]. In Japan, D3 LN dissection for advanced colon cancer requires the harvesting of LNs at the root of the principal artery, such as the superior mesenteric artery in right-sided colon cancer and the inferior mesenteric artery (IMA).
in left-sided colon cancer [4]. IMA was commonly ligated and cut in D3 LN dissection for left-sided colon cancer. Some reports proposed D3 LN dissection with preservation from the IMA root to the left colic artery (LCA) for sigmoid and rectal cancers [5–8]. In descending colon cancer, whether IMA root to the superior rectal artery (SRA) should be preserved represents a clinical problem. Nonetheless, to our best knowledge, no reports focusing on D3 LN dissection have investigated whether the SRA should be preserved in descending colon cancer.

Transverse and descending colon cancers were excluded from most previous prospective studies related to laparoscopic surgery [9–11] because of complex anatomy and technical difficulties [12]. However, with the recent improvement in the understanding of surgical anatomy and laparoscopic surgical techniques, some retrospective studies reported laparoscopic surgery for descending colon cancer to be safe and feasible [13, 14]. Hence, in our institute, laparoscopic surgery has been routinely performed for descending colon cancer even if D3 LN dissection is required. The present retrospective study aimed to compare the short- and long-term outcomes of laparoscopic D3 LN dissection between ligation of the IMA (LIMA) and preservation of the SRA (PSRA) for descending colon cancer using propensity score matching analysis.

**Materials And Methods**

**Study design and patient population**

The present retrospective observational study was performed using a single-center surgical database. This study was approved by the Human Research Ethics Committee of Hakodate Municipal Hospital, Hokkaido, Japan (reference number 2021-56), and was conducted in accordance with the tenets of the 1964 Declaration of Helsinki and its later amendments. The requirement for the acquisition of informed consent from patients was waived owing to the retrospective nature of the study. The study and the manuscript adhered to the STROBE guidelines for observational studies.

Data of patients diagnosed with descending colon cancer, who underwent elective radical surgery for primary tumors in our department between January 2005 and March 2022, were collected from our database. The exclusion criteria were as follows: laparotomy, absence of D3 LN dissection, pathological stages IV, multicentric cancer, and multivisceral resection. Preoperative chemotherapy was not administered to this cohort. The patients were classified into the LIMA and PSRA groups.

**Study endpoints**

The primary endpoint was the difference in the long-term outcomes between LIMA and PSRA. The secondary endpoint was the difference in the surgical outcomes between LIMA and PSRA.

**Surgical technique**

The patients were placed in the lithotomy position. In most cases, the operation was performed using the conventional five-port method. However, in some cases, the procedure was carried out using the reduced-
port technique. Mobilization of the sigmoid and descending mesocolon was initiated using a medial-to-lateral approach. The procedure for laparoscopic D3 LN dissection in PSRA (ligation of LCA) was previously reported by our department [15]. In contrast, the procedure for LIMA involved ligation of the IMA root. The schema for D3 dissection and representative laparoscopic images after D3 LN dissection in LIMA and PSRA were shown in Fig. 1. The selection of either LIMA or PSRA was decided based on the preoperative surgeons’ discussion. In the PSRA group, the selection of arteries (LCA, the first sigmoid artery [SA] or both) for ligation was determined by preoperative computed tomography (CT) and intraoperative evaluation of dominant tumor vessel. Mobilization of the colon at the splenic flexure was completed by dividing the greater omentum and dissecting the mesentery at the lower edge of the pancreas. After mobilization, the colon was pulled out at the umbilical site and transected at the proximal and distal margins. For LIMA, the level of the distal bowel transection was near the rectosigmoid junction. The anastomosis method was selected at the surgeons’ discretion. In most cases, stapled anastomosis, including triangular anastomosis (TA) and functional end-to-end anastomosis, was performed extracorporeally. The procedure for TA was previously reported by our department [16]. No cases of diverting stoma were identified. All surgeries were performed under the supervision of specialized laparoscopic surgeons who were qualified by the endoscopic surgical skill qualification system of the Japan Society for Endoscopic Surgery [17].

**Data collection and assessments**

The following clinicopathological data were collected from the hospital database: patients’ age and sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), tumor location, ligation of artery, operative time, estimated blood loss, number of harvested LNs, conversion, type of anastomosis, postoperative hospital stay, histological type, maximum tumor diameter, stage, depth of tumor invasion, LN metastasis, lymphatic invasion, vascular invasion, induction of adjuvant chemotherapy, and observation period. Staging was performed according to the third English edition of the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma [18]. Tumor location was categorized into descending colon and sigmoid-descending colon (SD) junction. Descending colon was defined as the segment fixed to the retroperitoneum extending from the left colic flexure to the height of the iliac crest, and SD junction was defined as the segment fixed to the retroperitoneum below the iliac crest based on barium enema examination and CT [18]. Postoperative complications were assessed within 30 days after surgery using the Clavien-Dindo classification [19].

LN distribution was assessed according to Japanese classification [18]. After tumor removal, the surgeons isolated the LNs and recorded their distribution. LN distribution was classified in the guidelines as follows: LN 221, pericolic LNs along the transverse colon; LN 222Lt, intermediate LNs along the left branch of the middle colic artery; LN 231, pericolic LNs along the descending colon; LN 232, intermediate LNs along the LCA; LN 241, pericolic LNs along the sigmoid colon; LN 242, intermediate LNs along the sigmoid arteries; LN 252, intermediate LNs along the superior rectal artery (SRA); and LN 253, LNs at the IMA root. The lengths of the proximal and distal margins were measured and recorded prior to formalin fixation.
Adjuvant chemotherapy was determined by gastrointestinal oncologists based on the pathological stage and general condition according to Japanese guidelines [4]. For all patients with high-risk stage II or III disease, 5-fluorouracil-based chemotherapy was considered. The patients were followed up in our department every 3 months for 3 years and every 6 months thereafter. Tumor markers, including serum carcinoembryonic antigen and carbohydrate antigen 19–9, were examined at each follow-up, and chest and abdominal CT was performed every 6 months. Total colonoscopy was performed every 2 years. Recurrence was diagnosed by radiological detection of an increase in the lesion size or by histological confirmation.

**Statistical analysis**

Propensity scores were calculated using a logistic regression model based on the following clinical variables: age, sex, BMI, ASA-PS, location of tumor, and clinical stage. We performed 1:1 nearest-neighbor matching without replacement with an optimal caliper width of 0.25 logit of the standard deviation of the propensity score [20]. Standardized mean differences (SMD) were assessed to determine whether sufficient balance was achieved after matching (SMD < 0.2).

Between-group comparisons were performed using the Mann-Whitney U test for quantitative data and Fisher’s exact test for categorical data. Recurrence-free survival (RFS), overall survival (OS), and cancer-specific survival (CSS) rates were estimated using the Kaplan-Meier method and compared between the groups using the univariate log-rank test in the matched cohort. Statistical significance was set at \( P < 0.05 \). All statistical analyses were performed using EZR version 1.50 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R version 3.6.3 (The R Foundation for Statistical Computing, Vienna, Austria), which is a modified version of R Commander (version 2.6-2) designed to add statistical functions frequently used in biostatistics [21].

**Results**

**Patient characteristics**

A total of 175 patients who underwent elective radical surgery for descending colon cancer between January 2005 and March 2022 were eligible in this study. However, 33 patients who underwent surgery by laparotomy and 26 patients who did not undergo D3 LN dissection were excluded. Moreover, 10 patients with pathological stage IV disease, four patients with multicentric cancer, and one patient who underwent multivisceral resection were excluded. Before 1:1 propensity-score matching, 101 patients (LIMA, \( n = 60 \) [59.4%]; PSRA, \( n = 41 \) [40.6%]) were enrolled in this study. After matching, 64 patients (LIMA, \( n = 32 \) [50%]; PSRA, \( n = 32 \) [50%]) were included in the analysis (Fig. 2).

Clinical characteristics of all patients and the LIMA and PSRA groups before and after matching were presented in Table 1. Before matching, the PSRA group included significantly more male patients and tumor location at descending colon than the LIMA group. After matching, these differences in the clinical characteristics improved and the SMD of all variables became < 0.2.
Surgical outcomes

The surgical outcomes before and after matching were summarized in Table 2. In the PSRA group, ligation of artery was LCA, SA, and both, in 24, 10, and 7 patients, respectively. After matching, no significant differences in operative time, estimated blood loss, number of total harvested LNs, and harvested LN 253 were observed between the LIMA and PSRA groups. Regarding the anastomosis method, double stapling technique and TA were performed most often in the LIMA and PSRA groups, respectively. Although the lengths of the resected proximal and distal margins of the colon were not significant differences between the two groups, significantly more patients with a distal margin of ≥15 cm were present in the LIMA group than in the PSRA group. Postoperative complication rate was not significantly difference between the two groups. No major complications occurred in the PSRA group, whereas three patients in the LIMA group developed major complications. The length of postoperative hospital stay was not significantly different between the LIMA and PSRA groups.

Pathological outcomes and distribution of LN metastasis

The pathological outcomes before and after matching were summarized in Table 3. One patient with 253 LN metastasis was present in each study group. After matching, no significant differences in pathological outcomes were observed between the LIMA and PSRA groups. The distribution of pathological LN metastasis was shown in Fig. 3. The principal LNs at the IMA root (LN 253) included metastatic LNs at 2.0%. The intermediate LNs along the sigmoid arteries (LN 242) and superior rectal artery (LN 252) had metastatic LNs at only SD junction tumor.

Recurrence and survival

The median observation period was 52.8 (range, 3.0-150.6) months. The overall 3-year RFS, 5-year OS, and 5-year CSS were 88.4%, 71.4%, and 88.6%, respectively. Table 4 presented the results of univariate analyses for RFS, OS, and CSS in the matched cohort. LIMA or PSRA was not significantly associated with RFS, OS, and CSS. Before matching, the 3-year RFS, 5-year OS, and 5-year CSS rates were not significantly different between the LIMA and PSRA groups (3-year RFS: 86.3% vs. 91.5%, \(P = 0.476\); 5-year OS: 72.4% vs. 69.9%, \(P = 0.908\); 5-year CSS: 91.2% vs. 84.8%, \(P = 0.928\)) (Fig. 4). After matching, the 3-year RFS, 5-year OS, and 5-year CSS rates were also not significantly different between the LIMA and PSRA groups (3-year RFS: 78.7% vs. 88.9%, \(P = 0.335\); 5-year OS: 69.8% vs. 63.4%, \(P = 0.888\); 5-year CSS: 84.2% vs. 82.8%, \(P = 0.607\)) (Fig. 5).

Ten patients (seven in the LIMA group and three in the PIMA group) experienced cancer recurrence. Among the seven patients in the LIMA group with cancer recurrence, three had peritoneal metastasis, two had liver metastasis, one had lung metastasis, and one had para-aortic LN metastasis. Among the three patients in the PSRA with cancer recurrence, one had metastasis to the LN of the porta hepatis, one had liver metastasis, and one had multiple organs (liver, lung, spleen, peritoneal metastasis). No recurrence of LN metastasis was observed around the IMA root.
Discussion

To our best knowledge, this is the first report to compare the short- and long-term outcomes between LIMA and PSRA for descending colon cancer focusing on laparoscopic D3 LN dissection. Irrespective of whether the IMA was ligated or the SRA was preserved, no significant differences were observed in the operative time, estimated blood loss, number of harvested LNs, and number of harvested LN 253. The complication rate was not significantly different between the two groups. Long-term outcomes were not significantly different between the two groups. Although this was a retrospective, single-center study with a relatively small cohort, we performed propensity-score matching and eliminated selection biases as much as possible.

CME with CVL has been suggested by several studies to have prognostic importance in localized colon cancer [1–3]. D3 LN dissection and CME with CVL were based on similar oncologic principles [1]. According to the Japanese guidelines, D3 LN dissection, including the central LN, is required for clinical stage II and III CRC [4]. In descending colon cancer, the central LN is located at the IMA root. Conventionally, the IMA is transected at the root for D3 LN dissection. However, a wide range of the left-sided colon and upper rectum is fed by the IMA. When the IMA root is ligated, the blood supply to the residual left-sided colon may be insufficient. Several previous studies on rectal cancer reported D3 LN dissection with preservation from the IMA root to the LCA to maintain the blood supply to the residual oral-side colon [22–24]. In descending colon cancer, a lack of blood supply to the residual anal-side colon could occur as a result of IMA ligation. Nonetheless, few reports have reviewed the preservation from the IMA root to the SRA for descending colon cancer. Lee et al. reported the short- and long-term outcomes of SRA-preservation and IMA-ligation for descending colon cancer [2]. However, no reports focusing on D3 LN dissection for descending colon cancer have investigated whether the SRA should be preserved.

Kobayashi et al. reported that laparoscopic D3 LN dissection with PSRA was a safe and applicable method in five cases of descending and proximal sigmoid colon cancer [25]. Nevertheless, we consider this procedure to be complex. According to some studies, D3 LN dissection with preservation of LCA for sigmoid or rectal cancer required a longer operative time than with IMA ligation [6, 8, 24]. We previously showed that this procedure could be simplified by using our step-by-step approach [15]. The present study revealed that short-term outcomes, including operative time, bleeding, and complication rate, were not significantly different between LIMA and PSRA after propensity matching. Hence, our surgical procedure is safe and feasible.

When the IMA is ligated at the root, the blood supply to the remnant anal-side colon is considered to be preserved by up to approximately 10 cm from peritoneal reflection on the oral side [26]. In the study conducted by Munechika et al., indocyanine green (ICG) examination of the blood supply in IMA-root ligation revealed a distance of 17–66 cm from the peritoneal reflection to the ICG contrast limit [27]. Based on these reports, a wide variation of the blood supply to the anal-side colon in IMA-root ligation was considered. The extent of anal-side bowel resection may be increased to avoid ischemia, which would result in the shortening of the remnant bowel and difficulty in creating a tension-free anastomosis.
without wide mobilization. Our results indicated that the LIMA group had significantly more patients with a distal margin of ≥ 15 cm than the PSRA group. Regarding anastomotic complications, few studies have reported no occurrence of anastomotic leakage in IMA ligation or SRA preservation for descending colon cancer [2, 27]. However, in this study, postoperative anastomotic leakage occurred in two patients who underwent LIMA. Wakahara et al. reported that although anastomotic leakage in laparoscopic sigmoidectomy did not differ irrespective of IMA ligation or SRA preservation, one patient who underwent IMA ligation developed anastomotic leakage [28]. While the leakage rate was not significant because there were very few cases of leakage in either group, we consider that PSRA, rather than LIMA, is safer for anastomosis.

There are few reports on the rate or distribution of LN metastasis in descending colon cancer. According to the report that became the basis of the Japanese guidelines, the rate of central LN metastasis in pathological T3 colon cancer was 2.4%. Nonetheless, these data included right-sided colon cancer [4]. Rao et al. reported a rate of 5.7% (2/35 cases) for central LN metastasis in descending colon cancer [29]. Conversely, Lee et al. investigated the distribution of LN metastasis and reported that there was no metastasis of LN 253 in 26 cases [2]. Our data indicated 2.0% of all patients (2/101 cases) had metastatic LN 253. Among all studies, the present report included the largest number of cases Elucidation of the rate of central LN metastasis in descending colon cancer is a topic of future research.

Some studies on D3 dissection for rectal and sigmoid colon cancers revealed no significant difference in OS and disease-free survival between the IMA ligation and IMA preservation groups [7, 24, 30]. Previous reports on descending and sigmoid colon cancers that investigated the long-term outcomes have shown no significant difference, irrespective of whether the IMA was ligated at the root or not [2, 28]. Our study revealed no significant difference in oncological outcomes between the LIMA and PSMA groups in the overall and matched cohorts. There were three cases of recurrence in PIMA; however, there were no cases of LN recurrence around the IMA root or para-aorta.

Our study had some limitations. First, this study was a single-center retrospective study of patients with different backgrounds and potential for selection bias in the choice of either LIMA or PSRA by surgeons existed. Therefore, propensity-score matching was performed. Austin et al. reported that SMD < 0.1 was considered a sufficient balance of variables [31]. However, such methods are difficult to work with a small sample size as our matched cohort became too small. In these cases, the SMD is sometimes set at < 0.2 [32]. An SMD > 0.2 is reported to cause an imbalanced matching cohort [20]. Therefore, this study set the SMD at < 0.2. Second, the sample size of the overall cohort was relatively small. Third, there were a few cases of metastasis at LN 253. Hence, this study could not investigate whether D3 LN dissection with PSRA achieved sufficient outcomes in cases with LN 253 metastasis. Despite these limitations, this study could be worth reporting because there are few reports on descending colon cancer. Multicenter cohort studies or randomized controlled trials should be conducted in the future to verify the surgical and oncological outcomes.

Conclusions
In conclusion, laparoscopic D3 dissection in PSRA was comparable to that in LIMA in terms of short- and long-term outcomes. The PSRA procedure is safe and feasible. However, considering the several limitations of this study, the optimal LN dissection for descending colon cancer should be investigated in future large-scale studies.

Declarations

Conflict of interest statement

Drs. Aya Sato, Ken Imaizumi, Hiroyuki Kasajima, Kentaro Ichimura, Kentaro Sato, Daisuke Yamana, Yosuke Tsuruga, Minoru Umehara, Michihiro Kurushima, and Kazuaki Nakanishi declare no conflict of interest.

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Authors’ contributions

AS, KIm, HK, Klc, KS, DY, YT, MU, MK, and KN conceptualized and designed the study. AS and KIm wrote the manuscript. AS performed statistical analyses. AS, KIm, HK, Klc, KS, DY, YT, MU, MK, and KN performed the operations and collected clinicopathological data. KN supervised the study. AS, KIm, HK, Klc, KS, DY, YT, MU, MK, and KN interpreted the results and wrote the report. All authors have read and approved the final version of the manuscript.

Ethics approval

This study was approved by the Human Research Ethics Committee of Hakodate Municipal Hospital, Hokkaido, Japan (reference number 2021-56), and was conducted in accordance with the tenets of the 1964 Declaration of Helsinki and its later amendments. The requirement for the acquisition of informed consent from patients was waived owing to the retrospective nature of the study. The study and the manuscript adhered to the STROBE guidelines for observational studies.

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References


Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures
Figure 1

Representative images of D3 LN dissection. The upper panels represented schemas of the procedures, whereas the lower panels were intraoperative photographs. (a) Ligation of the inferior mesenteric artery (LIMA). (b) Preservation of the superior rectal artery (PSRA). Selection of arteries (LCA or SA or both) for ligation was determined by preoperative computed tomography and intraoperative evaluation of dominant tumor vessel. IMA, inferior mesenteric artery; IMV, inferior mesenteric vein; LCA, left colic artery; LN, lymph node; SA, 1st sigmoid artery; SRA, superior rectal artery.
Figure 2

Study population and patient flow chart. IMA, inferior mesenteric artery; SRA, superior rectal artery.
Figure 3

Distribution of LN metastasis. (a) Total cases. (b) The cases of cancer at descending colon. (c) The case of cancer at the sigmoid–descending colon (SD) junction. LN, lymph node.
Figure 4

Kaplan-Meier curves between ligation of the inferior mesenteric artery (PIMA) vs. preservation of the superior rectal artery (PSRA) in the overall cohort. (a) Recurrence-free survival. (b) Overall survival. (c) Cancer-specific survival.
Figure 5

Kaplan-Meier curves between ligation of the inferior mesenteric artery (PIMA) vs. preservation of the superior rectal artery (PSRA) in the matched cohort. (a) Recurrence-free survival. (b) Overall survival. (c) Cancer-specific survival.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

- Table1PSM.xlsx
- Table2PSM.xlsx
- Table3PSM.xlsx
- Table4PSM.xlsx