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ORIGINAL ARTICLE

A multicenter prospective observational study of lymph node metastasis patterns and short-term outcomes of extended lymphadenectomy in right-sided colon cancer

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Abstract

Background: The lymph node metastasis rate in right-sided colon cancer is unknown, and the optimal central vascular ligation level remains controversial. We aimed to determine the lymph node metastasis rate and short-term results of radical surgery with extended lymph node dissection in right-sided colon cancer.

Methods: This prospective multicenter observational study included patients with stage II/III right-sided colon cancer from five cancer hospitals. The metastasis rate of each node station was analyzed according to tumor location and main feeding artery.

Results: Between April 2018 and August 2021, 208 patients underwent dissection around the superior mesenteric artery (SMA) and vein (SMV). In transverse colon cancer, 7.5% and 2.5% of metastases occurred around the SMV and SMA at the root of the middle colic artery (MCA), respectively; 6.7% and 6.7% at the root of the right colic artery. In caecal cancer, 1.9% of metastases occurred around the SMV and 1.9% around the SMA. In ascending colon cancer, the rate was 1.1% around the SMV. Of the tumors, 17% fed mainly by the ileocolic artery had node metastases along the middle or right colic artery, as did 66.7% fed mainly by the right colic artery and 41.2% fed by the MCA ($p = 0.01$). Postoperative complications occurred in 42 patients (20.2%).

Conclusion: Routine prophylactic extended lymphadenectomy around the SMA might not be necessary in caecum and ascending colon cancer. Dissection around the SMA may be necessary in cases of transverse colon cancer or when the feeding artery is the MCA.

KEYWORDS
lymph node metastasis, lymphadenectomy, main lymph nodes, observational study, right-sided colon cancer

1 | INTRODUCTION

In recent years, reports from Western countries have indicated that complete mesocolic excision (CME) reduces the risk of local recurrence of advanced colon cancer and has a positive impact on prognosis.[1,2] CME consists of (1) resection of the mesentery containing the tumor within a complete envelope of mesenteric fascia, (2) resection of apical lymph nodes with high-level ligation of blood vessels (central vascular ligation, CVL), and (3) resection of an adequate length of bowel to remove the pericolic lymph nodes. Cancer cells can micro-metastasize from the main tumor to the surrounding area via lymphatics and blood vessels in the mesentery. This provides the rationale for CME, namely, dissection between the mesenteric plane and the parietal fascia and removal of the mesentery.

The frequency of lymph node metastasis according to the site along the artery feeding the tumor is important when performing CVL but has not been investigated in detail. When CME was first reported in Europe, not only the lymph nodes along the superior mesenteric artery (SMA) and superior mesenteric vein (SMV) but also the peripancreatic and gastroepiploic lymph nodes were dissected.[3] In recent years, the extent of dissection has decreased because of concerns about prolonged operation times and complications. Positive results were reported in the United States and South Korea when extended lymph node dissection was performed with exposure of the SMA and SMV.[4,5] However, there has been no in-depth study of which lymph nodes are involved in metastasis. D3 lymph node dissection, similar to CVL, has been performed in Japan for a long time. Whereas the CME technique emphasizes preservation of the anatomical planes of resection, the Japanese technique emphasizes anatomical lymph node dissection. In the Japanese guidelines, regional lymph nodes in colon cancer are classified as pericolic, intermediate, or main lymph nodes. D3 lymph node dissection aims to remove the maximal number of metastatic lymph nodes by resecting up to the main lymph node at the root of the feeding artery.[6] However, in right-sided colon cancer, lymph node dissection around the SMA is technically difficult and very likely to result in complications, so most surgeons dissect only up to around the SMV.[7,8] Therefore, the frequency of metastasis to the lymph nodes surrounding the SMA located to the left of the SMV is unclear and the appropriate CVL level in the blood vessels remains controversial. Furthermore, even in right-sided colon cancer, the appropriate CVL level may depend on the location of the tumor (e.g., the caecum, ascending colon, transverse colon), which has not been investigated.

The aim of this multicenter prospective observational study was to determine the frequency and location of lymph node metastasis and the short-term results of radical surgery with extended lymph node dissection including exposure of the SMV and SMA for right-sided colon cancer in Japan.

2 | MATERIALS AND METHODS

2.1 | Patients

Five specialist cancer hospitals in Japan where extended lymph node dissection is routinely performed (National Cancer Center Hospital, Aichi Cancer Center Hospital, Kanagawa Cancer Center Hospital, Osaka International Cancer Institute Hospital, and Niigata Cancer Center Hospital) participated in this study. The study protocol was approved by the institutional review boards of all participating hospitals. All patients provided written informed consent before enrolment. The clinical trial registration number is UMIN000047356. The eligibility criteria were as follows: (1) primary tumor located in the caecum, ascending colon, or right side of the transverse colon; (2) stage II or III disease according to the Union for International Cancer Control TNM Classification of Malignant Tumors (8th edition); (3) mainly lymph nodes around the SMA and SMV to be dissected; and (4) bowel resection margin >10 cm beyond the tumor on both the oral and anal sides planned. Patients with a history of chemotherapy or multiple cancers were excluded.

2.2 | Procedures

Patient underwent surgery for right-sided colon cancer with D3 lymph node dissection, which was defined as dissection of at least the main lymph node around the root of the main feeding artery of the tumor. Studies in Japan have shown that pericolic lymphatic spread >10 cm beyond the tumor rarely occurs in right-sided colon cancer; thus, in this study the minimum bowel resection margin was set as 10 cm on each of the oral and anal sides.[9,10] The main feeding artery was defined as the vessel identified to be flowing closest to the tumor intraoperatively. In this study, the artery flowing into the ileocaecal portion was defined as the ileocolic artery (ICA), the artery flowing into the ascending colon as the right colic artery (RCA), and the artery flowing into the transverse colon or hepatic flexure as the middle colic artery (MCA). Lymph nodes were classified according to the third English edition of the Japanese Classification of Colorectal Carcinoma,[6] whereby the pericolic lymph nodes are at station 201 for the ICA, station 211 for the RCA, and station 221 for the MCA and the intermediate lymph nodes are at stations 202, 212, and 222, respectively. In the Japanese classification, there is no distinction between the main lymph nodes around the SMV and those around the SMA. In this study, the main lymph nodes were divided into those around the SMA and those around the SMV (Figure 1) in order to clarify the frequency of metastasis around these vessels. If the RCA was missing due to anatomical variation, we divided the area between the ICA/ICV and MCA/MCV into three equal portions and defined stations 213A and 213V as the middle of these portions.

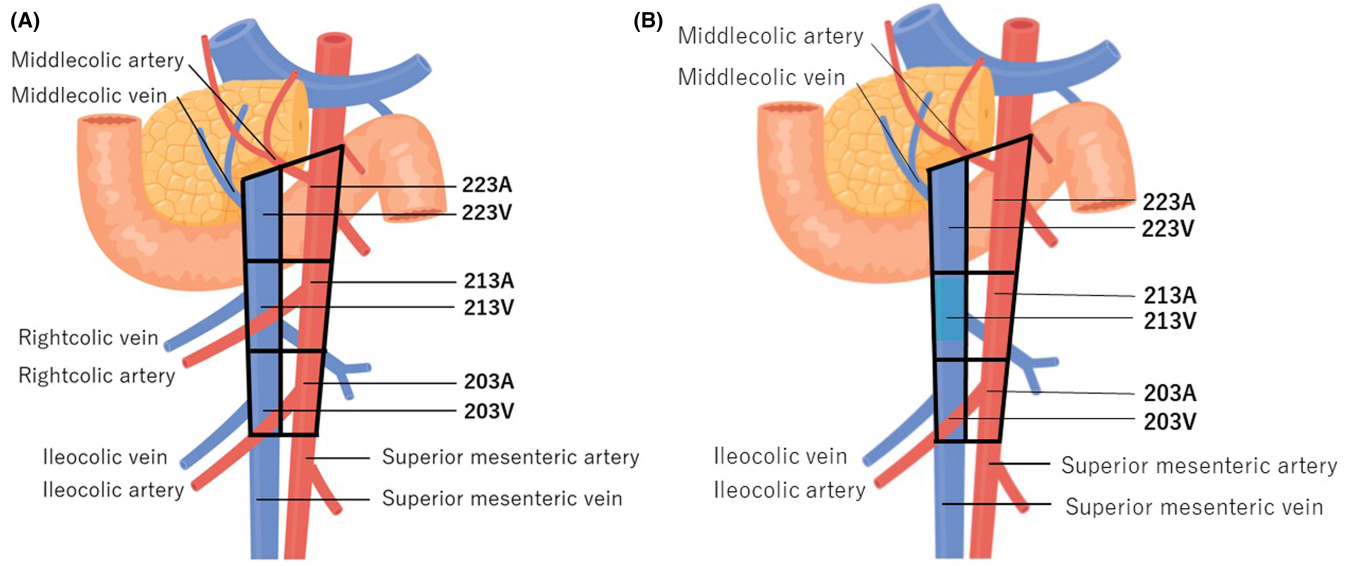

FIGURE 1 Lymph node station numbers classified by vascular anatomy: (A) cases with the ileocolic artery, right colic vessels, and middle colic artery, and (B) cases with the right colic artery missing.

The main lymph nodes were specifically marked intraoperatively to clarify the metastatic sites. In open surgery, the main lymph nodes were divided in the surgical field. In laparoscopic surgery, where the main lymph nodes could not be divided in the abdominal cavity, they were marked intraoperatively so that their boundaries could be seen. Lymph nodes other than the main ones were submitted for pathological examination after completion of surgery.

The surgeries were categorized as follows, depending on which main feeding arteries were within the resection area: resection of the ICA alone was defined as ileocaecal resection; resection of the ICA, the RCA, and the right branch of the MCA was defined as right hemicolectomy; and resection of the left branch of the MCA in addition to these was defined as extended right hemicolectomy.

2.3 | Outcomes

The primary endpoint was the metastasis rate at each lymph node station according to tumor location and main feeding artery. Secondary endpoints were postoperative complications according to the Clavien–Dindo classification, the R0 resection rate, 5-year overall survival, and 5-year relapse-free survival according to metastatic status in each node station. This report summarizes the short-term outcomes; overall survival and relapse-free survival rates will be reported after 5 years of follow-up.

2.4 | Statistical analysis

Differences between groups were examined using the chi-squared test. All statistical analyses were performed using SPSS for Windows (version 23.0; IBM Corp.). A *p*-value of 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Patient and tumor characteristics

Between April 2018 and August 2021, 208 Japanese patients with right-sided colon cancer were enrolled. Their characteristics are shown in Table 1. The tumor was located in the caecum in 52 patients (25.0%), the ascending colon in 114 (54.8%), and the right side of the transverse colon in 42 (20.2%). The main feeding artery was the ICA in 130 patients (62.5%), the RCA in 27 (13.0%), and the MCA in 51 (24.5%). The RCA was recognized intraoperatively in 37.5% of cases and absent in the remaining 62.5%. Pathologic lymph node metastasis was not found in 126 patients (60.6%), and 57 (27.4%) had N1 disease and 25 (12.0%) had N2 disease. No evidence of distant metastasis was found on preoperative imaging or intraoperative examination in any patient. R0 resection was achieved in 207 cases (99.5%); in one case (0.5%), R1 resection of the radial margin of the primary tumor was performed.

3.2 | Surgical outcomes

The surgical outcomes are shown in Table 2. Open surgery was performed in 47 cases (22.6%) and laparoscopic surgery in 161 (77.4%). The surgical procedures performed were ileocaecal resection ($n = 18$; 8.7%), right hemicolectomy ($n = 172$; 82.7%), extended right hemicolectomy ($n = 17$; 8.2%), and partial resection of the transverse colon ($n = 1$; 0.5%). The median operation time was

TABLE 1 Patient characteristics.

Age, years	
Median (range)	70 (23–89)
Sex	
Male	90 (43.3%)
Female	118 (56.7%)
Tumor location	
Caecum	52 (25.0%)
Ascending colon	114 (54.8%)
Transverse colon	42 (20.2%)
Feeding artery	
Ileocolic	130 (62.5%)
Right colic	27 (13.0%)
Middle colic	51 (24.5%)
Right colic artery	
Absent	130 (62.5%)
Present	78 (37.5%)
Pathological T status	
T0/1	13 (6.3%)
T2	31 (14.9%)
T3	122 (58.7%)
T4	42 (20.2%)
Pathological N status	
N0	126 (60.6%)
N1	57 (27.4%)
N2	25 (12.0%)
Final M status	
M0	208 (100.0%)
M1	0 (0.0%)
Margin status	
R0 resection	207 (99.5%)
R1 resection	1 (0.5%)
R2 resection	0

TABLE 2 Surgical outcomes.

Surgical approach	
Open	47 (22.6%)
Laparoscopic	161 (77.4%)
Surgery	
Ileocaecal resection	18 (8.7%)
Right hemicolectomy	172 (82.7%)
Extended right hemicolectomy	17 (8.2%)
Partial resection of transverse colon	1 (0.5%)
Operation time, min (median, range)	213 (102–447)
Blood loss, ml (median, range)	20 (0–513)
Retrieved nodes, *n* (median, range)	38 (12–107)
Proximal margin, cm (median, range)	14 (6–55)
Distal margin, cm (median, range)	15 (2–41)
Postoperative complication	42 (20.2%)
Ileus	14 (6.7%)
Wound infection	8 (3.8%)
Abdominal infection	6 (2.9%)
Chylous ascites	5 (2.4%)
Hemorrhage	2 (1.0%)
Anastomotic leak	1 (0.5%)
Femoral neuropathy	1 (0.5%)
Urinary retention	1 (0.5%)
Gastric ulcer	1 (0.5%)
Pneumonitis	1 (0.5%)
Cardiac disorders	1 (0.5%)
Eczema	1 (0.5%)
Mortality	0 (0.0%)

213 (range, 102–447) min, the median blood loss was 20 (range, 0–513) ml, and the median number of harvested lymph nodes was 38 (range, 12–107). The median length of the proximal margin was 14 (range, 6–55) cm and that of the distal margin was 15 (range, 2–41) cm. Postoperative complications of any grade were recorded in 42 patients. The most common complication was ileus (6.7%), followed by wound infection (2.9%), abdominal infection (2.9%), chylous ascites (2.4%), and hemorrhage (1.0%). The mortality rate was 0%.

3.3 | Metastasis rates at each lymph node station and pathway along blood vessels

Figure 2 shows the frequency of lymph node metastasis according to location of the main tumor. Among all patients, six (2.9%) had metastasis in the main lymph nodes. In patients with caecal cancer, the overall frequency of metastasis to the main lymph nodes was 3.8%, with the same frequency around the SMA and SMV. Except for the lymph nodes along the ICA, nodes at station 211 were involved in 4.8% of cases of caecal cancer, but no metastasis to other lymph nodes was observed. In patients with cancer in the ascending colon, the only main lymph nodes with metastasis were at station 223V (in 1.1% of cases). However, paracolic and intermediate lymph node metastases were found around the ICA, RCA, and MCA. In patients with transverse colon cancer, metastasis to the main lymph nodes was found at stations 213 and 223; around the SMA, 6.7% of nodes at station 213A and 2.5% of those at station 223A showed metastasis; 2.4% of metastases around the ICA were found at station 201.

Table 3 shows the rate of lymph node metastasis for each tumor site according to the main feeding artery in all patients. To calculate the rates in the table, the denominator was the number of cases in which a given station was dissected, and the numerator was the number of those cases in which metastasis was detected. Among six patients with metastasis in the main lymph nodes, the mean number of metastatic lymph nodes was 12 (range 5–32), and all of these

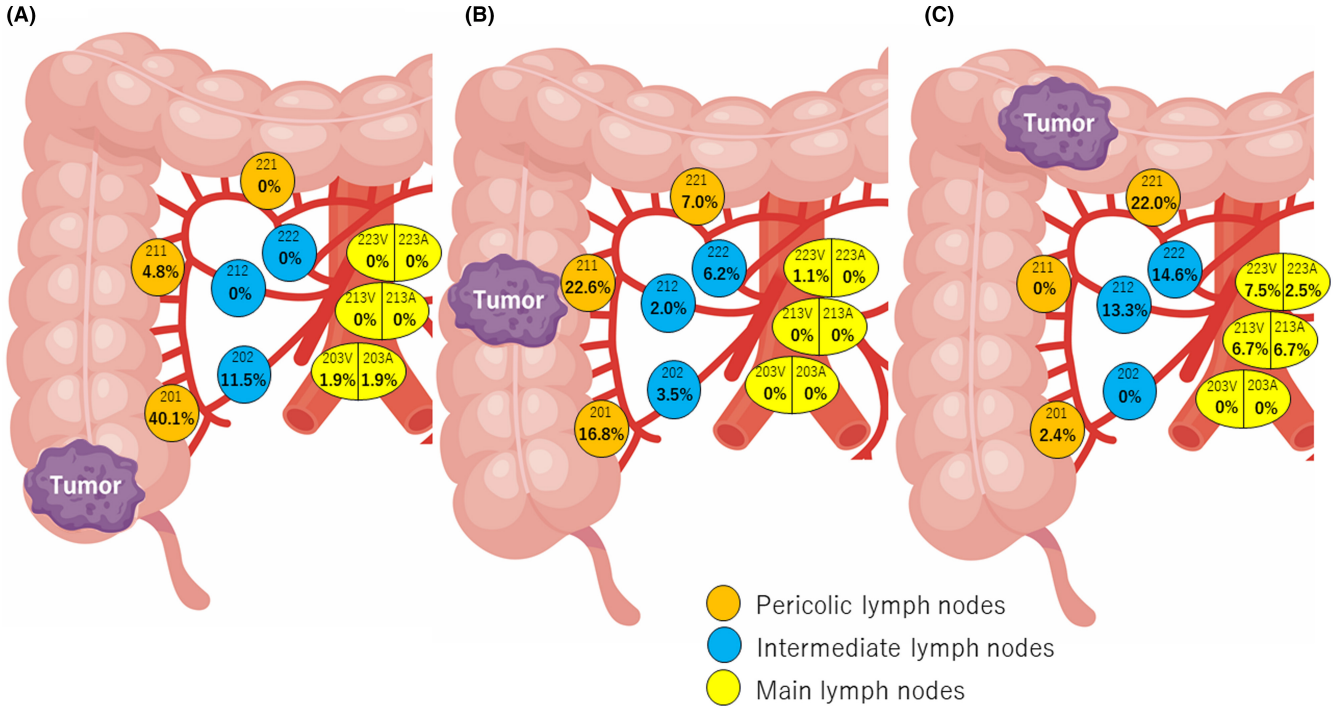

FIGURE 2 Lymph node metastasis rate in (A) 52 patients with caecal cancer, (B) 114 patients with ascending colon cancer, and (C) 42 patients with transverse colon cancer.

TABLE 3 Metastases for each lymph node station according to main feeding artery.

			Main feeding artery		
	Node station	Overall	ICA	RCA	MCA
Pericolic lymph nodes	201	24.4% (50/205)	35.4% (46/130)	11.5% (3/26)	2.0% (1/49)
	211	16.0% (15/94)	14.6% (7/48)	19.2% (5/26)	15.0% (3/20)
	221	9.3% (16/172)	4.1% (4/97)	8.3% (2/24)	19.6% (10/51)
Intermediate lymph nodes	202	4.9% (10/205)	6.9% (9/130)	3.8% (1/26)	0% (0/49)
	212	3.8% (3/79)	2.5% (1/40)	0% (0/26)	15.4% (2/13)
	222	7.2% (12/167)	1.1% (1/92)	12.5% (3/24)	15.7% (8/51)
Main lymph nodes	**203**	1.0% (2/205)	1.5% (2/130)	0% (0/26)	0% (0/49)
	203V	0.5% (1/205)	0.8% (1/130)	0% (0/26)	0% (0/49)
	203A	0.5% (1/205)	0.8% (1/130)	0% (0/26)	0% (0/49)
	213	1.3% (1/77)	0% (0/38)	0% (0/26)	7.7% (1/13)
	213V	1.3% (1/77)	0% (0/38)	0% (0/26)	7.7% (1/13)
	213A	1.3% (1/77)	0% (0/38)	0% (0/26)	7.7% (1/13)
	223	2.6% (4/156)	0% (0/84)	4.8% (1/21)	5.9% (3/51)
	223V	2.6% (4/156)	0% (0/84)	4.8% (1/21)	5.9% (3/51)
	223A	0.6% (1/156)	0% (0/84)	0% (0/21)	2.0% (1/51)

Abbreviations: ICA, ileocolic artery; MCA, middle colic artery; RCA, right colic artery.

patients had metastases in the pericolic and/or intermediate lymph nodes. Of these six patients, four had metastases in only the main lymph node around the SMV. The remaining two patients had metastases around the SMA: 1 with extensive lymph node metastases around the SMA and SMV, and the other with no lymph node metastases around the SMV but numerous metastases in the mesenteric lymph nodes.

There were 189 patients who underwent right hemicolectomy and extended right hemicolectomy in whom the status of lymph node metastasis could be fully evaluated. In 13 of these patients with a T0/T1 tumor, there was one case (7.7%) each of metastasis in the pericolic and intermediate lymph nodes, but no metastasis in the main lymph nodes. Table 4 shows the rate of lymph node metastasis according to tumor depth from T2 to T4 for each tumor location.

TABLE 4 Metastasis rates for each lymph node station according to the main feeding arteries for the patients with right hemicolectomy or extended right hemicolectomy.

		pT2 tumor				pT3 tumor				pT4 tumor			
			Tumor location				Tumor location				Tumor location		
	Node Station	Overall ($n=27$)	Cecum ($n=8$)	ASCENDING COLON ($n=12$)	Transverse colon ($n=7$)	Overall ($n=111$)	Cecum ($n=18$)	Ascending colon ($n=68$)	Transverse colon ($n=25$)	Overall ($n=38$)	Cecum ($n=11$)	Ascending colon ($n=22$)	Transverse colon ($n=5$)
Pericolic lymph nodes	201	3 (11.1%)	2 (25.0%)	1 (8.3%)	0	22 (19.8%)	6 (33.3%)	16 (23.5%)	0	18 (47.4%)	7 (63.7%)	10 (45.5%)	1 (20.0%)
	211	1 (3.7%)	1 (12.5%)	0	0	10 (9.0%)	0	10 (14.7%)	0	4 (10.5%)	0	4 (18.2%)	0
	221	2 (7.4%)	0	1 (8.3%)	1 (14.3%)	8 (7.2%)	0	3 (4.4%)	5 (20.0%)	6 (15.8%)	0	3 (13.6%)	3 (60.0%)
Intermediate lymph nodes	202	1 (3.7%)	1 (12.5%)	0	0	4 (3.6%)	1 (5.6%)	3 (4.4%)	0	4 (10.5%)	3 (27.3%)	1 (4.5%)	0
	212	1 (3.7%)	0	0	1 (14.3%)	2 (1.8%)	0	1 (1.5%)	1 (4.0%)	0	0	0	0
	222	1 (3.7%)	0	0	1 (14.3%)	4 (3.6%)	0	3 (4.4%)	1 (4.0%)	6 (15.8%)	0	2 (9.0%)	4 (80.0%)
Main lymph nodes	203	0	0	0	0	0	0	0	0	1 (2.6%)	1 (9.1%)	0	0
	203V	0	0	0	0	0	0	0	0	0	0	0	0
	203A	0	0	0	0	0	0	0	0	1 (2.6%)	1 (9.1%)	0	0
	213	1 (3.7%)	0	0	1 (14.3%)	0	0	0	0	0	0	0	0
	213V	1 (3.7%)	0	0	1 (14.3%)	0	0	0	0	0	0	0	0
	213A	1 (3.7%)	0	0	1 (14.3%)	0	0	0	0	0	0	0	0
	223	1 (3.7%)	0	0	1 (14.3%)	1 (0.9%)	0	0	1 (4.0%)	2 (5.3%)	0	1 (4.5%)	1 (20.0%)
	223V	1 (3.7%)	0	0	1 (14.3%)	1 (0.9%)	0	0	1 (4.0%)	2 (5.3%)	0	1 (4.5%)	1 (20.0%)
	223A	1 (3.7%)	0	0	1 (14.3%)	0	0	0	0	0	0	0	0

TABLE 5 Pathway of lymph node metastasis along arteries.

	Lymph node metastasis		
	Along one artery	Along two arteries	*p*-Value
Tumor location			
Caecum	20 (95.2%)	1 (4.8%)	<0.01
Ascending colon	29 (60.4%)	19 (39.6%)	
Transverse colon	9 (69.2%)	4 (30.8%)	
Feeding artery			
Ileocolic artery	44 (83.0%)	9 (17.0%)	0.01
Right colic artery	4 (33.33%)	8 (66.7%)	
Middle colic artery	10 (58.8%)	7 (41.2%)	

There was one case (3.7%) of metastasis to a main lymph node in patients with a T2 tumor, but this patient had metastases in all of the 213A, 213V, 223A, and 223V regions. Among patients with T3 tumors, there was only one case (0.9%) with metastasis to a main lymph node (223V). Three patients (7.9%) with T4 tumors had main lymph node metastases: one with a caecal lesion at 203A and two with a transverse colon lesion at 223V. Among 189 cases, there were five cases (2.6%) with metastasis in the intermediate lymph nodes despite the absence of metastasis in the pericolic lymph nodes.

Table 5 shows the number of regions that were found to be metastatic according to tumor location and the main feeding artery among the cases that had lymph node metastasis. Lymph node metastasis involving two of the above three arteries was detected in only 4.8% of patients with caecal cancer but was found in 39.6% of patients with cancer of the ascending colon and 30.8% of those with transverse colon cancer ($p < 0.01$). Lymph node metastasis along two arteries was present in 17% of tumors with the ICA as the main feeding artery, as well as in 66.7% with the RCA and 41.2% with the MCA as the main feeding artery ($p = 0.01$).

4 | DISCUSSION

Lymphatic spread in the colon typically follows the feeding artery to the central lymph node.[11] CME as performed in Western countries and D3 lymph node dissection as performed in Japan are considered similar surgical procedures for dissection of the central lymph nodes, and there are many reports on their surgical outcomes.[5,12,13] The important common goal of CVL and D3 lymph node dissection is to ensure that metastatic lymph nodes are removed. However, there have been only a few small studies of the distribution of lymph node metastasis around the SMA in right-sided colon cancer, and the extent of lymph node dissection has been controversial.[14,15] To the best of our knowledge, this is the first prospective study that has attempted to classify metastases to the main lymph nodes in detail. Overall, we found that only a small number of cases (2.9%) had metastasis to the main lymph nodes. However, in patients with transverse colon cancer, 6.7% had metastasis to station 213V and 7.5% to station 223V around the SMV and 6.7% had metastasis to station 213A and 2.5% to station 223A around the SMA. On the other hand, the rate of main lymph node metastasis was 1.9% to stations 203V and 203A in caecal cancer and 1.1% to station 223V in ascending colon cancer. In this study, only 2.6% of the patients who underwent right hemicolectomy or extended right hemicolectomy had metastasis in the intermediate lymph nodes without metastasis in the pericolic lymph nodes. No patient had metastasis in the main lymph nodes despite the absence of metastasis in the intermediate lymph node. Therefore, it may not be necessary to dissect the main lymph nodes out of concern about missing metastasis. In addition, in the case with metastasis to 203A, numerous lymph node metastases were found in the mesentery. These findings suggest that routine prophylactic extended lymphadenectomy around the SMA is not necessary in caecum and ascending colon cancer but is appropriate when many metastatic lymph nodes are found.

The high incidence of metastases to the main lymph nodes, including those around the SMA, in patients with transverse colon cancer may reflect anatomical variation; however, the incidence was low in patients with cancer of the caecum or ascending colon. Surgery is more difficult to perform in the transverse colon, which is located between the hepatic flexure and the splenic flexure, than in the area near the ileum because of the complex anatomy of the vascular and lymphatic vessels involved.[16,17] In the present study, there was considerable variation in vascular anatomy, and an RCA was found in only 37.5% of cases. A significant correlation between distribution of lymph nodes and the crossing pattern of the colic arteries was found in a post-mortem study.[18] Another autopsy study showed many lymph nodes and short lymphatic vessels arising from the MCA and connecting to lymph nodes in front of the SMV and SMA whereas the lymphatic vessels running from the areas of the ICA and ileocolic vein into the SMA were relatively simple.[19] This may reflect the fact that tumors with the MCA as a main feeding artery also have more main lymph node metastases than tumors fed by the RCA or ICA. Another histological and electron microscopic study has shown that the transverse colon, unlike the ascending colon, has no submesocolic fascia and tends to have lymphatic flow spread over a wider area.[20] This may be one of the reasons for the more extensive lymph node metastasis in transverse colon cancer. When performing CVL or D3 dissection for right-sided colon cancer, it may not be advisable to determine the extent of dissection uniformly without considering the tumor location. After confirming the location of the tumor and the vascular anatomy, it may even be necessary to dissect around the SMA in cases of transverse colon cancer or when the feeding artery is the MCA.

Both central and pericolic lymph node metastases should be considered in lymph node dissection. Studies in Japan have shown that pericolic lymphatic spread >10 cm beyond the tumor occurs in only 1%–4% of right-sided colon cancers.[9,10] Therefore, a Japanese surgeon must achieve a minimum bowel resection margin of 10 cm. However, longer lengths of intestinal tract are often resected by CME in Europe than by D3 dissection in Japan.[21] In our study, 17% of tumors fed by the ICA showed metastasis, mainly to other feeding arteries, whereas 66.7% of those fed by the RCA and 41.2% of those fed by the MCA showed metastasis to other feeding arteries. The distance between the main tumor and the pericolic metastatic lymph nodes was not measured in this study. For the bowel

resection margin, consideration should be given to both apical and pericolic lymph node metastasis data. Thus, the length of the bowel resection margin cannot be determined in this study.

There have been reports on the long-term outcomes in Japanese patients who have undergone D3 dissection.[22,23] However, in Japan, D3 dissection of right-sided colon cancer has traditionally been limited to the area around the SMV. The importance of dissecting pathologically positive main lymph nodes, including when D3 dissection is performed around the SMA, is controversial in terms of survival and recurrence.[24] It has been reported that the prognosis of right-sided colon cancer improves as the number of retrieved lymph nodes increases, but the prognostic impact of dissecting lymph nodes at a specific anatomical location is unclear.[25–27] The improved survival achieved by extended dissection in our study may be limited considering that only a few cases had metastasis in the lymph nodes around the SMA. However, survival may have been improved in some of our patients, and we plan to analyze the relationship between the extent of lymph node metastasis and long-term prognosis after completion of the 5-year follow-up period.

Studies of CME have reported postoperative complication rates in the range of 5.7%–19.7%.[3,28,29] Two recently published randomized controlled studies, one conducted in China[30] and the other in Italy,[31] have shown that CME for right-sided colon cancer does not have increased postoperative complications compared with less extensive surgery. Complication rates vary widely according to ethnicity. A large-scale Chinese study recently reported a complication rate of 19.8%, which is very similar to the rate of 20.2% in our present study, in which extended dissection was performed around the SMA.[13] Therefore, the risk of complication was not increased with extended lymph node dissection compared with other studies conducted in Asians. However, 2.4% of the patients in our study developed ascites, a finding that has not been reported previously and suggests that lymphatic leakage may be caused by resection of the lymphatic vessels around the SMA. Extended lymphadenectomy should be performed only in patients who will truly benefit in order to reduce the occurrence of such complications.

This study demonstrates that there is variability in lymph node metastasis in right-sided colon cancer, and it is desirable to be able to confirm the extent of metastasis intraoperatively in individual patients. It has been reported that indocyanine green (ICG) fluorescence imaging during surgery for right-sided colon cancer could identify the optimal extent of lymph node dissection; visualization of lymphatic flow using ICG may allow for more personalized lymph node dissection.[32,33] Lymphatic flow and lymph node metastasis were not assessed by ICG in this study. However, it is difficult to determine the extent of lymph node dissection needed based on ICG findings alone because the lymph nodes visualized by ICG do not accurately correspond to pathologic lymph node metastases.[34] Use of this technique in the future, especially for right-sided transverse colon cancer, where the vascular and lymphatic anatomy is complex, may clarify which lymphatic pathways should be dissected along from the tumor and in which direction.

This study has several limitations. First, with a total of 208 cases and only a 2.9% rate of metastasis to the main lymph node, the number of lymph node metastases to the SMA and the SMV was small. Moreover, the caecum, ascending colon, and transverse colon subgroups were small. Further studies of metastasis to the main lymph nodes should include larger populations. Second, lymph nodes in areas other than the mesentery, such as the gastroepiploic and peripancreatic areas, were not dissected. Given that the metastatic status of these lymph nodes is unknown, further imaging studies are needed to determine the likelihood of recurrence in nearby lymph nodes outside of the dissected area. Third, the study did not collect information on preoperative imaging and intraoperative findings because of differences among institutions in lymph node imaging methods and criteria for intraoperative assessment. If it were possible to obtain accurate information on pre- and intraoperative lymph node metastases, it might be helpful in determining the indication for extended lymph node dissection.

In conclusion, the rate of metastasis to main nodes around the SMV and SMA is low in caecal cancer and ascending colon cancer but higher in transverse colon cancer. This result suggests that routine prophylactic extended lymphadenectomy around the SMA is not necessary in the caecum and ascending colon cancer. In contrast, it may be necessary to dissect around the SMA in cases of transverse colon cancer or when the feeding artery is the MCA.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article.

ETHICS STATEMENTS

Approval of the research protocol: The study protocol was approved by the institutional review boards of all participating hospitals.
Informed Consent: All patients provided written informed consent before enrolment.
Registry and the Registration No. of the study/trial: The clinical trial registration number is UMIN000047356.
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