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〔Original Paper〕

Clinical evaluation of para-aortic lymph node dissections for sigmoid colon and rectal cancers

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SUMMARY

This retrospective study evaluated clinical outcome with regard to para-aortic lymph node dissection in patients with sigmoid colon cancer and rectal cancer.

A total of 348 consecutive colorectal cancer patients consisting of 158 patients with sigmoid colon cancer and 190 with rectal cancer were reviewed. There were significant differences in operative blood loss and duration of surgery between conventional and extended lymph node dissection. The incidence of metastasis to inferior mesenteric root nodes (#253) was 1.1% (4/348), and 2.9% (10/348) to para-aortic nodes (#216). The cumulative survival rate of the patients with metastatic #216 nodes was 56% at 12 months, 33% at 18 months, and 0% at 24 months. The outcome of the patients with metastatic para-aortic or inferior mesenteric root nodes was very poor, because they usually had several incurable factors, such as liver or peritoneal metastasis. Male sexual dysfunction is often caused by para-aortic dissection because of sacrificing lumbar splanchnic and hypogastric nerves, and it is very important to avoid extended dissection in patients without metastatic para-aortic or inferior mesenteric root nodes. General rules for the indications for para-aortic dissection are needed, and a regimen of postoperative therapy for patients with metastatic nodes is also needed. Thus a multi-institutional randomized control clinical trial is required to evaluate the actual outcome of extended dissections as a meaning of enabling more effective and more appropriate lymph node dissections for sigmoid colon and rectal cancers.

Key words : colorectal cancer, para-aortic lymph node, lymphadenectomy

Abbreviations : D2, lymph node dissection of group 1 and 2 lymph nodes
D3, lymph node dissection of group 1, 2, and 3 lymph nodes
D4, para-aortic lymphadenectomy (extended lymphadenectomy)

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I. Introduction

D2 dissection for gastric cancer and D3 dissection for colorectal cancer seem to be a standard operative procedure in Japan. There is no gold standard for extended dissections (para-aortic dissection) for gastrointestinal cancers in all institutions. This radical procedure for advanced colorectal cancer has both improved survival and decreased local recurrence, but genitourinary dysfunction following this procedure has proved to be a serious problem.

The aim of this retrospective study was to evaluate the clinical significance of para-aortic lymph node dissection and to clarify the outcome of patients with metastatic para-aortic (#216) or inferior mesenteric root nodes (#253). We also retrospectively analyzed the postoperative outcome and complications in sigmoid colon and rectal cancer patients.

There is no consensus concerning the indications for para-aortic lymphadenectomy or how to deal with patients with metastatic #253 and #216 lymph nodes[1,2].

After reviewing all the sigmoid colon and rectal cancer cases together with the case with metastatic para-aortic or inferior mesenteric root nodes, the indications for para-aortic lymphadenectomy and the actual therapeutic value of extended lymphadenectomy are evaluated.

II. Patients and Methods

We operated on five hundred and seven colorectal cancer patients between July 1992 and February 1997. Among these 507 patients, 348 patients had primary solitary lesions located below the sigmoid colon. There were 155 patients with sigmoid colon tumors and 190 patients had rectal tumors (Rs 59, Ra 58, Rb 73). The general rules in the evaluation of colorectal cancer were performed in accordance with Japanese Classification of Colorectal Carcinoma[2]. The cases were analyzed according to tumor location, pathological findings (Table 1), and macroscopic curability (Table 2).

Table 1. Tumor location and #253, #216 metastasis

	D4 performance rate	#253	#216
Sigmoid (n=158)	48/158 (30.4%)	4 (2.5%)	4 (205%)
Rs (n= 59)	21/ 59 (35.6%)	0 (0%)	0 (0%)
Ra (n= 58)	21/ 58 (36.2%)	0 (0%)	5 (8.6%)
Rb (n= 73)	23/ 73 (31.5%)	0 (0%)	1 (1.4%)
	113/348 (32.5%)	4 (1.1%)	10 (2.9%)

D4 performance rate and #253 and #216 lymph node metastasis rates are shown according to tumor location. The overall D4 performance rate was 32.5% (113/348), and the #253 and #216 lymph node metastasis rate were 1.1% and 2.9%, respectively.

Table 2. Macroscopic curability of patients with metastatic #253 and #216 lymph nodes

		#253 (n=4)	#216 (n=10)
P	P0	2 (50%)	9 (90%)
	P1-3	2 (50%)	1 (10%)
H	H0	3 (75%)	9 (90%)
	H1-3	1 (25%)	1 (10%)
curability	A	1 (25%)	2 (20%)
	B	2 (50%)	4 (40%)
	C	1 (25%)	4 (40%)

The precise operative findings in patients with metastatic #253 and #216 lymph nodes are shown. Long-term disease-free survivors are found in the curability A group.

We also evaluated the duration of surgery, intraoperative blood loss, duration of hospital stay, morbidity rate, etc. The curability of surgical resection is defined as follows. Curability A means "no residual tumors (Cur A)", curability B means "no residual tumors but not evaluable as curability A (Cur B)", and curability C means "definite residual tumors (Cur C)"[2]. No metastatic #253 or #216 lymph nodes were identified

intraoperatively in the macroscopically curative A patients but after the final pathological diagnosis was reported, these patients turned out to have metastases of para-aortic or inferior mesenteric root lymph nodes (microscopically curative B cases). We evaluated patients with metastatic #253 or #216 lymph nodes according to macroscopic curability. Our indications for para-aortic lymphadenectomy (extended dissection) for sigmoid colon and rectal cancer are as follows.

1) Preoperative criteria

Significant enlargement of the lymph nodes along the aorta (#216) or the inferior mesenteric artery (#252, #253)

2) Intraoperative criteria

Metastatic lymph nodes beyond group 1 and 2 lymph nodes.

Our standard procedure for para-aortic lymphadenectomy is dissection of the para-aortic lymph nodes below the inferior mesenteric root (#216 b2 inter and lateral) and extension of the dissection to the median sacral nodes (#270) and to the aortic bifurcation nodes (#280), depending on tumor localization and local spread.

The lumbar splanchnic and hypogastric nerves are usually resected simultaneously. The para-aortic area between the renal vein and inferior mesenteric root (#216 b1) is not dissected for ordinary sigmoid colon and rectal cancer.

The statistical analysis was performed by the x-squared test, and P values less than 0.05 were considered significant.

Ⅲ. Results

The rate of completion of para-aortic dissection was 30.4% (48/158) in sigmoid colon cancer, 35.6% (21/59) in Rs, 36.2% (21/58) in Ra and 31.5% (23/73) in Rb rectal cancer, respectively. The total para-aortic dissection rate was 32.5% (113/348) (Table 1). There was a significant difference in the duration of the operation between the extended dissection and the conventional dissection. The average operating time for extended dissection was 331 min, versus 238 min for conventional dissection ($P<0.01$).

There was also a significant difference in the intraoperative blood loss between the two groups. Average blood loss during extended dissection was 949 g, versus 438 g for conventional dissection ($P<0.01$).

There were no significant differences in duration of postoperative hospital stay and morbidity rate between the two groups.

Only sigmoid colon cancer patients had metastatic #253 lymph nodes. The proportion of patients with metastatic #253 lymph nodes was 2.6% (4/158) of the sigmoid colon cancer patients and 1.1% (4/348) of all cases.

The proportion of metastatic #216 lymph nodes was 2.6% (4/158) of the sigmoid colon cancer patients, and 0% (0/59) of those with Rs lesions, 8.6% (5/58) of those with Ra lesions, 1.4% (1/73) of those with Rb lesions. The total proportion of patients with metastatic #216 lymph nodes was 2.9% (10/348) (Table 1).

With regard to macroscopic curability, there were great differences in outcome between the macroscopically curative A patients and the B and C patients.

The numbers of patients with metastatic #253 lymph nodes that were macroscopic curability A, B, and C were 1, 2 and 1, respectively. The reasons for curability B and C were peritoneal dissemination in 2 patients and liver metastasis in 1 patient.

The numbers of macroscopic curability A, B, and C patients with metastatic #216 lymph node were 2, 4, and 4, respectively.

Table 3. #253 Patients with metastatic

Location	Preop. N	Intraop. N	Path.	Met. rate	#253 met	Recurrence	Survival
1. Sigmoid	N1	N3	mod.	7/56	1/6	+	dead
2. Sigmoid	N2	N2	mod.	3/17	1/3	+	alive
3. Sigmoid	N0	N2	mod.	6/36	1/9	+	alive
4. Sigmoid	N0	N2	mod.	4/23	1/5	−	alive

Patients with metastatic #253 lymph nodes are shown. Patient No.4, who was considered to be macroscopically curative A, is the only disease-free survivor.

Table 4. #216 Patients with metastatic

Location	Preop. N	Intraop. N	Path.	Met. rate	#253 met	Recurrence	Survival
1. Sigmoid	N2	N4	mod.	8/12	2/ 4	+	dead
2. Sigmoid	N4	N4	mod.	24/34	13/ 5	+	dead
3. Sigmoid	N3	N4	mod.	22/93	10/29	+	alive
4. Sigmoid	N4	N4	por.	7/42	4/14	+	dead
5. Ra	N4	N4	mod.	45/84	33/44	+	dead
6. Ra	N2	N1	mod.	15/45	1/ 3	−	alive
7. Ra	N4	N4	por.	19/21	5/ 5	+	dead
8. Ra	N2	N4	por.	6/34	5/10	+	alive
9. Ra	N4	N4	por.	44/74	5/19	+	dead
10. Rb	N0	N3	por.	11/94	1/17	−	dead

Patients with metastatic #216 lymph nodes are shown. Only one patient who was macroscopically curative A was a long-term disease-free survivor.

The reasons for curability B and C were macroscopic #216 positive node in 5 patients, positive surgical margins in 2 patients and liver metastasis in 1 patient.

A detailed review of all patients with metastatic #253 lypmph nodes revealed only one disease-free survivor, the patient were convinced of having undergone a curative A resection intraoperatively. The other three patients had hepatic or peritoneal incurable factors (Table 3).

Similarly, a review of all 10 patients with metastatic #216 lymph nodes revealed only one disease-free survivor (Table 4).

These two disease-free survivors seemed not to have metastases to #253 or #216 lymph nodes intraoperatively based on macroscopic diagnosis, and only the final pathological diagnosis revealed them to have #253 or #216 lymph nodes metastasis.

All of the other patients were thought to have metastasis to #253 or #216 lymph nodes intraoperatively.

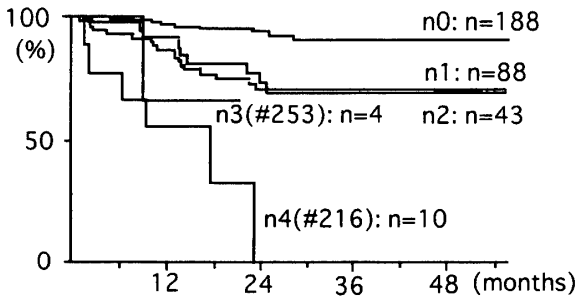

Fig. 1. Overall survival curves

Clinicopathological analysis of the patients with metastatic #216 lymph nodes revealed significant differences in histological type, vascular invasion (ly, v) and depth of invasion, but not in preoperative serum CEA level and tumor size.

The outcome of the patients with metastatic #253 lymph nodes was death in one patient and survival with recurrence in 2 patients, and there was 1 disease-free survivor (Fig. 1). The outcome of the patients

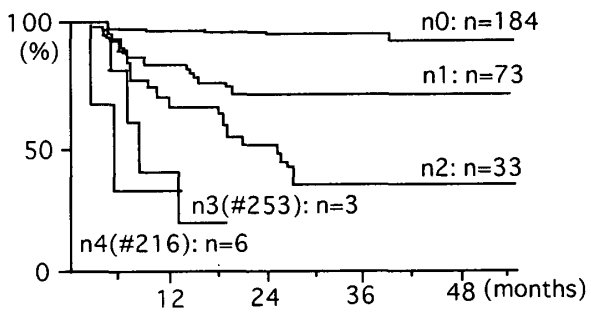

Fig. 2. Disease-free survival curves (curability A, B)

with metastatic # 216 lymph nodes was death in 7 patients and survival with recurrence in 2 patients, and there was only one disease-free survivor. The cumulative survival rates st 12, 18, and 24 months were 56%, 33%, and 0% respectively (Fig. 2).

IV. Discussion

According to the multi-institutional questionnaire study[3], the incidence of metastasis to #253 lymph nodes is 2.6% in the sigmoid colon cancer and 2.3% in rectal cancer. The incidence of metastasis to #216 lymph nodes is 2.1% in the sigmoid colon cancer and 1.9% in rectal cancer.

In our current analysis, the incidence of metastasis to #253 lymph nodes was 2.5% in the sigmoid colon cancer and 0% in rectal cancer, and the incidence of metastasis to #216 lymph nodes was 2.5% and 2.6%, respectively. In general, the outcome of patients with metastatic # 253 or # 216 lymph nodes is very poor. Only one of four patients with metastatic #253 lymph nodes (25%) and two out of ten patients with metastatic #216 lymph nodes (20%) had a curative resection macroscopically.

There are many papers have reported the benefit of para-aortic dissections[3-6]. While others have shown no statistical significance between the extended and conventional operation[7-9]. Many papers reported that there were no significant differences between operative procedures in duration of operation time, blood loss, morbidity, or mortality, but our present analysis revealed significant differences in operating time and blood loss.

According to all of the articles ever reported, the outcome of patients with metastatic #253 lymph nodes is just as poor as that of patients with metastatic #216 lymph nodes[10,11]. Patients with metastatic #253 or #216 lymph nodes should be treated with the same intensity as a very high risk group for recurrence. The average 5-year survival rate has been 10% to 20% and has never exceeded 20%. None of the patients in our analysis survived over two years.

The data in this study are derived from 1992 to 1997 and our present attitude toward extended dissection is rather negative. Using every modality, such as intraoperative pathological diagnosis by frozen sections, we have been trying to avoid unnecessary para-aortic dissection. Para-aortic dissection usually involves sacrificing the autonomic nerve (sympathetic inferior hypogastric nerve), and this procedure results in a severe sexual dysfunction (especially ejaculatory dysfunction). The degree of dysfunction is even mild compared to the injury to the pelvic nerve plexus (parasympathetic pelvic nerve) that occurs during the lateral node dissection for lower rectal cancer. If genitourinary dysfunction occurs after lateral lymph node dissection, strain voiding or self-catheterization is necessary for a long time, and male sexual function does not recover. Thus informed consent must be obtained after explaining the advantage and drawbacks of para-aortic and lateral lymph node dissection to patients.

Since many patients with metastatic #253 or #216 lymph nodes have multiple incurable

factors, we cannot easily conclude that para-aortic lymph node metastasis is of pure prognostic value. The presence of #253 or #216 lymph node metastasis may signal the start of occult systemic disease.

The indications for extended dissection are not clear yet, and they differ in every institution. Preoperative imaging diagnosis and intraoperative exploration to detect lymph nodes metastasis are not very accurate, and these modalities are of no benefit in selecting the operative procedure. Para-aortic dissection in patients with overtly metastatic #253 and #216 lymph nodes is somewhat ineffective, and the outcome of these patients is very poor. Disease-free survivors are only found when few #253 or #216 lymph nodes are involved and in macroscopic curative A cases. The incidence of #253 and #216 lymph node metastasis is between 2.0% and 3.0%. In any event, to avoid these functional complications, it is necessary to decide preoperatively and intraoperatively whether the patient will benefit from extended radical dissection.

Therefore, multi-institutional randomized, controlled trials of para-aortic extended lymph node dissection and conventional lymph node dissection are needed to confirm the standard criteria, i.e., in which cases and to what extent extended dissection should be performed, to reevaluate the real prognostic meaning of para-aortic dissection[12]. It can be concluded that patients with metastatic #253 and #216 lymph nodes are a very high risk group for recurrence and in a state of impending systemic disseminated disease, and thus close follow-up and intensive postoperative treatment, such as adjuvant chemotherapy, is needed to reduce recurrence.

要　旨

S状結腸，直腸癌に対する大動脈周囲リンパ節郭清の適応とその臨床的意義に関しては未だに明確にされていない点も多い。今回 retrospective に S 状結腸，直腸癌症例を対象とし，大動脈周囲リンパ節郭清と253，216陽性症例につき検討を行った。対象は最近4年7ケ月間に手術を施行した大腸癌症例507例のうち病変がS状結腸以下の症例348例とした。S状結腸158例と直腸190例である。大動脈周囲リンパ節郭清（以下D4）の適応はこの時期は，①術前に大動脈周囲や主幹動脈にリンパ節が指摘されている症例，②術中にN2以上の転移があると判断された症例としている。D4の施行率であるが全体では32.5%（113/348）であった。D4施行群と非施行群（以下D3以下）を比較すると手術時間（D4 331min vs D3以下238 min），出血量（D4 949g vs D3以下438g）の両群で有意差を認めた。次に大動脈周囲転移陽性例についてであるが，253陽性症例はS/Cに2.6%（4/158）にのみ認められ直腸にはみられなかった。216陽性症例はS/Cで2.6%（4/158），Rsで0%（0/59），Raで8.6%（5/58），Rbで1.4%（1/73）であり，全体では2.9%（10/348）であった。根治度でみると253陽性症例では根治度A，B，Cがそれぞれ1例，2例，1例であり，腹膜播種2例と肝転移1例が根治度B，Cの原因となっていた。一方216陽性症例では根治度A，B，Cが3例，3例，4例であり，根治度B，Cの原因として残存216が4例，ewが2例，肝転移が1例であった。予後についてであるが，253陽性症例では再発死亡1，再発生存2，無再発生存1である。216陽性症例では死亡7，再発生存2，無再発生存1であり，累積生存率は12，18，24ケ月でそれぞれ56%，33%，0%であった。今後術前大動脈周囲リンパ節転移診断の向上および危険群の抽出を行い効率的なD4郭清を行う必要があり，再発危険群でもあり術後の強力な補助療法も必要と考えられた。

References

1) Leggeri A, Roseano M, Balani A, Turoldo A. Lumbo-aortic and iliac lymphadenectomy: what is the role today? Dis Colon Rectum 1994; 37: 54-61.
2) Japanese Society for Cancer of the Colon and Rectum. Japanese Classification of Colorectal Carcinoma. First English Edition, 1997
3) Masaki T, Muto T, Yasutomi M. Clinicopathological characteristics of sigmoid colon and rectal cancers with central node involvement－multi institutional questionnaire study－. J Jpn Soc Coloproctol 1997; 50: 318-330.
4) Enker WE, Heilweil ML, Hertz REL, Pilipshen SJ, Stearns, Jr MW, Sternberg SS, Janov AJ. En bloc pelvic lymphadenectomy and sphincter preservation in the surgical management of rectal cancer. Ann Surg 1986; 203: 426-33.

5) Sterns MW, Deddish MR. Five year results of abdominopelvic lymph node dissection for carcinoma of the rectum. Dis Colon Rectum 1959; 2: 169-72.
6) Koyama Y, Moriya Y, Hojo K. Effect of extended systematic lymphadenectomy for adenocarcinoma of the rectum—significant improvement of survival rate and decrease of local recurrence. Jpn J Clin Oncol 1984; 14: 623-32.
7) Hojo K, Sawada T, Moriya Y. An analysis of survival and voiding, sexual function after wide ileopelvic lymphadenectomy in patients with carcinoma of the rectum, compared with conventional lymphadenectomy. Dis Colon Rectum 1989; 32: 128-33.
8) Grinnell RS. Results of ligation of inferior mesenteric artery at the aorta in resection of carcinoma of the descending and sigmoid colon and rectum. SGO 1965; 120: 1031-6.
9) Glass RE, Ritchie JK, Thompson HR, Mann CV. The results of surgical treatment of cancer of the rectum by radical resection and extended abdominoiliac lymphadenectomy. Br J Surg 1985; 72: 599-601.
10) Deddish MR. Surgical procedures for carcinoma of the left colon and rectum, with five-year end results following abdominopelvic dissection of lymph nodes. Am J Surg 1960; 99: 188-91.
11) Nagao J, Sumiyama Y. Para-aortic lymphadenectomy for advanced left colon cancer. Jpn J Gastroenterol Surg 1993; 26: 1246-50.
12) Nakagawa H, Kikkawa N, Yagyu T, Mishima H, Fukuda K, Shinn E, Hasuike Y, Kobayashi K. Study of para-aortic lymph node metastases of left side colon and rectal cancer. Jpn J Gastroenterol Surg 1996; 29: 2122-6.