TABLE 3 Univariate analysis of the clinicopathologic factors for peritoneal recurrence-free and cancer-specific survival in patients with stage II or III tumors ($N = 36$)

	No. of patients ($N = 36$)	Peritoneal recurrence-free 5-year survival	*P* value	Cancer-specific 5-year survival	*P* value
Age (years)					
<60	13	82.5	0.6127	53.8	0.5939
≥60	23	68.1		46.7	
Gender					
Male	21	81.4	0.1309	45.1	0.6552
Female	15	63.6		55.8	
Tumor size (cm)					
<5	13	81.5	0.2584	59.2	0.3185
≥5	23	67.8		43.2	
Tumor site					
Colon	19	75.7	0.8962	47.7	0.8196
Rectum	17	70.0		51.3	
Histologic grade					
Well	10	90.0	0.0258	90.0	0.0045
Others	26	59.5		31.7	
Depth of invasion					
T3	16	80.0	0.7804	73.1	0.0341
T4	20	65.3		31.7	
Regional lymph nodes					
N (−)	6	80.0	0.9614	80.0	0.1137
N (+)	30	72.2		43.1	
Lymphatic invasion					
No	7	80.0	0.2832	83.3	0.0572
Yes	29	65.5		41.0	
Venous invasion					
No	8	87.5	0.3778	80.0	0.0957
Yes	28	69.3		42.9	
Adjuvant chemotherapy					
No	8	70.0	0.5305	68.6	0.2399
Yes	28	74.3		44.6	
Intraperitoneal chemotherapy					
No	12	45.5	0.0047	16.7	0.0037
Yes	24	85.6		67.5	

Well well-differentiated adenocarcinoma, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma

cells in 3–28% of patients with CRC.[9,31,32] This wide range may be due to differences in patient populations, lavage cytology methods, or the criteria used for assessment. In the present study, only 52 patients (3.1%) were found to be positive for intraperitoneal cancer cells on cytologic evaluation. This positive rate is low because the strict definition used for identification of cancer cells excluded suspicious or borderline malignant cells. Some authors have used immunohistochemistry or reverse transcriptase-polymerase chain reaction (RT-PCR) to detect disseminated tumor cells in peritoneal lavage fluid.[33–37] In these studies, the detection rates of free cancer cells were comparatively high, ranging from 12% to 47%. Although immunohistochemical and RT-PCR techniques are more sensitive than conventional cytology in detecting cancer cells, their significance for survival is unclear. However, conventional cytology is a practical means of detecting cancer cells because it is a universal and inexpensive method that can be easily performed at any institution worldwide.[38]

Peritoneal recurrence is relatively rare. In this study, one thousand six hundred and twenty-five patients with stage I, II, III, or IV tumors showed negative cytology. In addition, one thousand five hundred and twenty of 1,625 patients had no clinically evident peritoneal dissemination. Overall, peritoneal recurrence was observed in 23 of 1520 patients (1.5%). In our previous study, peritoneal recurrence was observed in only 3.2% of patients (12 of 374 patients with stage II or III tumors). However, peritoneal recurrence was seen in 5 of 15 patients (33.3%) with positive peritoneal cytology and in 7 of 359 patients (1.9%) with negative peritoneal cytology.[12] Similarly, Yamamoto et al. reported the peritoneal recurrence rate to be 4.2% (8 of 189 patients with stage II or III tumors). Peritoneal recurrence was seen in 4 of 11 patients (36.4%) with positive peritoneal cytology and in 4 of 178 patients (2.2%) with negative peritoneal cytology.[9] As a result, 1 of the predictive factors for peritoneal recurrence may be a positive peritoneal lavage cytology finding.

We retrospectively investigated the significance of IPC with MMC in this study. In all patients, univariate analyses showed the 5-year peritoneal recurrence-free and cancer-specific survival rates to be significantly higher in patients with IPC than in patients without IPC ($P < 0.0005$). In multivariate analyses, IPC remained an independent prognostic factor for peritoneal recurrence-free survival ($P = 0.0274$). In 36 patients with stage II or III tumors, univariate analyses showed that the 5-year peritoneal recurrence-free and cancer-specific survival rates were significantly higher in patients with IPC than in patients without IPC ($P < 0.005$). In stage II or III patients with positive peritoneal lavage cytology, the overall peritoneal recurrence rate was 12.5% (3 of 24 patients) in the IPC (+) group and 50.0% (6 of 12) in the IPC (−) group. The incidence of peritoneal recurrence in the IPC (+) group was significantly lower than that of IPC (−) group ($P = 0.0362$). The histological grade is significantly associated with peritoneal recurrence-free and cancer-specific survival in all patients and in patients with stage II or III tumors. The reason may be that the histological grade has a strong correlation with IPC. Generally, lymph node metastasis is a powerful marker for a poor prognosis.

TABLE 4 Multivariate Cox regression analysis of the peritoneal recurrence-free and cancer-specific survival in all patients ($N = 52$)

Factors	Peritoneal recurrence-free survival			Cancer-specific survival		
	RR	95% CI	*P* value	RR	95% CI	*P* value
Histologic grade (Others:Well)	2.710	0.279–26.316	0.3903	2.062	0.644–6.579	0.2234
Depth of invasion (T4:T3)	–	–	–	1.290	0.556–2.992	0.5528
Regional lymph nodes (N(+):N(−))	–	–	–	1.842	0.518–6.579	0.3542
Lymphatic invasion (Yes:No)	–	–	–	5.435	0.399-71.429	0.2041
Venous invasion (Yes:No)	1.873	2.295–15.385	0.5576	1.570	0.220–11.236	0.6531
Distant metastasis (Yes:No)	–	–	–	5.236	2.320–11.905	<0.0001
Intraperitoneal chemotherapy (No:Yes)	5.319	1.205–23.256	0.0274	2.160	0.877–5.319	0.0938

Well well-differentiated adenocarcinoma, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, *RR* relative risk, *95% CI* 95% confidence interval

TABLE 5 Comparison of patterns of recurrent site in patients with stage II or III tumors ($N = 36$)

	Intraperitoneal chemotherapy (+) ($N = 24$)	Intraperitoneal chemotherapy (−) ($N = 12$)	*P* value
Lung	3	3	0.3781
Liver	1	1	0.9999
Lymph node	1	2	0.2527
Local	1	0	0.9999
Peritoneum	3	6	0.0362

However, in this study, lymph node metastasis was not a prognostic factor for peritoneal recurrence-free and cancer-specific survival in all patients or patients with stage II or III tumors. This is because this study investigated selected patients with positive peritoneal cytology whose prognosis was poor.

The timing of IPC is important. Postoperative adhesion formation is the major concern. In order to allow optimal contact between tumor cells and IP drug, treatment is preferred in the early postoperative period. Sugarbaker et al. performed a prospective randomized trial of intravenous versus IP 5-FU in patients with advanced primary CRC.[18] Although there was no difference in the disease-free or overall survival between the 2 groups, IP 5-FU decreased the incidence of peritoneal carcinomatosis significantly. In our study, IPC prolonged the prognosis; however, adjuvant chemotherapy did not improve the prognosis. One of the reasons may be the chemotherapeutic agents. With respect to adjuvant chemotherapy, further investigation is therefore necessary.

Although the effectiveness of cytoreductive surgery and hyperthermic IPC is clear, the optimum chemotherapeutic agents for IP treatment have not yet been defined. While several drugs have been used for IPC, the most common drugs used in hyperthermic IPC protocols worldwide for patients with colorectal peritoneal carcinomatosis are MMC or oxaliplatin.[22–24,26,27] In a mouse model, IPC with MMC or irinotecan provided a survival benefit compared with intravenous FOLFIRI therapy. Furthermore, combination IP therapy with MMC, panitumumab, and irinotecan was superior to all other agents tested alone or in combination.[39] However, with regard to the combination IPC, further phase I clinical trials will be necessary to integrate into clinical practice.

In conclusion, it appears that IPC with MMC is therefore an effective treatment for the prevention of peritoneal recurrence in CRC patients who had no clinical evidence of peritoneal dissemination and whose status of peritoneal lavage cytology was positive. However, adjuvant chemotherapy was not found to be effective. IPC with MMC is an easy, safe, and feasible treatment. However, the number of cases studied so far evaluated is relatively limited, and they were also investigated at a single institution. Therefore, a prospective trial where patients with positive cytology could be randomized to IPC plus the best systemic therapy versus the best systemic therapy alone is necessary to justify our results.

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Original Article

Adequate Lymph Node Examination Is Essential to Ensure the Prognostic Value of the Lymph Node Ratio in Patients with Stage III Colorectal Cancer

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Abstract

Purpose. This study aimed to assess the prognostic value of the lymph node ratio (LNR), estimated by dividing the number of positive lymph nodes (LNs) by the number of LNs examined, for stage III colorectal cancer in comparison to the new tumor, nodes, and metastasis (TNM) system, and to evaluate the relationship between the number of LNs examined and the prognostic value of the LNR.

Methods. We retrospectively reviewed the clinicopathological data of a cohort of 266 patients with stage III colorectal cancer. We assessed the impact of LNR on the prediction of cancer recurrence in comparison to the TNM system, as well as the prognostic value of LNR in patients with a low LN count.

Results. In multivariate analysis, the LNR was found to be an independent risk factor of cancer recurrence. The application of the LNR, in addition to the new TNM system, was more predictive of survival than the TNM system alone. A prognostic separation by LNR was observed in patients who had an adequate number of LNs examined, but not in patients with a low LN count.

Conclusions. A stronger prognostic separation can be obtained by using the LNR together with the new TNM system. Adequate lymph node examination is important to ensure the prognostic value of LNR in patients with stage III colorectal cancer.

Key words Colorectal cancer · Lymph node ratio · Lymph node examination · TNM 7th edition

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Introduction

The presence of lymph node (LN) metastasis is one of the most important prognostic factors in patients who undergo surgery for colorectal cancer with curative intent. According to the TNM staging system proposed by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), cancer with nodal disease is defined as stage III, and N categories are determined by the number of positive LNs (N1, 1–3; N2, 4 or more).[1] However, recent evidence indicates that the total number of LNs examined is also an important prognostic factor for colorectal cancer outcome, with potential for stage migration depending on the degree to which specimens are examined and the total number of LNs removed.[2] Hence, the N category of the current TNM system, which disregards the number of LNs examined, has been suggested to be a potential limitation to predicting cancer survival.[3,4] The lymph node ratio (LNR), estimated by dividing the number of positive LNs by the number of LNs examined, has recently been proposed as a potentially more accurate prognostic indicator for solid tumors including gastric,[5] breast,[6,7] and pancreatic cancers.[8] Berger et al. first described the LNR as a prognostic factor for colon cancer in a large retrospective study of the Intergroup trial 0089, a study investigating adjuvant chemotherapeutic regimens.[9] To date, several other studies have reported the prognostic significance of the LNR in colorectal cancer.[3,4,9–27] It has also been suggested that the LNR can predict survival more accurately than the number of positive LNs.[3,4,11,13,16,19] Furthermore, the application of the LNR, together with the TNM system, may be more predictive of cancer recurrence and survival.[18,23]

In December 2009, a new TNM grading system (7th edition) revised by the AJCC and UICC was released in which the nodal stage was further divided into

subgroups according to the number of positive LNs in stage III colorectal cancer.[1] Although the current guidelines and new TNM system recommend the excision and evaluation of a minimum of 12 LNs in the tumor specimen to adequately assess the tumor stage, the N category of the new TNM system does not reflect the number of LNs examined or the LNR. The LNR can be easily influenced by the completeness of LN evaluation and the adequacy of surgical resection, and therefore, the real prognostic value of the LNR remains unclear. Two conflicting studies of large populations have been published. Berger et al. found that the LNR was not predictive of disease-free survival (DFS) or overall survival (OS) in patients with 10 or fewer LNs examined,[9] whereas Wang et al. found the LNR to be a significant predictor of outcome even for patients in whom 11 or fewer LNs were examined.[18] Therefore, the prognostic value of the LNR in patients with a low LN count remains controversial.

The aim of this study was to assess the prognostic impact of the LNR for stage III colorectal cancer according to the new TNM staging system (7th edition), and to evaluate the influence of the number of LNs examined on the prognostic value of the LNR in patients with stage III colorectal cancer in a single institution.

Patients and Methods

We retrospectively reviewed 266 patients with stage III colorectal cancer who underwent curative resection from January 1991 to December 2008 in the Department of Surgery of Hiroshima University. Curative resection was defined by pathologically clear margins on the resected specimen, with no evidence of metastatic spread on preoperative computed tomography scans of the chest, abdomen, and pelvis. Patients were identified from a prospective database of all patients undergoing therapy for colorectal cancer. Patients with metastatic disease and inflammatory bowel disease were excluded. The tumor location was categorized as right colon (from the cecum to the distal transverse colon), left colon (splenic flexure colon to rectosigmoid colon), or rectum. All patients underwent standard resection of the colon and rectum with regional lymphadenectomy according to the Japanese General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus, 7th Edition (JGR),[28] and all procedures were performed by colorectal surgeons. Individual demographic and clinicopathological data were collected, including age, sex, tumor location, tumor stage (depth of invasion), nodal stage, tumor histology, tumor size, presence of lymphovascular invasion, preoperative serum carcinoembryonic antigen (CEA) level, administration of adjuvant chemotherapy, disease recurrence, and the survival rate. In addition, the number of LNs examined, number of metastatic LNs, and the LNR were determined for each patient. Receiver operating characteristic (ROC) curve analysis for cancer recurrence was performed to obtain the area under the ROC curve (AUC) and optimal cutoff point of the LNR for predicting cancer recurrence. The optimal cutoff point was defined as the point on the ROC curve nearest to the point where the both sensitivity and specificity were 1.

All specimens were examined as follows. After tumor removal, the excised specimen was opened along the antimesenteric border by the surgeon. The surgeon identified the lymph nodes, isolated them, and recorded both their number and distribution according to the JGR. After formalin fixation, a pathologist examined the specimens and lymph nodes, and histological diagnosis was determined according to JGR. Each tumor stage was coded according to the new TNM system, as described in the UICC (7th edition) revised in 2009. Although we did not analyze tumor deposits (satellites without regional nodes) defined by the new TNM system (new N category, N1c), the N1c status does not influence the N category classification (N1 and N2) or stage grouping of node-positive colorectal cancer patients.

The differences between the two groups were analyzed by the chi-square test and the Mann–Whitney *U*-test. Survival curves were plotted by the Kaplan–Meier method, and univariate analyses of DFS were estimated using the log-rank test. The Cox proportional hazard model was used for multivariate analyses. In all analyses, statistical significance was set at $P < 0.05$. All statistical analyses were performed using the JMP 8 software package (version 8.02; SAS Institute, Cary, NC, USA).

Results

Clinicopathological Features

The clinicopathological features of the 266 patients are summarized in Table 1. One hundred and fifty-one male (56.8%) and 115 female (43.2%) patients were included in this study, with a median age of 64.0 years (range, 24–92 years). The median follow-up time of the population was 42.4 months (range, 0.59–183.7 months). The distribution of tumor locations included 164 colon (61.2%; right colon: 61, left colon: 103) and 102 rectal cancers (38.7%). Of the 266 patients, 56 had stage IIIA disease (21.0%), 176 had stage IIIB disease (66.2%), and 34 had stage IIIC disease (12.8%). The tumor stage (depth of invasion) was classified as T1 in 28 patients (10.5%), T2 in 36 (13.5%), T3 in 171 (64.3%), T4a in 26 (9.8%), and T4b in 25 (9.4%). The median size of tumors

Table 1. Clinicopathological features of the 266 patients

	Total: 266 patients
Sex	
Male/female	151/121
Age (median) years	64.0 (range, 24–92)
Tumor location	
Right/left/rectum	61/103/102
UICC stage 7th edition	
IIIA/IIIB/IIIC	56/176/34
Tumor stage	
T1	28
T2	36
T3	171
T4a	26
T4b	5
Nodal stage	
N1a	110
N1b	89
N2a	42
N2b	25
Size (median) mm	40 (range, 9.9–108)
Histological type	
Well differentiated adenocarcinoma	81
Moderately differentiated adenocarcinoma	155
Poorly differentiated adenocarcinoma	10
Mucinous adenocarcinoma	19
Undifferentiated adenocarcinoma	1
Lymphatic invasion	
Negative/positive	54/212
Venous invasion	
Negative/positive	123/143
Serum CEA level (median) ng/ml	4.0 (range, 0.5–84.9)
Adjuvant chemotherapy	
No/yes/unknown	61/199/6
LNs examined (median)	14 (range, 1–76)
LNs involved (median)	2 (range, 1–27)
Proportion of patients with 12 or more LNs examined	175 (65.8%)
LNR (median)	0.16 (range, 0.01–1)
Low (0.01–0.20)	164
High (0.21–1)	102

UICC, Union Internationale Contre le Cancer; CEA, carcinoembryonic antigen; LN, lymph node; LNR, lymph node ratio

was 40 mm (range, 9.9–108 mm). The tumor was classified as well-differentiated adenocarcinoma in 81 patients (30.5%), moderately differentiated adenocarcinoma in 155 (58.3%), poorly differentiated adenocarcinoma in 10 (3.8%), mucinous adenocarcinoma in 19 (7.1%), and undifferentiated adenocarcinoma in 1 (0.4%). Lymphatic invasion was observed in 212 patients (79.7%), and venous invasion was observed in 143 patients (53.8%). The median preoperative serum CEA level was 4.0 ng/ml (range, 0.5–84.9 ng/ml).

The median number of LNs examined was 14 (range, 1–76). Eleven or fewer LNs were examined in 91 patients (34.2%). The median number of tumor-positive LNs was 2 (range, 1–27). One to three positive LNs (N1 disease) were observed in 199 patients (74.8%), and four or more positive LNs (N2 disease) were observed in the remaining 67 patients (25.2%). The LNR ranged from 0.1 to 1, with a median of 0.16. The best LNR cutoff value was selected as 0.20 based on ROC analysis. Therefore, patients were divided into two groups: LNR-low (0–0.2) and LNR-high (0.21–1). One hundred and sixty-four patients (61.7%) were classified as LNR-low, and 102 patients (38.3%) were classified as LNR-high. The median number of LNs examined in cases of colon and rectal cancer was 16 (range, 1–76) and 13 (range, 2–73), respectively ($P = 0.0699$). The median LNR values for cases of colon and rectal cancer were 0.13 (range, 0.01–1) and 0.17 (range, 0.04–1), respectively ($P = 0.0102$).

Adjuvant chemotherapy, administered according to pathological stage and the physical condition of the patient, was performed in 199 patients (76.5%). The

most common regimen before 2000 was oral tegafur/uracil therapy (100 patients, 50.2%). The standard regimens recommended by the current guidelines of the National Comprehensive Cancer Network such as 5-fluorouracil/leucovorin therapy, oral tegafur-uracil/folinate therapy, and capecitabine therapy, were performed after 2001 (99 cases, 49.8%). Oxaliplatin-based regimens, such as FOLFOX, were not administered to any of the patients in this study. In the LNR-low group, 43 patients received no chemotherapy (26.2%), and 118 patients (73.3%) received chemotherapy. In the LNR-high group, 17 patients received no chemotherapy (21.0%), and 81 patients (82.7%) received chemotherapy. No statistically significant difference in the frequency of the application of adjuvant chemotherapy was observed between the LNR groups ($P = 0.0833$). No patient received chemotherapy or radiation therapy before surgery.

Cancer recurrence was observed in 90 patients (33.8%). The sites of first recurrence (including overlapped cases) were the liver ($n = 36$), lung ($n = 30$), local recurrence ($n = 20$), lymph node ($n = 18$), peritoneal dissemination ($n = 7$), brain ($n = 3$), and bone ($n = 3$).

Risk Factors for Disease-Free Survival: Univariate and Multivariate Analyses

To estimate the risk factors for DFS, univariate analysis was performed for the following variables: sex (male vs female), tumor location (colon vs rectum), tumor stage (T1–T2 vs T3–T4), nodal stage (N1 vs N2), size of the tumor (≤30 mm vs >30 mm), histological type (well-differentiated adenocarcinoma vs other types), lymphatic invasion (negative vs positive), venous invasion (negative vs positive), serum CEA level (≤5.0 ng/ml vs >5.0 ng/ml), the administration of adjuvant chemotherapy (no vs yes), number of LNs examined (≤11 vs. ≥12), and LNR (low vs high). Tumor location (rectum, $P = 0.0002$), tumor stage (T3–T4, $P = 0.0118$), nodal stage (N2, $P = 0.0031$), lymphatic invasion (positive, $P = 0.0117$), the serum CEA level (>5.0 ng/ml, $P = 0.0199$), and the LNR (high, $P < 0.0001$) were identified as significant risk factors of reduced DFS (Table 2).

In a multivariate analysis of the selected variables found to be significant in the univariate analysis, only the tumor location (rectum, $P = 0.0047$) and the LNR (high, $P = 0.0003$) were identified as independent predictive factors for DFS (Table 3).

Five-Year Survival

The 5-year DFS for patients with stage IIIA, IIIB, and IIIC disease was 88.2%, 56.5%, and 38.4%, respectively ($P < 0.0001$). The 5-year OS for patients with stage IIIA, IIIB, and IIIC disease was 92.4%, 71.5%, and 41.7%, respectively ($P = 0.0001$). According to the LNR grading, the 5-year DFS in the LNR-low and LNR-high groups was 70.1% and 46.4%, respectively ($P < 0.0001$), and the 5-year OS in the LNR-low and LNR-high groups was 81.3% and 59.7%, respectively ($P = 0.0032$) (Fig. 1).

For patients with colon cancer, the 5-year DFS and the 5-year OS were 69.9% and 78.1%, respectively. According to the LNR grading, the 5-year DFS in the LNR-low and LNR-high groups was 79.8% and 53.8%, respectively ($P = 0.0009$), and the 5-year OS in these groups was 84.5% and 67.1%, respectively ($P = 0.121$) (Table 4A). For patients with rectal cancer, the 5-year DFS and OS was 45.9% and 63.7%, respectively. According to the LNR grading, the 5-year DFS in the LNR-low and LNR-high groups was 51.8% and 35.6%, respectively ($P = 0.0165$), and the 5-year OS in these groups was 75.3% and 49.7%, respectively ($P = 0.0179$) (Table 4B). Although there was no statistically significant difference in the 5-year OS in cases of colon cancer, a substantial prognostic separation was observed when we considered the LNR for both colon and rectal cancers.

For patients with stage IIIA disease, the 5-year DFS in the LNR-low and LNR-high groups was 91.2% and 82.4%, respectively ($P = 0.1861$). The 5-year OS in the LNR-low and LNR-high groups was 95.7% and 85.6%, respectively ($P = 0.4934$). For patients with stage IIIB disease, the 5-year DFS in the LNR-low and LNR-high groups was 64.6% and 41.7%, respectively ($P = 0.0019$). The 5-year OS in the LNR-low and LNR-high groups was 79.2% and 59.3%, respectively ($P = 0.0394$). For patients with stage IIIC disease, the 5-year DFS in the LNR-low and LNR-high groups was 54.7% and 33.4%, respectively ($P = 0.0166$), and the 5-year OS in the LNR-low and LNR-high groups was 72.9% and 35.4%, respectively ($P = 0.2244$) (Table 5). A stronger prognostic separation was observed in the DFS and OS of patients with stage IIIB disease by the application of LNR in addition to the new TNM system, than by the new TNM staging system alone. Conversely, no prognostic separation was seen in the DFS and OS of patients with stage IIIA and stage IIIC disease.

Relationship Between the Clinical Impact of the LNR and the Number of LNs Examined

To clarify the prognostic value of the LNR in patients with a low LN count (11 or fewer LNs examined), we separately analyzed patients with 11 or fewer LNs examined and patients with 12 or more LNs examined. For patients with a low LN count, the 5-year DFS in the LNR-low and LNR-high groups was 65.9% and 60.7%, respectively ($P = 0.3910$) (Fig. 2A), and the 5-year OS in the LNR-low and LNR-high groups was 76.2% and

Table 2. Risk factor of DFS: univariate analysis

Factor		5-year DFS (%)	*P* value
Sex	Male	65.4	0.1804
	Female	57.4	
Location	Colon	69.9	0.0002
	Rectum	45.9	
TNM tumor stage	T1, T2	79.0	0.0118
	T3, T4	55.3	
TNM nodal stage	N1	66.2	0.0031
	N2	43.9	
Size (mm)	≤30	68.5	0.0857
	>30	56.7	
Histological grade	Well	65.6	0.1543
	Others	58.8	
Lymphatic invasion	Negative	82.0	0.0117
	Positive	57.0	
Venous invasion	Negative	66.0	0.402
	Positive	57.4	
Serum CEA level (ng/ml)	≤5.0	68.6	0.0199
	>5.0	48.2	
Adjuvant chemotherapy	No	60.2	0.3847
	Yes	64.4	
No. of LNs examined	≤11	63.0	0.6319
	≥12	60.0	
LNR	Low	70.2	<0.0001
	High	46.4	

DFS, disease-free survival

Table 3. Risk factor of DFS: multivariate analysis

Selected risk factor	*P* value	Hazard ratio	95% confidence interval
Location (rectum)	0.0047	1.8933	1.2195–2.9412
TNM tumor stage (T3, T4)	0.0779	1.7342	0.9158–3.2787
TNM nodal stage (N2)	0.9296	1.0231	0.6161–1.7007
Lymphatic invasion (positive)	0.1080	1.7670	0.8396–0.3717
Serum CEA level (>5.0ng/ml)	0.1048	1.4503	0.9259–2.2727
LNR (high)	0.0003	2.4247	1.4970–3.9216

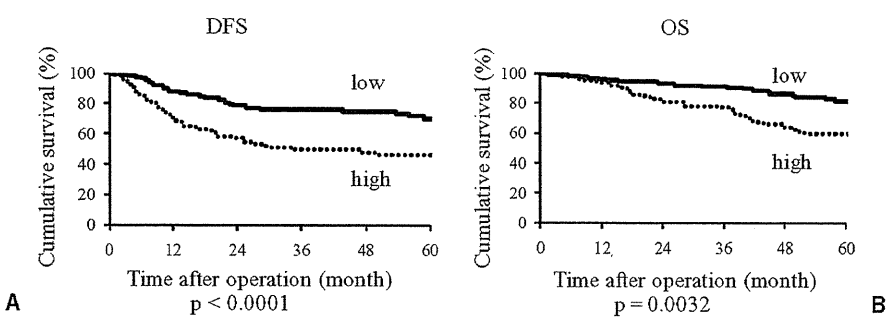

Fig. 1. Disease-free survival (*DFS*) (**A**) and overall survival (*OS*) (**B**) in the low lymph node ratio (LNR-low) and LNR-high patient subgroups

65.5%, respectively ($P = 0.9835$) (Fig. 3A). For patients with 12 or more LNs examined, the 5-year DFS in the LNR-low and LNR-high groups was 72.4% and 29.5%, respectively ($P < 0.0001$) (Fig. 2B), and the 5-year OS in the LNR-low and LNR-high groups was 82.7% and 52.2%, respectively ($P < 0.0001$) (Fig. 3B). Prognostic separation was not observed in the patients with a low LN count. The LNR was predictive of DFS and OS in patients with stage III colorectal cancer, especially when 12 or more LNs were examined.

Table 4. Five-year DFS and OS for colon cancer (A) and rectal cancer (B) according to LNR

LNR	5-year DFS (%)	*P* value	5-year OS (%)	*P* value
A. Colon cancer ($n = 164$)				
Total	69.9		78.1	
Low	79.8	0.0009	84.5	0.1207
High	53.8		67.1	
B. Rectal cancer ($n = 102$)				
Total	45.9		63.7	
Low	51.8	0.0165	73.5	0.0179
High	35.6		49.7	

OS, overall survival

Table 5. 5-year DFS and OS in the LNR-low and LNR-high groups according to TNM classification (7th edition)

Stage	LNR	5-year DFS (%)	*P* value	5-year OS (%)	*P* value
Stage IIIA ($n = 56$)	Total	88.2		92.4	
	Low	91.2	0.1861	95.7	0.4934
	High	82.4		85.6	
Stage IIIB ($n = 176$)	Total	56.5		71.5	
	Low	64.6	0.0019	79.2	0.0394
	High	41.7		59.3	
Stage IIIC ($n = 34$)	Total	38.4		41.7	
	Low	54.7	0.1661	72.9	0.2244
	High	33.4		35.4	

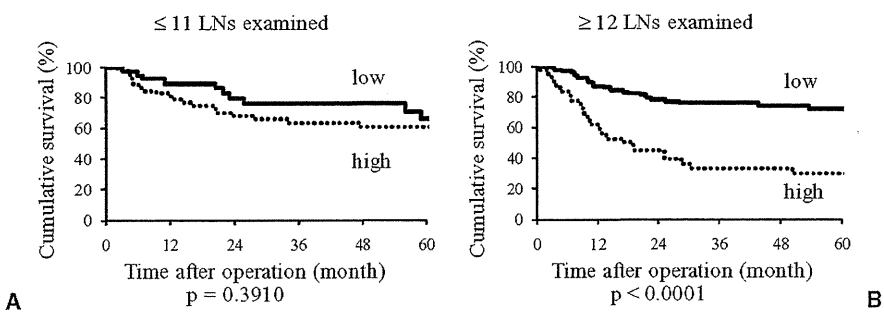

Fig. 2. Disease free survival (*DFS*) in the LNR-low and LNR-high subgroups analyzed separately for patients with 11 or fewer lymph nodes (*LNs*) examined (**A**) and 12 or more LNs examined (**B**)

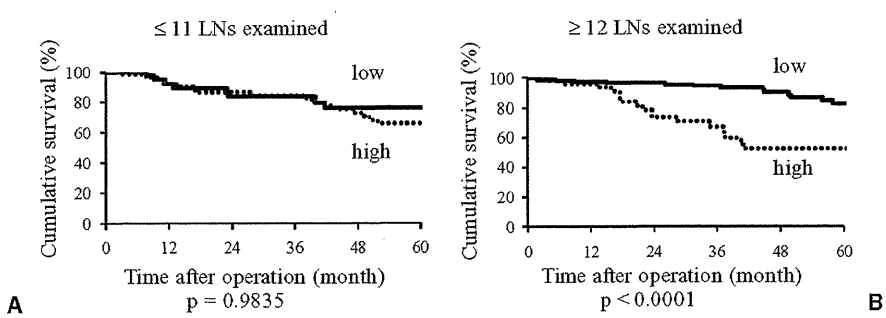

Fig. 3. Overall survival (*OS*) in the LNR-low and LNR-high subgroups analyzed separately for patients with 11 or fewer LNs examined (**A**) and 12 or more LNs examined (**B**)

Discussion

Because recent evidence has indicated that the number of positive LNs is an important factor in patients with colorectal cancer, N categories are determined by the number of positive LNs in the TNM staging system.[1] In addition, the current literature indicates that the accuracy of staging and OS in colorectal cancer patients

increases proportionally to the number of LNs examined in both node-negative and node-positive colorectal cancer,[2,29] because there is a potential for stage migration depending on the degree to which specimens are examined and the total number of LNs examined.[2] Although what constitutes adequate LN evaluation is still under debate,[2,30,31] the current guidelines issued by the AJCC and UICC recommend the excision and evaluation of a minimum of 12 LNs in the tumor specimen to adequately assess the tumor stage.[1] Therefore, the N category of the current TNM system, which disregards the number of LNs examined, has been suggested to be a potential limitation to the prediction of cancer survival, and the LNR has been proposed as a more accurate prognostic indicator in colorectal cancer. The LNR reflects the number of LNs examined, and may diminish stage migration and consequently predict survival more accurately than using only the number of positive LNs.[9] The presence of nodal disease influences the decision to recommend adjuvant chemotherapy, which is well known to improve survival in colorectal cancer patients with positive nodes. For many years, 5-fluorouracil/leucovorin therapy has been accepted as the standard adjuvant chemotherapy for stage III colorectal cancer.[32] Recently, oxaliplatin-based adjuvant chemotherapies, such as FOLFOX, have been shown to improve the outcome of colon cancer patients with positive nodes.[33,34] If patients with a high or low risk of recurrent disease could be accurately identified by the LNR, individual chemotherapeutic strategies might be utilized according to their risk of recurrence.

A new TNM grading system (7th edition) revised by the AJCC and UICC was released in December 2009.[1] In the new TNM system, stage III colorectal cancer was classified into stage IIIA (T1/2 and N1, T1 and N2a), IIIB (T3/T4a and N1, T2/3 and N2a, T1/2 and N2b), and IIIC (T4a and N2a, T3/4a and N2b, T4b and N1/2). N1a defines a tumor with only 1 metastatic LN, N1b defines a tumor with 2–3 metastatic LNs, N1c defines disease with satellites in the subserosa, without regional nodes, N2a defines tumors with 4–6 metastatic LNs, and N2b defines those with 7 or more metastatic LNs. In light of evidence that the number of LNs examined is an important prognostic factor for colorectal cancer, node-negative cases with a low LN count (11 or fewer) are now defined as pN0 by the new TNM system. However, for node-positive cases, neither the number of LNs examined nor the LNR are reflected as prognostic factors. In the present study, we demonstrated a stronger prognostic separation by the application of the LNR in addition to the new TNM system in patients with stage IIIB disease, although prognostic separation was not observed in patients with stage IIIA or IIIC disease. As shown in Table 1, our cohort consisted of 56 patients with stage IIIA disease, 176 patients with stage IIIB disease, and 34 patients with stage IIIC disease. According to the new TNM system, the proportion of patients with stage IIIB disease was relatively high, and that of patients with IIIA and IIIC disease was low. We speculated that this may be one of the reasons why no prognostic separation was observed in our patients with stage IIIA and IIIC disease. Further investigation is required to evaluate the possibility that prognostic separation can also be observed in patients with stage IIIA and IIIC disease by using the LNR.

The extent of LN dissection, surgical technique, the thoroughness of the pathologist, and the technique of LN isolation can all influence the assessment of the LNR.[27] Therefore, the prognostic impact of the LNR must be assessed cautiously. In particular, the prognostic value of the LNR in patients with a low LN count (11 or fewer examined) is still controversial. The present study supports the report of Berger et al.[9] that the LNR is not a predictive factor if there is a low LN count. Several studies have excluded patients with a low LN count, on the basis of insufficient LN examination according to the current guidelines.[12,13,19,25] Despite the existence of guidelines recommending that at least 12 LNs be examined, several published studies present median examined LN numbers of 11 or fewer.[9,13,27] Regardless of sufficient surgical resection and LN examination, other factors, such as tumor location, tumor stage, older age, and obesity may influence the number of LNs examined. In addition, the number of LNs examined may also be related to the immune response of the patient.[27] For this reason, we sometimes encounter cases of a low LN count even when adequate surgical resection and LN examination are performed. We therefore believe that clarification of the real prognostic value of the LNR in patients with a low LN count was meaningful.

To clarify this issue, we reviewed 21 articles concerning the prognostic impact of the LNR on colorectal cancer published to date in English.[3,4,9–27] A MEDLINE search was conducted to provide an overview of the literature concerning the prognostic impact of the LNR using the keywords "colorectal cancer" and "lymph node ratio." Of these 21 articles, 7 reports, including the present study, addressed the relationship between the prognostic impact of the LNR and the number of LNs examined.[3,4,9,16,18,24] Table 6 summarizes these seven reports, with an emphasis on the number of LNs examined and the proportion of patients with a low LN count. Four reports concluded that the prognostic value of the LNR was independent of the number of LNs examined[3,4,16,18] and three reports, including the present study, concluded that the prognostic value of the LNR was not significant in patients with a low LN count.[9,24] As shown in Table 6, the proportion of each TNM stage, the mean or median number of LNs examined, and the

Table 6. Summary of the seven reports investigating the relationship between the prognostic impact of LNR and the number of LNs examined in colorectal cancer patients

First author (year)[Ref.]	Study design	Cases	Location of tumor	Stage	Curability	Median no. of LNs examined	Proportion of patients with low LN count	Median positive LN	Median LNR	LNR cutoff value	Prognostic impact of LNR in patients with low LN count	Country
Berger (2005)[9]	Multiple center	3411	Colon	II, III	Curative	11	ND	ND	ND	0.05, 0.2, and 0.4 (based on quartile)	Not significant	USA
Wang (2008)[18]	Multiple center	24447	Colon	III	Curative	ND	39.26% (10 or fewer)	ND	ND	0.071, 0.25, and 0.50 (based on quartile)	Significant	USA
Peschaud (2008)[3]	Single center	307	Rectum	I–III	Curative	22 (mean)	19.20% (11 or fewer)	ND	0.10 (mean)	0, 0.07 and 0.2	Significant	France
Rosenberg (2008)[16]	Single center	3026	Colorectal	I–IV	Not curative (R0: 77.4%)	16	17.60% (11 or fewer)	2.6 (mean)	0.14 (mean)	0.17, 0.41, and 0.69 (based on Classification and regression trees technique)	Significant	German
Park (2009)[24]	Single center	318	Colon	III	Curative	24 (mean)	18.6% (11 or fewer)	ND	0.19	0.06, 0.12, and 0.24 (based on quartile)	Not significant	Korea
Vaccaro (2009)[4]	Single center	362	Colon	III	Curative	20	Less than 10% (10 or fewer)	2	0.11	0.06, 0.12, and 0.25 (based on quartile)	Significant	Argentina
Present study	Single center	266	Colorectal	III	Curative	14	34.2% (11 or fewer)	2	0.16	0.20 (based on ROC analysis)	Not significant	Japan

ND, not described; ROC, receiver operating characteristic

proportion of patients with a low LN count varied widely across studies. Thus, no clear tendency was reflected in the results. Although two conflicting studies comprised very large populations,[9,18] these series were multiple-center analyses that used registry-based data. These results may have been highly influenced by differences in surgical techniques, pathological thoroughness, and LN isolation techniques across institutions. By contrast, the influence of the degree of surgical and pathological variability may be minimized in single-center analyses. Five reports, including the present study, were single-center analyses.[3,4,16,24] Although three of these reports concluded that the prognostic value of the LNR was independent of the number of LNs examined,[3,4,16] two of these three reports included node-negative patients.[3,16] The prognostic impact of the LNR for populations including node-negative patients differs from that of a node-positive population, because the LNR of all node-negative patients is zero, and these patients have a relatively good prognosis. Of the three reports with a fully node-positive population, including the present study,[4,24] only one concluded that the prognostic impact of the LNR was independent of the LN count.[4] In this report, the median number of LNs examined was 20 and the proportion of patients with a low LN count (11 or fewer LNs examined) was extremely low, at fewer than 10%. Therefore, from this study the prognostic impact of the LNR in patients with low LN count could not be determined. From single-center analyses, therefore, the study by Park et al.[24] and the present study concluded that the prognostic impact of the LNR was not significant in patients with 11 or fewer LNs examined in fully node-positive populations. This review suggests that the prognostic impact of the LNR is not significant in node-positive populations with a low LN count when the influence of surgical and pathological variability is minimized.

The present study had several limitations, and therefore this finding should be considered with caution. First, both the present study and that of Park et al. had a relatively small sample size. Second, although no statistically significant difference in the frequency of the application of adjuvant chemotherapy was observed between the LNR groups, we cannot deny the influence of the variations in the regimens used for adjuvant chemotherapy. In addition, the cutoff value of the LNR varied across studies, as shown in Table 6. The optimal LNR cutoff value has not yet been determined. In the present study, to divide the study population into two groups, we used the two LNR cutoff values that were determined by the quartile-based classification, which is a well described method, and the ROC analysis. Better prognostic separation was observed when we used the LNR cutoff value determined by the ROC analysis (data not shown) and hence, we used this value of 0.20 for classification, as described by Galizia et al.[20] Further examination is required to determine the optimal cutoff value of LNR. Even with these limitations, however, our findings suggest that a powerful prognostic separation can be obtained using the LNR after exclusion of patients with a low LN count. Therefore, we conclude that the LNR can be used to predict survival in patients with stage III colorectal cancer, especially when an adequate number of LNs is examined.

Conclusions

The LNR is an important predictive factor for cancer recurrence in patients with stage III colorectal cancer. A stronger prognostic separation can be observed by the simultaneous application of the LNR and the new TNM system, especially for patients with stage IIIB disease. The LNR can predict cancer recurrence and survival in patients with stage III colorectal cancer, especially when 12 or more LNs are examined. From this point of view, we support the consensus that defines 12 LNs as the quality measure of surgical and pathological performance. To clarify the real prognostic value of the LNR, multiple-center analyses with a large population are required. Surgeons should strictly follow the guidelines for adequate lymphadenectomy, and an adequate examination is necessary to retrieve as many LNs as possible from the specimen to minimize the influence on the number of LNs examined across institutions.

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Conflict of Interest Statement. The authors have no conflicts of interest to declare.

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Glove法による単孔式内視鏡手術の術式の工夫 —胆嚢摘出術からadvanced surgeryへの応用—

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はじめに

単孔式内視鏡手術は2007年Navarraらの報告に始まり，2009年本邦へ導入された後は，胆嚢摘出術，虫垂切除術から他のadvanced surgeryへ応用展開が試みられている[1)~4)]。単孔式内視鏡手術は傷が著しく小さいという利点を有しながら，手元や，腔内でのconflictが少なからず発生することから内視鏡手術で得意としていた拡大視効果や鉗子での精緻な手技が損なわれるのではないかとの懸念があり，いまだ施行に躊躇している施設も少なくないと思われる。今回は視野の確保および器具操作を中心に，安全な単孔式内視鏡手術の導入とadvanced surgeryへの展開について述べる。

Ⅰ．単孔式内視鏡手術の方法

単孔式内視鏡手術への取り組みは施設によりさまざまである。気腹法として主には①マルチポート穿刺法，②SILSポートを中心としたプラットフォーム法，③glove（手袋）法の3種類がある。吊り上げ器具使用の施設もあるが応用展開は困難である。

それぞれの方法の利点と欠点を**表1**に列挙する。マルチポート穿刺法は廉価で特別な器具を必要としないが，1本目のトロカール挿入がblind操作になりやすいことと，狭い範囲に複数のトロカールを挿入する際，気腹漏れの恐れがあり，皮下の剝離も広めとなるため，創の整容性や痛みに対して不利な側面がある。すでに本邦で使用可能なプラットフォームとしてはディスポーサブルのSILS™ Port（コヴィディエン社）であるが，特殊なゴムでできており気腹漏れが少なく，ポートを回すことによりトロカール孔がconflictしづらい位置にすることができる。また12 mmトロカールへの変更も容易で，回収袋なども操作しやすい。一方トロカール挿入部の視認しづらさやコストの高いことは問題とされる。現時点では気腹チューブはあるものの排煙装置がついていないことも，視野確保の点で問題となる。

Ⅱ．Glove法の利点，欠点と対処法

Glove法はWound Retractor XS™と5.5 sizeの大きさの手袋を手首部分で切って，3~5本のHeadの小さなトロカール（LINA Portまたは Olympus SonoSurg Trocor）を用いている。廉価であるばかりでなく，トロカール位置の変更が容易に可能で，腹壁固定部分が薄いのでconflictは最小と考えられる。また複数のトロカールが誘導

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key words
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表1　単孔式内視鏡手術の利点，欠点

	利点	欠点
マルチポート穿刺法	1. 従来の器具を使用できる 2. 廉価である	1. 気腹漏れを起こすことがある 2. ポートの位置の変換が不可能 3. 皮下組織への影響
プラットフォーム法	1. 気腹が確実にできる 2. ポートをまわすことにより位置の変換が可能	1. トロカール挿入部が見えないことがある 2. コスト高 3. 排煙困難
Glove（手袋）法	1. 廉価である 2. 位置の変換が自由 3. 腹壁固定部分が薄い 4. 複数のトロカール挿入可 5. ステイプラー，屈曲鉗子の挿入可 6. 標本の取り出しやすさ 7. 創汚染予防	1. プラットフォームの欠落 2. トロカールの逸脱 →外科用シールなどでの疑似プラットフォーム作成

表2　Glove 法に必要な器具

- Alexsis Wound Retractor XS，5.5 glove
- Flexible fiber（5 mm）Olympus
- トロカール 3〜4 本（5 mm）（LINA Port，Olympus SonoSurg Trocar）
- 把持鉗子，剝離鉗子，Scissors etc.（Straight forceps）
- 可変式屈曲鉗子：Roticurator または Real Hand（Bending forceps）
- 造影鉗子（コラジオカテ，ペチニードル，クーマー etc.）
- 剝離器具；超音波凝固切開装置，ベッセルシーリングシステム，止血器具
  （SonoSurg, Harmonic Scalpel，Autosonics，LigaSure，Enseal，Bypolla scisors，VAIO Soft coag, ABC，Surgicel Nit etc.）
- 縫合結紮器具
  （Endo-loop, 持針器，Endo-Stitch，SILS-Stitch etc.）
- リニアステイプラー，サーキュラーステイプラー
- Mini-loop retractor，針糸，ペンローズドレーン，ネラトン，エンドマウス etc.
- 気腹装置，排煙装置，回収袋（スリムバッグ，エンドキャッチ etc.）

可能で，太いステイプラーや屈曲鉗子などの誘導も可能である。また欠点としてのプラットフォームの欠落，トロカールの逸脱については，外科用シールの添付や，孔を大きくしすぎないことで対処しうる。本法で胃や大腸などの大きな標本の症例では切開孔を 2.5〜4 cm 程度に作成することが可能であり，その大きさゆえに鉗子類の conflict が少なくなり，創汚染が防止されているため，標本回収が容易などの利点も挙げることができる。また傷については皮下周囲の剝離がないため，もっとも小さく美容的で，痛みも少ないと考えられる。

Ⅲ．手術に必要な器具

Glove 法での必要器具を表2に列挙する。皮膚汚染防御材としての Alexsis Wound Retractor XS は皮膚切開が 2 cm あると装着が可能で，皮膚縁までのロールアップにより適度な外側へのテンションがかかり，5.5 size の glove との適合はよい。気腹，排煙用のコック付き 5 mm トロカールを選択するか，後者を 1 本の指から別ルートとして排気させるか決め，basic skill では 3 本誘導し，2-0 絹糸で結紮固定する。Advanced surgery では 12〜13 mm トロカールや屈曲鉗子，ステイプラーを直接挿入し，固定する。Basic skill ではカメラとしては flexible fiber（5 mm）を挿入し，術者の鉗子類と conflict を起こさないように角度を変え把持する。鉗子類は直の剝離鉗子，把持鉗子と可変型屈曲鉗子を適宜使用する。われわれが通常行うコンバインド法の場合には右手は直の剝離鉗子，左手は屈曲型の把持鉗子を使用すること

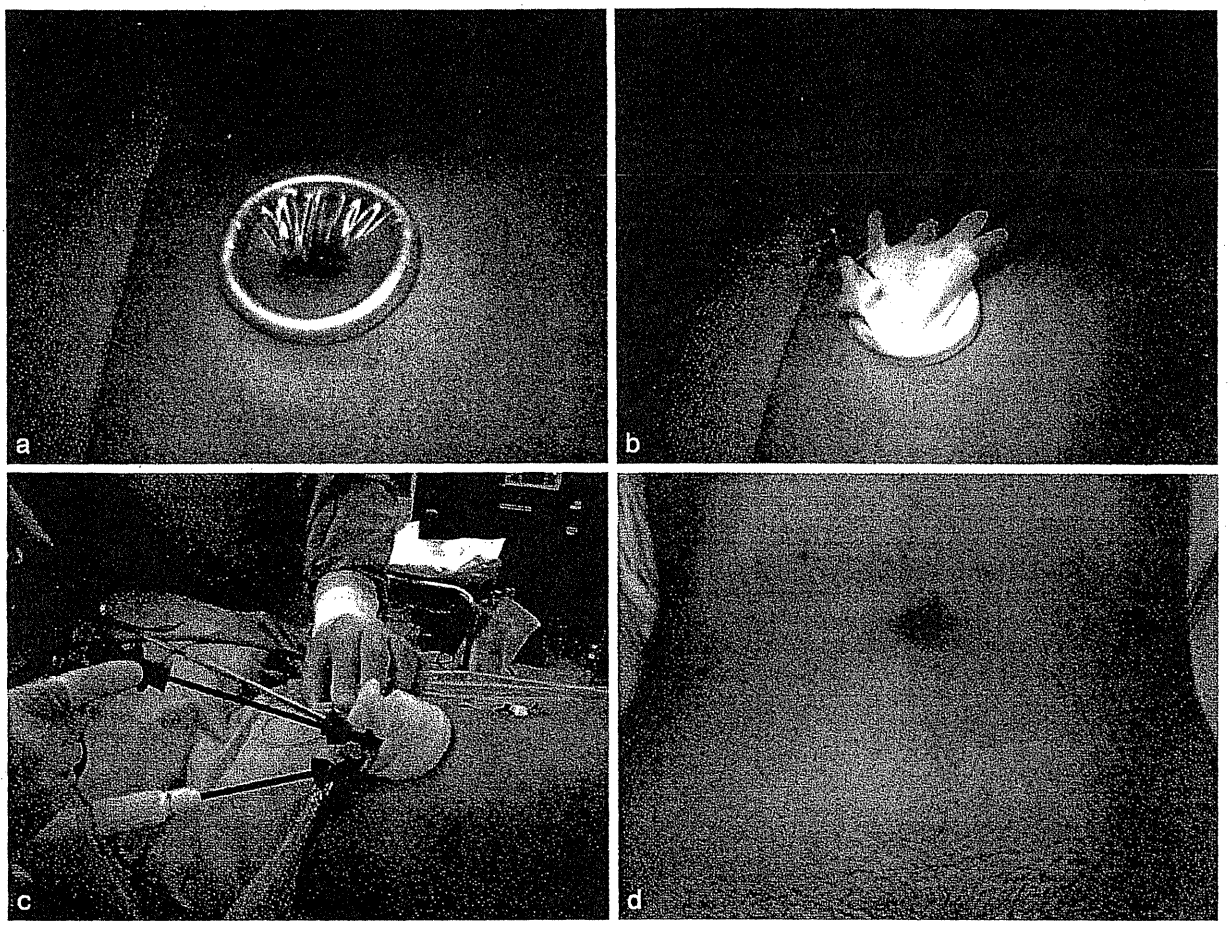

図1　Glove 法

Incision=2 cm（Lap. chole，TAPP，Appe）
a）Applied Alexis；Wound Retractor-XS を臍部に装着する。
b）Glove（5.5）から，3本の Lina Port（5 mm）を誘導する。
c）Flexible scope で視野を確保する。
d）術後の創部（臍）。

が多い（図1）。当院では胆嚢摘出術では胆道造影をルーチンワークとしているため造影鉗子およびチューブを用意しており，ヘルニア修復術（TAPP）では縫合結紮器具を必要とする。また本手技では出血を極力少なくするため，超音波凝固切開装置，ABC などの，止血器具も使用することも多くなる。

胃切除，大腸切除，肝切除などの advanced surgery には針糸，ペンローズドレーン，ネラトンチューブなどの胃腸または肝などによる把持挙上の工夫と器械縫合の導入が必要となる。今後も新たな器具が開発され使用されるようになると思われるが，創意工夫をしてコスト減となるような器具選択を心掛けなくてはならない。

Ⅳ．TANKO の症例

2010年6月から約1年4カ月間に施行した当院での TANKO（Port Reduced Surgery）は88例である。表3に胆嚢摘出術，ヘルニア修復術（TAPP），虫垂切除術の basic skill 症例を，また表4にそれ以外の advanced surgery 症例を提示する。

Ⅴ．Glove 法の手技

基本的には臍部を2 cm 縦切開し，Alexsis の Wound Retractor XS を装着する。5.5 size の glove に LINA Port を3本誘導し2〜0絹糸にて固定する。5 mm の flexible scope を誘導し，鉗子類と一定の距離をとるように屈曲させローテートさせる。

表3　Port Reduced Surgery 1

疾患	症例	平均年齢	平均手術時間（min.）	トロカール数	術式の工夫	術後入院期間
胆嚢摘出術	28例	60.6歳 (34～83)	92.8 min.	3 Assist=6 SILS P.=3	胆道造影＝23 Kumor=2 Petineedle＝5 Cholagiocathe＝15	3days
ヘルニア修復術	14例 (20側)	65.8歳 (34～72)	133 min. 初片=90 再片=109 両側=162	3 Assist=6 SILS P.=3	3D Mesh =7 Parietex Mesh=4	3days
虫垂切除術	7例	52.5歳 (10～83)	67.6 min.	2-3 Assist=4	Looping = 6 Stapler = 1	4.6 days

表4　Port Reduced Surgery 2

術式	症例	平均年齢	平均手術時間	疾患	術式内容	術後入院期間
胃部分切除術	10例	68歳	150 min.	GIST＝6 Shwanoma=1 平滑筋腫=1 Early Gastric Ca.=2	胃内手術 =6 吊り上げ法 =2 LADG =2 (S+2)	7.2 days
胃空腸吻合術	2例	68歳	136.5 min.	Panc Ca.＝1 Gastric Ca.＝1	Kajitani 式 =2	7 days
小腸切除術	1例	78歳	78 min.	Mecher's Diverticulitis＝1	出血→塞栓→準緊急	8 days
大腸切除術	10例	69歳	188 min.	Colon Ca=6 LST=1	Pure S.=1 +1Port =5 +2Port=1	8.8 days
脾臓摘出術	1例	71歳	108 min.	ITP=1	Pure S. =1	6 days
肝嚢胞開窓術	2例	69歳	208 min.	感染性肝嚢胞＝1 多発性肝嚢胞＝1	単発巨大＝1 多発＝1	8 days
肝切除術	1例	61歳	67 min.	肝血管腫＝1	肝血管腫＝1 SonoSurg=1	4 days

また剝離鉗子，把持鉗子も縦に少しずらして3次元的に右手，左手の conflict が少ないように移動する。創部が2 cm で5 mm トロカールを3本誘導した場合にはトロカールのねじ部分の摩擦のため逸脱が防止できる（図2a）。創部が大きすぎる場合には逸脱を防ぐため外科用シールにて1～2カ所を止め，疑似プラットフォームを作成する（図2b）。

1．胆嚢摘出術

胆嚢摘出術は胆嚢管の術前の画像診断を踏まえた解剖学的な理解と，安全な剝離手技が重要なことは充来の腹腔鏡下胆嚢摘出術と同じである[6]。右手は直の剝離鉗子，左手は屈曲型把持鉗子によるコンバインド法を主に用いている。胆嚢底部を Mini-loop retractor で把持挙上し，臍部創から挿入した屈曲鉗子にて胆嚢体部を挙上し，right turn, left turn を行い，サイドから剝離を開始する。胆嚢頸部から胆嚢管は left turn を明確に行い，胆嚢管右側のラインを出すことに専念する（図3a）。胆嚢管右側は左側の Callot's 三角と異なり，胆嚢動脈根部から遠いので出血に遭遇する可能性が少なく，安全な剝離が可能である。Critical view of safety の観点から広目に胆嚢体部まで剝

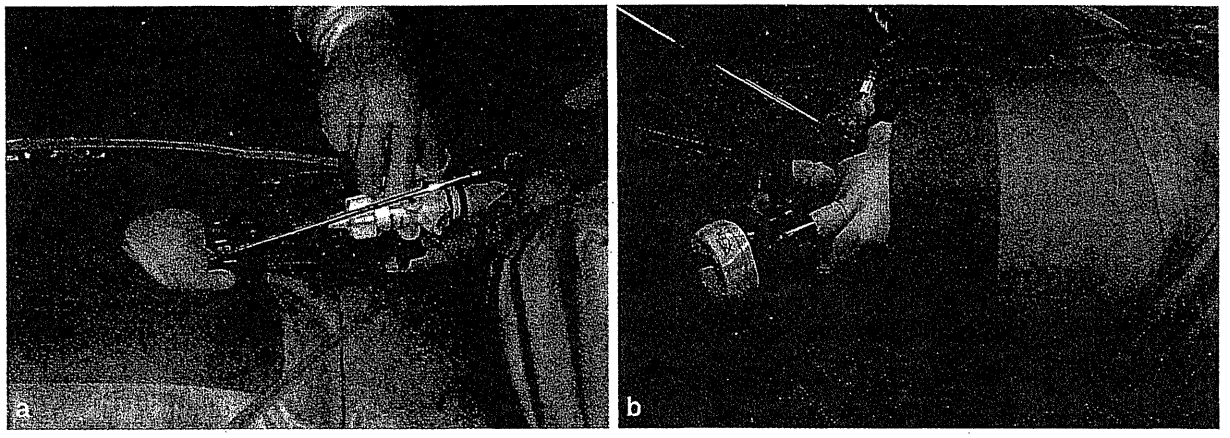

図2　Glove 法におけるポート部
a）Basic skill でのポート部
b）Advanced surgery でのポート部固定

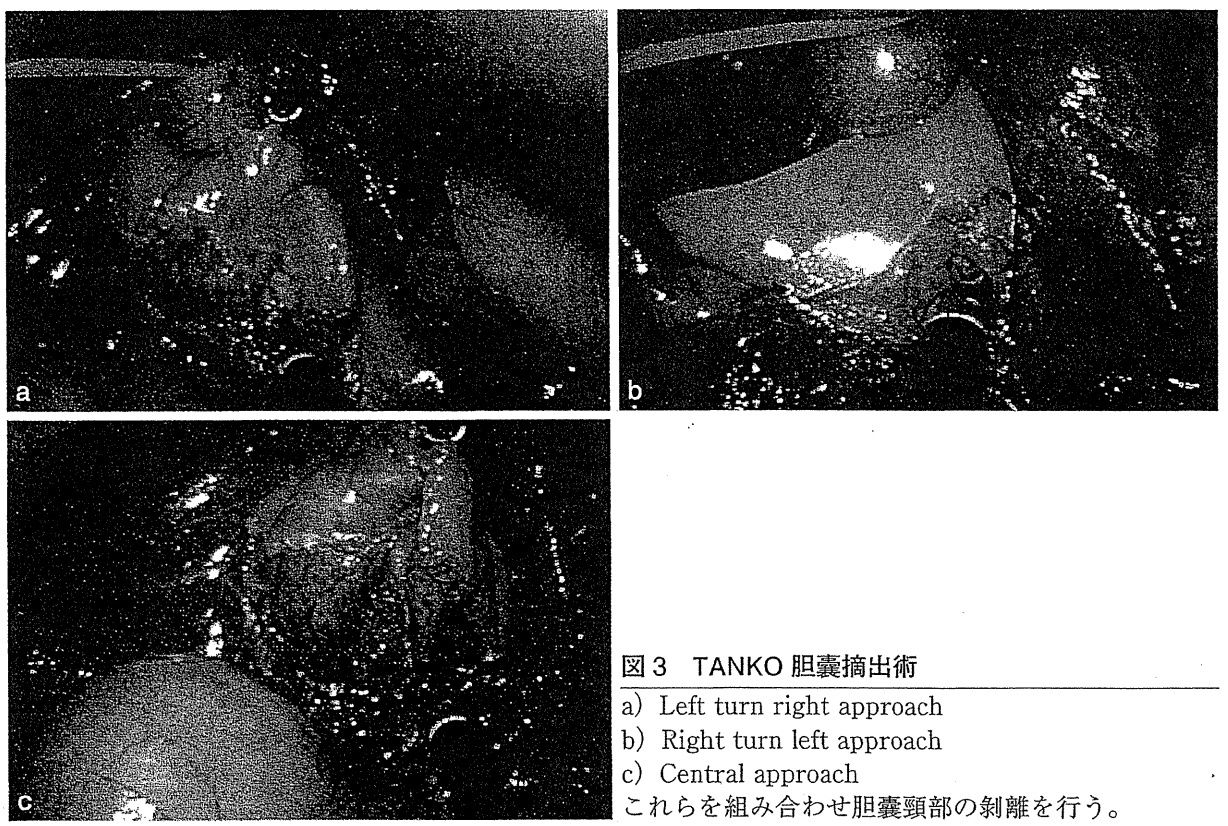

図3　TANKO 胆嚢摘出術
a）Left turn right approach
b）Right turn left approach
c）Central approach
これらを組み合わせ胆嚢頸部の剝離を行う。

離を進める。その後 right turn を行い，Callot's 三角内にて胆嚢動脈を剝離同定し，胆嚢管を背側から剝離する（図 3b）。胆嚢動脈をクリップ処理し，胆嚢管を血管から剝離する（図 3c）胆嚢管を慎重に半切してコラジオカテーテルによる術中胆道造影を行う。6 例目から全例造影を行っているが，いずれの方法でも造影は可能であった。現在は胆嚢穿刺法である Kumor 法 2 例，ペチニードル法 5 例，コラジオカテーテル法を 15 例に行っているが，コラジオカテーテルは角度の合いづらい時に，ラジフォーカスガイドワイヤー（0.025）を使用している（図 4）。胆嚢管を切離した後は胆嚢を挙上しつつ頸部側からの剝離を基本としているが（図 5a），困難な症例では底部からの Dome-down 法（6 例）で行っている。正中上部から補助ポートを挿入し＋1 となった症例は 6 例であった。肝床部からの止血に，時には ABC を用いている。腹腔内を洗浄し胆嚢は回収袋（スリ

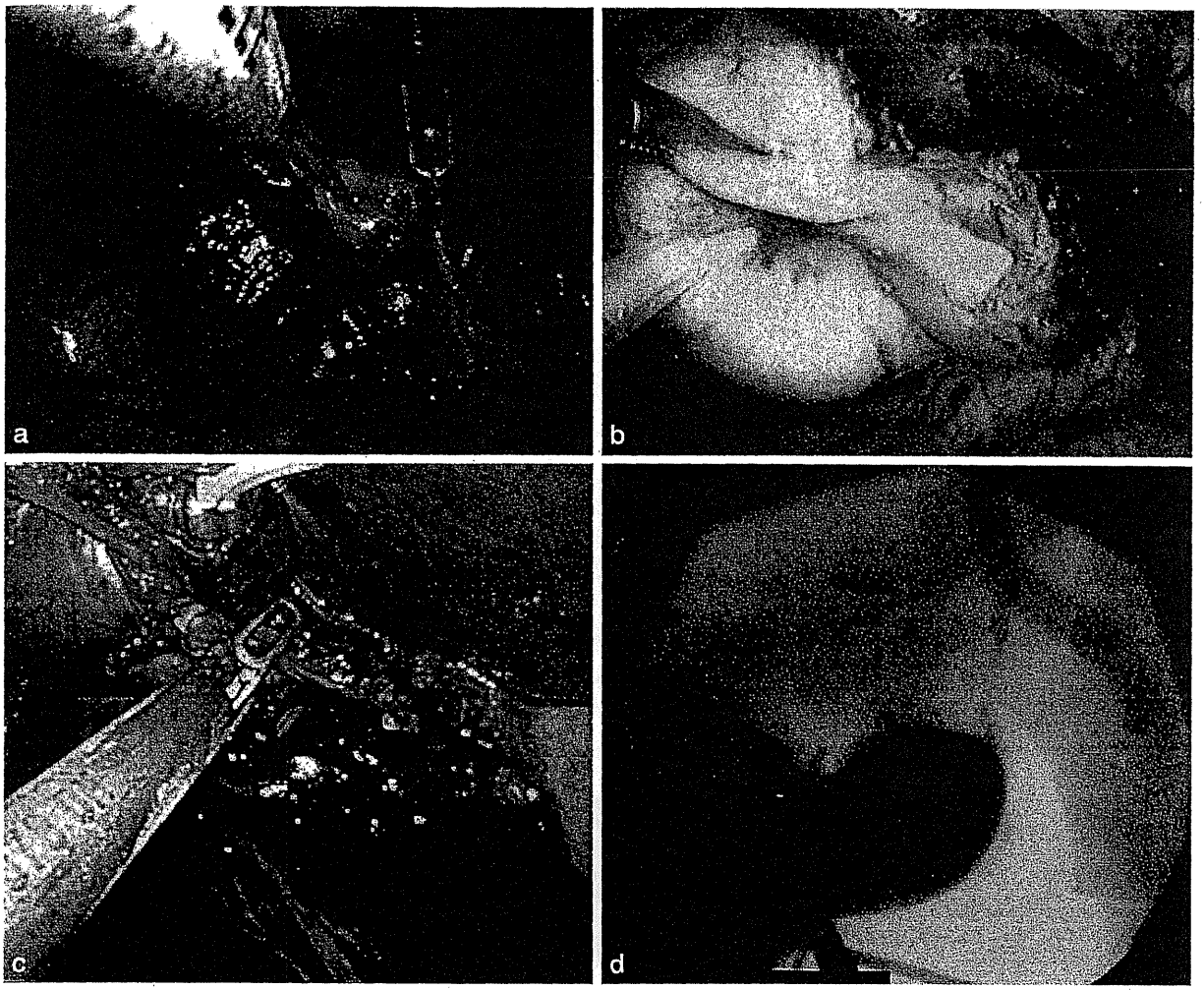

図 4　造影の工夫

a）胆道造影クランプ（Kumor 法）。
b）ペチニードル法（HAKKO）。
c）コラジオカテーテル法（HAKKO）。
d）術中胆道造影。

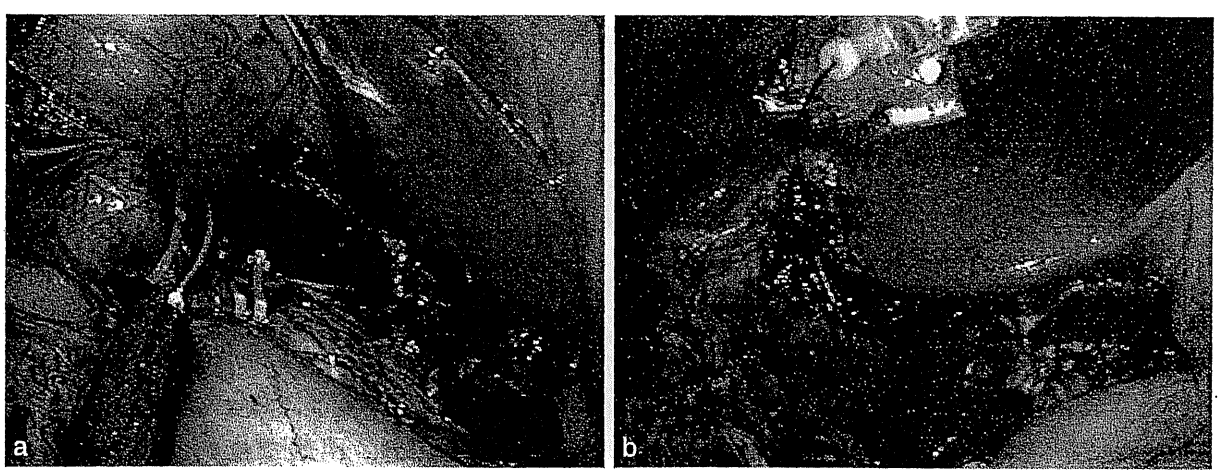

図 5　胆嚢摘出術

a）胆嚢管にクリップをかけ処理する。
b）胆嚢は回収袋（スリムバッグ）に入れて回収。