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Original Research Article

Prognostic Impact of Potentially Curative Resection for Synchronous Peritoneal Carcinomatosis with Lavage Cytology Positivity in Colorectal Cancer: A Retrospective Observational Study

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Abstract

Objectives: Although curative resection for synchronous peritoneal carcinomatosis has been reported to improve prognosis, cases with positive intraoperative lavage cytology have not been reported. In this study, we investigated the prognostic value of potentially curative resection based on colorectal cancer and lavage cytology positivity in patients with synchronous peritoneal carcinomatosis.

Methods: We retrospectively evaluated 72 patients who underwent intraoperative lavage cytology and one-stage potentially curative resection of primary and metastatic lesions (lavage cytology-positive, n = 21; lavage cytology-negative, n = 51) between July 2004 and December 2019. We compared the 5-year overall survival and 3-year recurrence rates between the lavage cytology-positive and lavage cytology-negative groups.

Results: No significant differences were observed in the 5-year overall survival (48.2% vs. 45.5%, P = 0.924) or 3-year recurrence rates (74.5% vs. 62%, P = 0.143) between the two groups. Univariate analysis for 3-year recurrence revealed that lavage cytology-positive status was not an explanatory variable (hazard ratio: 1.552, 95% confidence interval: 0.83-2.902, P = 0.169). Multivariate analysis identified colon cancer as an independent risk factor of recurrence.

Conclusions: In resectable cases, the resection of synchronous peritoneal carcinomatosis from colorectal cancer can be considered even if intraoperative lavage cytology is positive.

Keywords

peritoneal cytology, lavage cytology, colorectal cancer, prognosis

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Introduction

In colorectal cancer (CRC), intraoperative lavage cytology (LCY) is not a component factor in the TNM classification due to a lack of evidence[1]. Some studies have reported that intraoperatively positive LCY is a prognostic factor for recurrence and survival in patients with stage I-III CRC, and the significance of LCY as a staging factor has been discussed[2,3]. Although few studies have reported on the relationship between LCY and prognosis in patients with stage IV CRC[4,5], some have shown that LCY positivity is associated with a poor prognosis, even in stage IV cases. However, the evidence is currently insufficient.

Synchronous peritoneal carcinomatosis (PC) from CRC

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occurs in approximately 4-5% of patients[6,7]. The median duration of overall survival (OS) in patients with PC is reported to be 16.3 months[8], with a prognosis that is generally worse than that of patients with other metastases[7,8]. In addition, LCY positivity has been reported to be a prognostic factor in patients with PC of CRC[5]. However, therapeutic strategies for patients with stage IV LCY-positive CRC have not been sufficiently investigated. In particular, whether curative resection improves the prognosis of patients with LCY tumors remains controversial. To the best of our knowledge, researchers have yet to investigate the significance of potentially curative resection of both primary and metastatic lesions in synchronous PC from LCY-positive CRC. In this context, studies on LCY in CRC are relatively rare because intraoperative LCY is not a routine procedure, unlike in gastric cancer[9].

When LCY is diagnosed intraoperatively in patients with CRC, the decision to continue curative resection or to complete surgery with diagnostic laparoscopy and start systemic chemotherapy as soon as possible remains controversial. To address this challenge, this study aimed to investigate the prognostic value of potentially curative resection in patients with PC and LCY-positive CRC.

Methods

Study design and patients

This retrospective observational study reviewed clinicopathological data from our hospital database and was approved by the Institutional Review Board of the Cancer Institute Hospital of the Japanese Foundation for Cancer Research. The study was conducted in accordance with the 1964 Declaration of Helsinki and its amendments. The requirement for informed consent was waived due to the retrospective nature of the study. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies.

From the hospital database, we extracted data of adult patients with initial stage IV CRC and synchronous PC who underwent intraoperative LCY and surgical resection for both primary and metastatic lesions at the Cancer Institute Hospital, Japanese Foundation for Cancer Research, between July 2004 and December 2019. During the period, LCY was collected in all cases for CRC with resectable synchronous PC. The exclusion criteria were as follows: extra-abdominal metastasis, multiple cancers, multicentric cancer, non-potentially curative resection, and inability to follow-up postoperatively. Potentially curative resection was defined as a procedure in which both primary and metastatic lesions could be macroscopically resected. Patients with other intra-abdominal metastases (e.g. liver and para-aortic lymph nodes) were also included when potentially curative resection was performed for all lesions. Staging was performed according to the 8th edition of the Union for International Cancer Control (UICC) TNM classification[1].

Outcome measures

The 5-year overall survival (OS) and 3-year recurrence rates were evaluated to determine the prognosis of LCY positivity. Risk factors for poor OS and recurrence rates were also evaluated.

Data collection

Clinicopathological data were collected from the hospital databases. Sex, age, tumor location (colon or rectum), preoperative treatment, histological type of primary lesion, depth of tumor invasion, lymph node metastasis, area of PC, number of peritoneal nodule, size of peritoneal nodule, synchronous liver metastasis, synchronous para-aortic lymph node metastasis, adjuvant chemotherapy, duration between surgery and first follow-up computed tomography (CT), and surgical resection for recurrence were examined as clinicopathological factors. Histological grades were classified as low (well or moderately differentiated or papillary adenocarcinoma) or high (poorly differentiated or mucinous adenocarcinoma or signet-ring cell carcinoma). The area of PC was defined as follows: 'localized to the adjacent peritoneum' corresponds to P1 (metastasis localized to the adjacent peritoneum) in the JSCCR classification of peritoneal metastasis, and 'metastatic to the distant peritoneum' corresponds to P2 (limited metastasis to the distant peritoneum) and P3 (diffuse metastasis to the distant peritoneum)[10].

Cytology protocol

LCY was collected in all cases for CRC with resectable synchronous PC during the study period. The LCY protocols were in accordance with those reported by Matsui et al.[4]. Immediately after port insertion, 20 mL of physiological saline was instilled into the bottom of the pelvis in patients with rectal cancer and into the nearby side of the tumor in patients with colon cancer. The returned fluid was collected for peritoneal washing cytology. The fluids were immediately centrifuged for 5 min at 2500 rpm, the cell pellets were smeared on glass microscope slides, and Papanicolaou staining was performed according to conventional methods[11]. During surgery, cytological examinations were performed separately by two certified cytotechnologists and the final evaluation was performed by a cytopathologist.

In general, the results of cytological examinations are classified as "negative" when malignant cells are not observed, "suspicious" when atypical cells are present, and "positive" when malignant cells are present. In this study, the cytological results were defined as negative when malignant cells were not observed, and all other results (suspicious and positive) were considered positive.

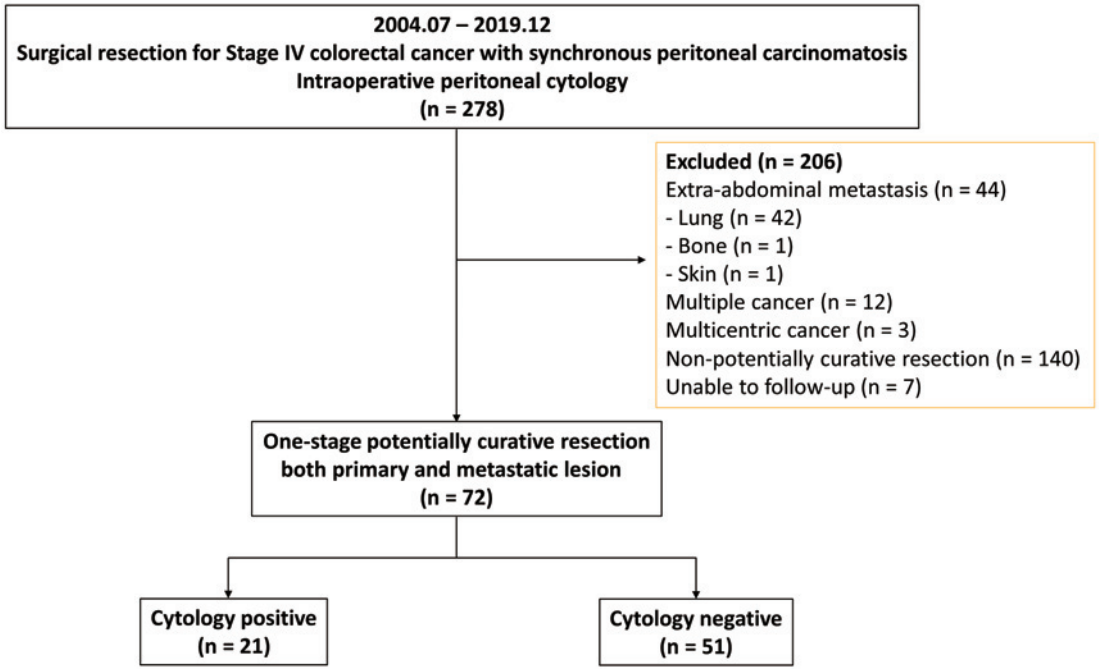

Figure 1. Study population and flowchart of patient enrollment.

Postoperative follow-up

Postoperative follow-up consisted of serum tumor marker measurements and CT scans approximately every three months for five years. In cases without recurrence more than two years after surgery, where the attending surgeon judged that the risk of recurrence was low, the interval for CT scans was extended to six months.

Statistical analysis

The clinicopathological parameters were analyzed using the Mann-Whitney U test and Fisher's exact test. The prognostic factors were analyzed using univariate and multivariate analyses. The 5-year OS rate was analyzed using a Cox proportional hazards regression model, while the 3-year recurrence rate was analyzed using a Fine-Gray proportional hazards regression model. Multivariate analysis included variables with $P < 0.1$ in the univariate analysis as covariates. The 5-year OS rate was estimated using the Kaplan-Meier method and compared between the groups using the log-rank test. The 3-year recurrence rate was estimated using the Gray's test. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan, version 1.50), a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria, version 3.6.3). More precisely, it is a modified version of R Commander (version 2.6-2), which is designed to add statistical functions that are frequently used in biostatistics[12]. Statistical significance was set at $P < 0.05$.

Results

Patient characteristics

Of the 278 patients, we excluded 44 with extra-abdominal metastasis (lung, n = 42; bone, n = 1; skin, n = 1), 12 with multiple cancer, three patients with multicentric cancer, 140 who underwent non-potentially curative resection, and seven patients who were unable to follow-up. Ultimately, 72 patients who underwent a one-stage potentially curative resection of both primary and metastatic lesions (LCY-positive, n = 21 [29.2%]; LCY-negative, n = 51 [70.8%]) were included in the analysis (Figure 1).

Table 1 shows the clinicopathological features of patients in the LCY-positive and LCY-negative groups. The median follow-up duration did not differ significantly between the two groups (38.3 months vs. 33.8 months, respectively; P = 0.577). No significant differences were observed between the LCY-positive and LCY-negative groups with respect to sex, age, tumor location, preoperative treatment, histological type, depth of tumor invasion, lymph node metastasis, rates of synchronous liver metastasis, rates of synchronous paraaortic lymph node metastasis, adjuvant chemotherapy, duration between surgery and first follow-up CT, surgical resection for recurrence, and area of PC (localized to the adjacent peritoneum: 57.1% vs. 60.8%; metastasis to distant peritoneum: 42.9% vs. 39.2%) (P = 0.797).

Table 1. Clinicopathological Features of All Patients and Comparison between LCY-Positive and LCY-Negative Patients.

Clinicopathological features		All cases n=72, n (%)	LCY-positive n=21, n (%)	LCY-negative n=51, n (%)	P-value
Follow-up duration (months), median (range)		34.3 (2.3-138.6)	38.3 (5.8-132.9)	33.8 (2.3-138.6)	0.577
Sex	Male	30 (41.7)	6 (28.6)	24 (47.1)	0.192
Age (years), median (range)		64.5 (25-89)	63 (28-81)	66 (25-89)	0.241
Location	Colon	41 (56.9)	13 (62)	28 (54.9)	0.613
	Rectum	31 (43.1)	8 (38)	23 (45.1)	
Preoperative treatment	None	70 (97.2)	21 (100)	49 (96.1)	1
	CRT	0 (0)	0 (0)	0 (0)	
	NAC	2 (2.8)	0	2 (3.9)	
Histological type	Low grade (tub, pap)	21 (29.2)	6 (28.6)	15 (29.4)	1
	High grade (por, sig, muc)	51 (70.8)	15 (71.4)	36 (70.6)	
Depth of tumor invasion	T3	8 (11.1)	1 (4.8)	7 (13.7)	0.423
	T4	64 (88.9)	20 (95.2)	44 (86.3)	
Lymph node metastasis	N0	11 (15.3)	2 (9.5)	9 (17.7)	0.57
	N1	31 (43)	11 (52.4)	20 (39.2)	
	N2	30 (41.7)	8 (38.1)	22 (43.1)	
Area of peritoneal metastasis	Localized to adjacent peritoneum	43 (59.7)	12 (57.1)	31 (60.8)	0.797
	Metastasis to distant peritoneum	29 (40.3)	9 (42.9)	20 (39.2)	
Number of peritoneal nodule	1	43 (59.7)	11 (52.4)	32 (62.7)	0.751
	2-4	25 (34.7)	9 (42.9)	16 (31.4)	
	≥ 5	4 (5.6)	1 (4.7)	3 (5.9)	
Size of peritoneal nodule*	< 10 mm	12 (31.6)	3 (25)	9 (34.6)	0.909
	≥ 10 mm, < 20 mm	14 (36.8)	5 (41.7)	9 (34.6)	
	≥ 20 mm	12 (31.6)	4 (33.3)	8 (30.8)	
Synchronous liver metastasis	Presence	14 (19.4)	5 (23.8)	9 (17.6)	0.532
Synchronous paraaortic lymph node metastasis	Presence	1 (1.4)	0 (0)	1 (2)	1
Adjuvant chemotherapy	Induced	55 (76.4)	18 (85.7)	37 (72.5)	0.361
Duration between surgery and first follow-up CT (months), median (range)		3.3 (0.8-9.5)	3.8 (1-8.5)	3.2 (0.8-9.5)	0.956
Surgical resection for recurrence **	Yes	11 (22.9)	5 (29.4)	6 (19.4)	0.486
	No	37 (77.1)	12 (70.6)	25 (80.6)	

LCY: lavage cytology, CRT: chemoradiotherapy, CT: computed tomography, NAC: neoadjuvant chemotherapy, tub: tubular adenocarcinoma, pap: papillary adenocarcinoma, por: poorly differentiated adenocarcinoma, sig: signet-ring cell carcinoma, muc: mucinous adenocarcinoma

*n = 38 (LCY-positive: n = 12, LCY-negative: n = 26)

**n = 48 (LCY-positive: n = 17, LCY-negative: n = 31), including cases who underwent preoperative therapy for recurrence

Prognostic impact of cytology positive for long-term outcomes

Figure 2 shows the Kaplan-Meier curves for 5-year OS in the LCY-positive and LCY-negative groups. No significant differences were observed in the 5-year OS rates between the two groups (48.2% vs. 45.5%, P = 0.924). The median OS in months was 48.4 months in the LCY-positive group and 51.3 months in the LCY-negative group. Table 2 shows the results of the univariate and multivariate Cox proportional hazard regression analyses for 5-year OS. Multivariate analysis identified age ≥ 70 years (HR: 2.896, 95% CI: 1.308-6.412, P = 0.009) and colon cancer (HR: 3.82, 95% CI: 1.139-12.82, P = 0.03) as independent prognostic factors for poor OS. LCY-positivity was not an independent prognostic factor for poor OS. Figure 3 shows the cumulative 3-year recurrence rates in the LCY-positive and LCY-negative groups. The recurrence rate was higher in the LCY-positive group (74.5%) than that in the LCY-negative group (60.8%); however, this difference was not statistically significant (P = 0.143). The median recurrence-free months were 9.8 months in the LCY-positive group and 18.7 months in the LCY-negative group. Table 3 shows the results of the univariate and multivariate fine-gray proportional hazard regression

analyses for 3-year recurrences. Multivariate analysis identified colon cancer (hazard ratio [HR], 2.92; 95% CI, 1.107-7.717; P = 0.03) as an independent risk factor for recurrence, and T4 tumors were associated with a lower risk of recurrence (HR, 0.408; 95% CI: 0.181-0.916, P = 0.03). LCY-positivity was not an independent risk factor for recurrence.

Relationship between cytology findings and recurrence types

Table 4 shows the types of recurrence in the LCY-positive and LCY-negative groups. The total recurrence rate in the LCY-positive group (81%) was higher than that in the LCY-negative group (60.8%); however, the difference was not statistically significant (P = 0.168). There were no significant differences in any recurrence types between the LCY-positive and LCY-negative groups.

Discussion

To our knowledge, this study is the first to investigate the prognostic impact of the potentially curative resection of synchronous PC in LCY-positive CRC. The long-term outcomes, especially OS, were found to be comparable between the LCY-positive and LCY-negative groups. Although this was a single-center retrospective study, the results provide

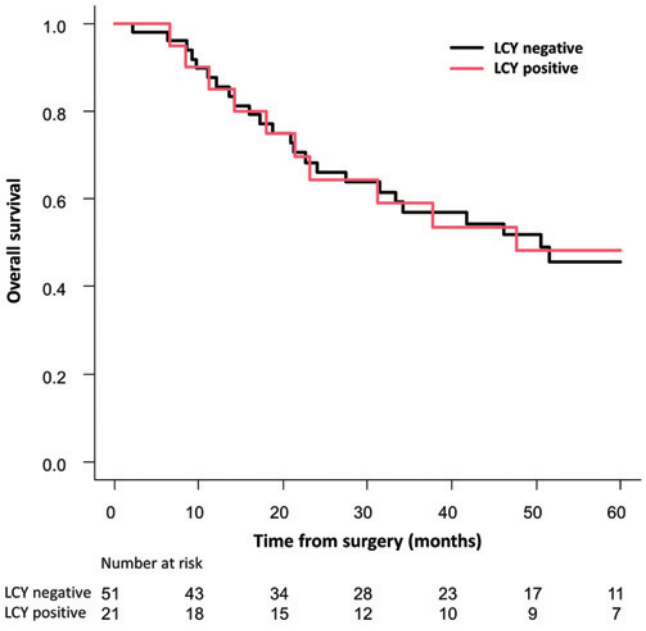

Figure 2. Kaplan-Meier curves for 5-year overall survival.

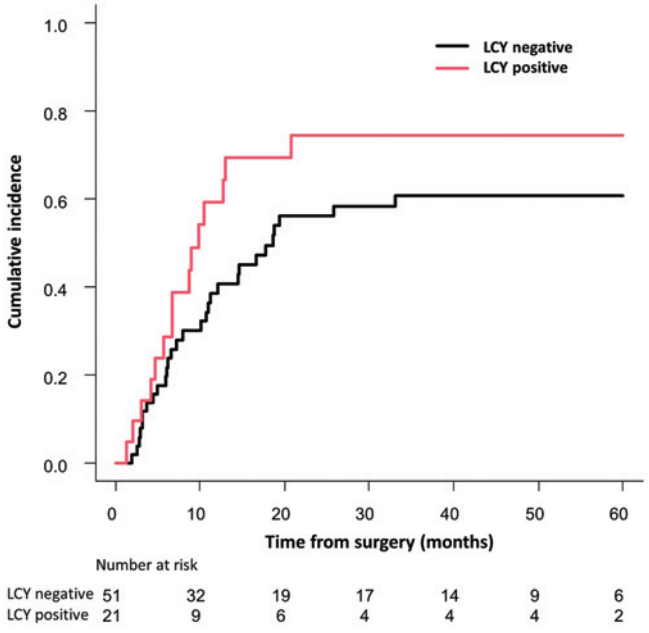

Figure 3. Cumulative 3-year recurrence rate.

Table 2. Cox Proportional Hazards Regression Analyses for 5-Year OS.

Prognostic factors (n = 72)		n	Univariate analysis		Multivariate analysis	
			HR (95% CI)	P-value	HR (95% CI)	P-value
Sex	Male	30	1.179 (0.595-2.335)	0.638	-	
Age	≥70 years	26	2.334 (1.182-4.608)	0.015	2.896 (1.308-6.412)	0.009
Location	Colon	41	4.224 (1.265-14.11)	0.019	3.82 (1.139-12.82)	0.03
Histological grade	High grade (por, sig, muc)	51	0.918 (0.428-1.968)	0.825	-	
Depth of tumor invasion	T4	64	0.715 (0.276-1.848)	0.489	-	
Lymph node metastasis	N2	30	1.313 (0.669-2.576)	0.429	-	
Area of peritoneal metastasis	Metastasis to distant peritoneum	29	1.474 (0.752-2.889)	0.259	-	
Number of peritoneal nodule	Multiple	29	1.339 (0.683-2.628)	0.396	-	
Size of peritoenal nodule*	≥ 20 mm	12	0.643 (0.249-1.661)	0.361	-	
Synchronous liver metastasis	Present	14	1.565 (0.729-3.355)	0.249	-	
Adjuvant chemotherapy	Not induced	17	1.309 (0.61-2.806)	0.489	-	
Cytology findings	Positive	21	0.965 (0.461-2.018)	0.924	-	

OS: overall survival, HR: hazard ratio, CI: confidence interval

*n = 38 (LCY-positive: n = 12, LCY-negative: n = 26)

Table 3. Fine-Gray Proportional Hazards Regression Analyses for 3-Year Recurrence.

Prognostic factors (n = 72)		n	Univariate analysis		Multivariate analysis	
			HR (95% CI)	P-value	HR (95% CI)	P-value
Sex	Male	30	1.12 (0.615-2.04)	0.71	-	
Age	≥70 years	26	1.525 (0.824-2.821)	0.18	-	
Location	Colon	41	3.381 (1.335-8.558)	0.01	2.92 (1.107-7.717)	0.03
Histological grade	High grade (por, sig, muc)	51	0.734 (0.376-1.433)	0.37	-	
Depth of tumor invasion	T4	64	0.474 (0.206-1.092)	0.08	0.408 (0.181-0.916)	0.03
Lymph node metastasis	N2	30	0.884 (0.482-1.624)	0.69	-	
Area of peritoneal metastasis	Metastasis to distant peritoneum	29	1.642 (0.917-2.942)	0.095	1.733 (0.793-3.79)	0.17
Number of peritoneal nodule	Multiple	29	1.256 (0.706-2.235)	0.44	-	
Size of peritoenal nodule*	≥ 20 mm	12	0.721 (0.284-1.828)	0.49	-	
Synchronous liver metastasis	Present	14	1.695 (0.854-3.365)	0.13	-	
Adjuvant chemotherapy	Not induced	17	0.989 (0.463-2.112)	0.98	-	
Cytology findings	Positive	21	1.594 (0.849-2.993)	0.15	-	

HR: hazard ratio, CI: confidence interval

*n = 38 (LCY-positive: n = 12, LCY-negative: n = 26)

Table 4. Sites of Recurrence.

Variables	All cases n = 72, n (%)	LCY-positive n = 21, n (%)	LCY-negative n = 51, n (%)	P value
Total	48 (66.7)	17 (81)	31 (60.8)	0.168
Peritoneal*	26 (36.1)	10 (47.6)	16 (31.4)	0.28
Liver*	16 (22.2)	6 (28.6)	10 (19.6)	0.534
Lung*	5 (6.9)	2 (9.5)	3 (5.9)	0.625
Distant lymph nodes*	15 (20.8)	4 (19)	11 (21.6)	1
Local recurrence*	1 (1.4)	1 (4.8)	0 (0)	0.292
Spleen*	1 (1.4)	1 (4.8)	0 (0)	0.292

LCY: lavage cytology

*There are some duplications

useful insights for the development of therapeutic strategies for PC from LCY-positive CRC.

According to a previous study, patients with stage IV CRC with initial PC and cytological positivity have a particularly poor prognosis[5]. The cytology-positive group demonstrated poorer cancer-specific survival (CSS) than the cytology-negative group (3-year CSS: 14.6% vs. 50.2%; 5-year CSS: 0% vs. 32.5%; all $P < 0.001$). At present, therapeutic strategies for improving the prognosis of patients with stage IV CRC with PC and LCY-positivity remain controversial. A previous study conducted at our institution evaluated the poorer prognosis following curative resections in patients with stage III or IV CRC[4]. However, in that study, not all Stage IV patients had PC, and the LCY-positive group included more cases with PC (62.5% vs. 9.2%), while most of the LCY-negative cases had liver metastasis (87.5%). Differences in metastatic types may have influenced the results. In the present study, all patients had synchronous PC, so the patient background was more consistent compared to the previous study. Therefore, the results of the present study seem to better reflect the true prognostic value of LCY. On the other hands, prognostic value of LCY seems to be different for stage III cases. In Stage III cases with curative resection and LCY-negative, it can be judged that the tumor cells have been completely resected. However, when the LCY result is positive, it is considered that microscopic residual tumor cells remain, even if the tumor has been macroscopically resected. Therefore, in cases with a positive LCY, the prognosis is closer to that of stage IV, and LCY positivity is considered to be a prognostic factor.

In CRC, the potentially curative resection of synchronous PC has been reported to improve long-term outcomes[13-16]. In addition, the prognostic impact of curative resection for the peritoneal recurrence of CRC has also been reported[17]. The clinical challenge addressed in the present study was whether potentially curative resection of the primary lesion and PC improves prognosis, even if LCY is positive. Our results may suggest a certain significance for achieving comparable long-term outcomes to LCY-negative group. Considering the results, potentially curative resection

seems to be beneficial for improving prognosis, even in LCY-positive cases. In particular, the OS was comparable between the LCY-positive and LCY-negative groups. Shida et al. reported that the 5-year OS rate after the curative resection of synchronous peritoneal metastases without distant metastases was 28.7%[15]. In our study, the 5-year OS rates were 48.2% in the LCY-positive group and 46.4% in the LCY-negative group (Figure 2), despite the fact that the cohort included patients with other intra-abdominal metastases. However, whether curative resection improves the recurrence rates should be carefully considered. Although there were no significant differences, the 3-year recurrence rate (74.5% vs. 62%, P = 0.143) and the rate of peritoneal recurrence (47.6% vs. 31.4%, P = 0.28) were found to be slightly worse in the LCY-positive group. The reason for the satisfactory OS compared to recurrence rates in the LCY-positive group may be the aggressive resection of metastatic lesions[18] in our hospital. In the present study, five patients (29.4%) in the LCY-positive group and six patients (19.4%) in the LCY-negative group underwent surgical resection for recurrence (Table 1). In addition, intensive adjuvant therapies and careful postoperative follow-up also should be considered in cases of LCY-positive to introduce appropriate therapy for recurrence. In our institution, postoperative follow-up CT scans are conducted every three months after the resection of PC, regardless of LCY positivity. This frequent CT follow-up may contribute to the early detection of recurrence. In addition, frequent follow-up using second-look diagnostic laparoscopy has been reported to be useful for the early detection of peritoneal recurrence[17], and surgical resection for localized peritoneal recurrence may improve survival[19]. When peritoneal recurrence is suspected, a second-look diagnostic laparoscopy is an optional diagnostic modality.

In the present study, peritoneal metastasis distant from the primary lesion and multiple PC were not found to be an independent risk factor for poor OS or recurrence (Table 2, 3). Based on these findings, surgical resection of both primary and metastatic lesions can be considered in cases of LCY positivity, even in cases of PC located in the distant peritoneum or multiple PC. However, peritoneal metastasis to the distant peritoneum may be a risk factor for recurrence, as the univariate analysis demonstrated a higher HR. To improve OS, postoperative management for the early detection of recurrence, such as intended early postoperative second-look diagnostic laparoscopy, may be important, especially in cases of distant peritoneal metastasis. In this context, it may also be useful to search for early recurrence using ctDNA[20]. Hyperthermic intraperitoneal chemotherapy (HIPEC) is effective in improving the prognosis of diffuse metastases to the distant peritoneum[21,22]. However, a recent multicenter randomized phase III trial (PRODIGE 7) reported that HIPEC did not improve OS and increased the 60 days grade 3 or worse adverse events compared with cytoreductive surgery alone[23]. Based on these results, surgical resection may be safer and more widely available than HIPEC. Thus, the therapeutic strategies for metastasis to the distant peritoneum should be discussed further.

The present study included 14 patients (19.4%) with both PC and liver metastases. In Cox proportional hazards regression analyses, synchronous liver metastasis was not an independent risk factor for poor OS or recurrence (Table 2, 3). Even though a previous study found that liver metastasis is an independent risk factor for poor OS in patients with CRC and synchronous PC[13], our results suggested that resection of liver metastasis does not significantly contribute on prognostic improvement regardless of LCY positivity.

This study has a strange result that the T4 tumors were associated with a lower risk of recurrence (Table 3). The reasons are controversial; however, the induction rates of adjuvant chemotherapy were significantly higher in the T4 cases than T3 cases (81.3% vs. 37.5%, P = 0.015). This higher induction rate of adjuvant chemotherapy may influence the results.

This study has some limitations. First, this was a retrospective single-center study. However, no significant differences in patient backgrounds existed between the LCY-positive and LCY-negative groups (Table 1). Second, the median follow-up duration of the entire cohort was relatively short (34.3 months). Thus, the data obtained from our cohort may be insufficient to draw definitive conclusions. However, the median follow-up duration for the survivors was 56 months, and our results were significant. Third, the diagnostic accuracy may vary depending on the collection method of the LCY by each surgeon. Fourth, the sample size of the LCY-positive patients was small (n = 21). Because intraoperative LCY is not routinely performed for CRC, most cytological studies have small sample sizes and may suffer from selection bias[2]. In particular, the number of patients with stage IV disease in previous studies[4,5]. Our department routinely performs intraoperative LCY for approximately 95% of patients with CRC[4] and all patients with resectable synchronous PC. Therefore, selection bias was minimized. However, in the future, multicenter large-scale studies will need to be conducted to verify our results.

In conclusion, the present study investigated the potential of prognostic impact of potentially curative resection in LCY-positive patients with peritoneally disseminated stage IV CRC. Although concerns regarding worsened recurrence rates remain, OS was found to be comparable between the LCY-positive and LCY-negative groups. If possible, the potentially curative resection of both primary and metastatic lesions of synchronous PC from CRC may be considered, even if intraoperative LCY is positive.

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Conflicts of Interest

There are no conflicts of interest.

Author Contributions

Conceptualization: Kentaro Sato, Shimpei Matsui, Tomohiro Chiba, Tatsuki Noguchi, Takashi Sakamoto, Toshiki Mukai, Tomohiro Yamaguchi, Takashi Akiyoshi, and Yosuke Fukunaga; methodology: Kentaro Sato, Shimpei Matsui, and Tomohiro Chiba; formal analysis and investigation: Kentaro Sato; writing - original draft preparation: Kentaro Sato and Shimpei Matsui; writing - review and editing: Kentaro Sato and Shimpei Matsui; funding acquisition: not applicable; resources: not applicable; supervision: Yosuke Fukunaga.

Approval by Institutional Review Board (IRB)

This study was approved by the Institutional Review Board of the Cancer Institute Hospital, Japanese Foundation for Cancer Research (Tokyo, Japan; reference no. 2024-GB-022).

Consent to Participate

The need for informed consent to participate in the study was waived due to the retrospective nature of the study.

Consent for Publication

The need for informed consent was waived due to the retrospective nature of the study.

Availability of Data and Material

The data supporting this study's findings are available upon request from the corresponding author.

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