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ORIGINAL ARTICLE

Influence of hospital type on survival in stage IV colorectal cancer

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Abstract
Purpose Hospital factors along with various patient and surgeon factors are considered to affect the prognosis of colorectal cancer. Hospital volume is well known, but little is known regarding other hospital factors.
Methods We reviewed data on 853 patients with stage IV colorectal cancer who underwent elective palliative primary tumor resection between January 2006 and December 2007. To detect the hospital factors that could influence the prognosis of incurable colorectal cancer, the relationships between patient/hospital factors and overall survival were analyzed. Among hospital factors, hospital type (Group A: university hospital or cancer center; Group B: community hospital), hospital volume, and number of colorectal surgeons were examined.
Results In univariate analysis, Group A hospitals showed significantly better prognosis than Group B hospitals ($p = 0.034$), while hospital volume and number of colorectal surgeons were not associated with overall survival. After adjustment for patient factors in multivariate analysis, hospital type was significantly associated with overall survival (hazard ratio: 1.31; 95 % confidence interval: 1.05–1.63; $p = 0.016$). However, there was no significant difference in short-term outcomes between hospital types.
Conclusions Hospital type was identified as a hospital factor that possibly affects the prognosis of stage IV colorectal cancer patients.

Keywords Colorectal neoplasms · Survival · Stage IV · Hospital factors

Introduction

Many reports have observed that hospital factors along with various patient and surgeon factors affect the short-term and long-term outcomes of patients undergoing surgery for colorectal cancer [1, 2]. Hospital volume is the best known example of a hospital factor [3, 4]. Patients with stage IV colorectal cancer need support from various medical professionals with diverse backgrounds and skills, including colorectal surgeons, medical oncologists, radiologists, and palliative care physicians. Accordingly, their prognosis is possibly influenced by many factors [5–8]. However, little is known regarding the hospital factors that may affect the prognosis of patients with incurable colorectal cancer. Therefore, in this study, we assessed certain hospital factors that potentially affected the prognosis of patients with stage IV colorectal cancer who underwent palliative primary tumor resection.

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Table 1 Patient background characteristics

Patient factor	Category	Number	%
Age (years)	<75	693	81.2
	≥75	160	18.8
Sex	Male	492	57.7
	Female	361	42.3
Tumor depth	T2-3	476	55.8
	T4	377	44.2
Lymph node metastasis	−	138	16.5
	+	700	83.5
Hepatic metastasis	−	227	26.7
	+	623	73.3
Peritoneal metastasis	−	625	73.5
	+	225	26.5
Distant metastasis	−	475	56.1
	+	371	43.9
Tumor location	Right colon	281	33.5
	Left colon	392	46.7
	Rectum	167	19.9
Surgical approach	Open	637	74.7
	Laparoscopy	216	25.3
Scope of lymph node dissection	D2	176	21.0
	D3	663	79.0
Preoperative intestinal stenosis	−	441	52.9
	+	392	47.1
CEA (ng/mL)	<5	173	20.4
	≥5	674	79.6
CA19-9 (U/mL)	<37	427	50.7
	≥37	415	49.3
ASA-PS	1	396	46.9
	2-3	448	53.1
Preoperative chemotherapy	−	799	93.7
	+	54	6.3
Postoperative chemotherapy	−	140	16.4
	+	713	83.6

ASA-PS American Society of Anesthesiologists - Physical Status, *CA19-9* carbohydrate 19–9, *CEA* carcinoembryonic antigen

Materials and methods

Patients

The Japan Society of Laparoscopic Colorectal Surgery (JSLCS) retrospectively collected data on 968 patients with stage IV colorectal cancer who underwent palliative tumor resection at 41 participating hospitals between January 2006 and December 2007. All surgeons were experienced in laparotomy, and most of them performed over 100 laparoscopic surgeries [9]. From the 968 patients, we excluded 37 patients who had active cancer in other organs, 5 patients with a performance status of 4, 51 patients who underwent emergency operation, and 23 patients who underwent insufficient lymph node dissection (D0 or D1). We included only patients undergoing D2 or D3 lymph node dissection. The scope of lymph node dissection was classified between D0 and D3 according to guidelines from the Japanese Society for Cancer of the Colon and Rectum [10]. D2 lymph node dissection indicates the removal of pericolic and intermediate lymph nodes, and D3 involves removal of pericolic, intermediate, and main lymph nodes around the root of the regional artery. Hepatic and peritoneum metastases were distinguished from distant metastasis according to Japanese classification [10]. Finally, 853 patients who underwent elective palliative tumor resection with sufficient scope of lymph node dissection were included in the analyses.

Table 2 Hospital characteristics

Hospital factor	Category	Hospitals		Patients	
		n	%	*n*	%
Hospital type	Group A	28	68.3	626	73.4
	Group B	13	31.7	227	26.6
Hospital volume (operations/year)	≥200	10	24.4	350	41.0
	<200	31	75.6	503	59.0
Number of colorectal surgeons	≥5	20	48.8	396	46.4
	<5	21	51.2	457	53.6

Hospital factors

This study included 41 hospitals that participated in the JSLCS study. We focused on three hospital factors, namely hospital type (university hospital, cancer center, or community hospital), hospital volume, and number of colorectal surgeons. In Japan, university hospitals and cancer centers play a leading role in cancer care, and we divided the hospitals into the following two groups according to the hospital type: (1) group A, which included university hospitals and cancer centers, and (2) group B, which included community hospitals. Hospital volume was defined as the average annual number of colorectal cancer patients who underwent surgery in each institution.

Statistical analysis

Continuous variables were compared by Student's *t* test. Categorical valuables were compared by Fisher's exact test. Survival analyses were performed with Kaplan-Meier estimates, and they were compared by the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model. Overall survival (OS) was defined as the time between the date of primary tumor resection and the

Table 3 Patient factors associated with overall survival

Patient factor	Category	Number	Event (*n*)	Median survival (day)	*p* value
Age (years)	<75	692	380	788	<0.001
	≥75	159	104	442	
Sex	Male	489	264	784	0.074
	Female	360	220	667	
Tumor depth	T2-3	473	241	852	<0.001
	T4	376	243	636	
Lymph node metastasis	−	138	54	1072	<0.001
	+	696	418	694	
Hepatic metastasis	−	227	105	976	<0.001
	+	619	378	668	
Peritoneal metastasis	−	623	341	787	0.002
	+	223	142	620	
Distant metastasis	−	472	254	804	0.010
	+	370	227	647	
Tumor location	Right colon	278	180	619	<0.001
	Left colon	391	207	798	
	Rectum	167	90	825	
Surgical approach	Open	634	375	703	0.047
	Laparoscopy	215	109	860	
Scope of lymph node dissection	D2	173	127	466	<0.001
	D3	662	349	831	
Preoperative intestinal stenosis	−	440	237	831	0.006
	+	390	237	631	
CEA (ng/mL)	<5	172	74	1025	<0.001
	≥5	671	407	674	
CA19-9 (U/mL)	<37	424	202	909	<0.001
	≥37	414	276	599	
ASA-PS	1	393	201	904	<0.001
	2–3	447	277	631	
Preoperative chemotherapy	−	795	449	737	0.185
	+	54	35	555	
Postoperative chemotherapy	−	137	97	308	<0.001
	+	712	387	798	

ASA-PS American Society of Anesthesiologists - Physical Status, *CA19-9* carbohydrate 19–9, *CEA* carcinoembryonic antigen

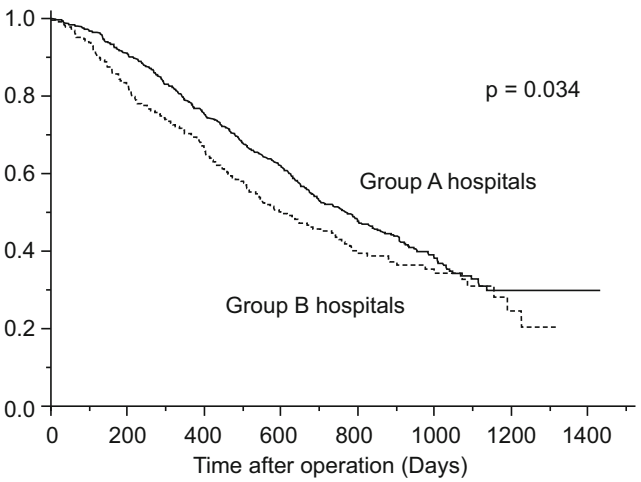

Fig. 1 Overall survival of patients stratified by hospital type

date of death. All *p* values were two-sided, and *p* values less than 0.05 were considered statistically significant. All statistical analyses were performed using JMP Statistical Software Version 11 (SAS-Institute Inc., Cary, NC).

Results

The clinicopathological characteristics of the 853 patients are shown in Table 1, and the characteristics of the 41 participating hospitals are described in Table 2. Groups A and B comprised 28 and 13 institutions, respectively, and the numbers of patients treated in each hospital group were 626 and 227, respectively. Hospital volume was classified into two categories of ≥200 and <200 operations/year, with 10 institutions

Table 4 Hospital factors associated with overall survival

Hospital factor	Category	Number	Event (*n*)	Median survival (day)	*p* value
Hospital type	Group A	622	344	772	0.034
	Group B	227	140	616	
Hospital volume (operations/year)	≥200	350	201	751	0.713
	<200	499	283	683	
Number of colorectal surgeons	≥5	392	210	761	0.186
	<5	457	274	732	

(350 patients) and 31 institutions (503 patients) classified into the respective categories. The number of colorectal surgeons in each institute was divided into two categories of ≥5 and <5, with 20 institutions (396 patients) and 21 institutions (457 patients) classified into the respective categories.

Among patient factors, age, tumor depth, regional lymph node metastasis, hepatic metastasis, peritoneal metastasis, distant metastasis, tumor location, surgical approach, scope of lymph node dissection, preoperative intestinal stenosis, carcinoembryonic antigen (CEA), carbohydrate 19–9 (CA19-9), American Society of Anesthesiologists - Physical Status (ASA-PS) score, and postoperative chemotherapy were significantly associated with OS (Table 3). Among hospital factors, only hospital type was significantly associated with

Table 5 Factors associated with overall survival

Factor		Category	HR	95 % CI	*p* value
Patient	Age (years)	<75	Ref		<0.001
		≥75	1.58	1.23–2.02	
	Tumor depth	T2-3	Ref		0.011
		T4	1.30	1.06–1.59	
	Lymph node metastasis	−	Ref		<0.001
		+	1.62	1.22–2.22	
	Hepatic metastasis	−	Ref		<0.001
		+	1.71	1.33−2.21	
	Peritoneal dissemination	−	Ref		0.045
		+	1.28	1.01–1.63	
	Distant metastasis	−	Ref		0.002
		+	1.36	1.12–1.65	
	Tumor location	Right colon	Ref		0.073
		Left colon	0.77	0.62–0.96	
		Rectum	0.88	0.66–1.16	
	Surgical approach	Open	Ref		0.739
		Laparoscopy	1.04	0.82–1.30	
	Scope of lymph node dissection	D2	Ref		<0.001
		D3	0.60	0.48–0.76	
	Preoperative intestinal stenosis	−	Ref		0.084
		+	1.19	0.98–1.44	
	CEA (ng/mL)	<5	Ref		0.250
		≥5	1.18	0.89–1.59	
	CA19-9 (U/mL)	<37	Ref		<0.001
		≥37	1.56	1.28–1.92	
	ASA-PS	1	Ref		0.006
		2–3	1.31	1.08–1.60	
	Postoperative chemotherapy	−	Ref		<0.001
		+	0.51	0.39–0.66	
Hospital	Hospital type	Group A	Ref		0.016
		Group B	1.31	1.05–1.62	

ASA-PS American Society of Anesthesiologists - Physical Status, *CA19-9* carbohydrate 19–9, *CEA* carcinoembryonic antigen, *Ref* reference

Table 6 Short-term outcomes

Hospital type		Group A	Group B	*p* value
Factor	Hospitals (*n*)	28	13	
	Patients (*n*)	626	227	
	Category			
Resumption of oral intake (days)	Median (range)	2 (1–42)	2 (1–21)	0.575
Length of hospital stay (days)	Median (range)	15 (1–142)	17 2–110)	0.134
Conversion to open surgery	−	136	62	0.645
	+	19	6	
Intraoperative complications	−	620	227	0.350
	+	6	0	
Postoperative complications	−	482	187	0.109
	+	144	40	

OS, and OS was significantly higher in the group A hospitals than in the group B hospitals (median survival time: 772 vs. 616 days, $p = 0.034$) (Fig. 1). The other hospital factors—hospital volume and number of colorectal surgeons—were not associated with OS (Table 4). In multivariate analysis, hospital type remained significantly associated with OS even after adjusting for patient factors (Table 5).

Short-term outcomes after primary tumor resection were compared between the group A and B hospitals; these results are shown in Table 6. There were no significant differences between the two groups in terms of resumption of oral intake, length of postoperative hospital stay, conversion from laparoscopic to open surgery, intraoperative complications, or postoperative complications (National Cancer Institute Common Terminology Criteria for Adverse Events v3.0 ≥ grade 2).

Discussion

Outcomes of patients with colorectal cancer are believed to be influenced by hospital factors as well as tumor, patient, and surgeon factors [1, 2]. Many reports have described an effect of hospital volume on both short-term and long-term outcomes in patients with colorectal cancer [3, 4]. Recently, hospital type has been focused on as an influential factor in various disease groups, such as pediatric disease, urologic cancer, breast cancer, and hepatocellular carcinoma [11–14]. With respect to colorectal cancer, Elferink et al. [15] reported that different hospital types showed significant differences in treatment and long-term outcomes. The treatment of incurable stage IV colorectal cancer shows greater diversity than that of other, curable stages because these patients are treated with multimodality therapy, including medical oncology, radiology, and symptomatic palliative care [6]. Therefore, the survival of patients with stage IV colorectal cancer is expected to be highly influenced by hospital factors. However, little is known regarding the impact of hospital type on the prognosis of patients with stage IV colorectal cancer. In this study, we examined several hospital-related factors, and only hospital type was significantly associated with prognosis, while hospital volume and number of colorectal surgeons were not.

Regarding the reason for better OS in the group A hospitals than in the group B hospitals, we consider that the main difference is the number and variety of cancer specialists apart from surgeons. In Japan, university hospitals and cancer centers (group A hospitals) have many specialists from various fields who are actively involved in cancer care, as compared with community hospitals (group B), which have fewer cancer specialists. Specialized cancer care has been reported to improve outcomes in various cancers, including colorectal cancer, breast cancer, and ovarian cancer [16]. In particular, systemic chemotherapy has been reported to improve survival in patients with incurable colorectal cancer [17, 18], but there are considerable variations in the administration of chemotherapy across hospitals [19]. Japan has faced a chronic shortage of medical oncologists, similar to many other countries [20, 21]. In the present study period (2006–2007), more intensive and toxic chemotherapy, such as FOLFOX and FOLFORI, were introduced into clinical practice in Japan, leading to a greater need for medical oncologists specialized in colorectal cancer chemotherapy. In this study, postoperative chemotherapy significantly improved OS ($p < 0.001$), but there was no significant difference between group A and B hospitals in the proportion of patients who received postoperative chemotherapy (84.0 vs. 80.6 %, $p = 0.174$). Therefore, the management of chemotherapy by the oncologists might affect patients' prognosis. An inhomogeneous distribution of such specialists across hospitals might contribute to the prognostic differences between group A and B hospitals.

Supportive care is also an essential factor in cancer care. Such care is reported to improve the patients' condition and can help in continuing cancer therapy [7, 8]. Although it is difficult to assess the quality of supportive care, it has been reported that there might be large disparities between hospitals [22]. Higher quality supportive care in group A hospitals might improve the postoperative prognosis of patients with

stage IV colorectal cancer who undergo palliative primary tumor resection.

On the other hand, we did not observe any differences between the hospital types in short-term outcomes, including postoperative complication rates and length of hospital stay, which are well-known indicators of the quality of curative colorectal surgery. A possible explanation for this finding is that our study only included hospitals with experienced specialists in colorectal surgery, and so the quality of surgery did not differ by hospital type. Further, in the management of patients with incurable colorectal cancer, the impact of the primary cancer surgery on patient survival might be relatively small compared with the impact of multimodality treatment [23, 24].

This study has some limitations, including its retrospective nature and a possible selection bias, although we made adjustments to minimize the effects of both surgeon factors and patient diversity. Therefore, it may be difficult to generalize our findings. Another limitation is that we lacked information on the patients' comorbidities and details of postoperative therapies. These factors might influence patient outcomes, but we made best effort to minimize the effect of disease other than colorectal cancer by excluding the patients with insufficient lymph node dissection, which was often performed in patients with severe comorbidities. Despite these limitations, we believe that the results of this study help in resolving medical inequality across hospitals.

In conclusion, hospital type was identified as a significant prognostic factor for OS in patients with stage IV colorectal cancer undergoing palliative primary tumor resection.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animal rights and informed consent For this type of study formal consent is not required.

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