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Prevalence of Synchronous Colorectal Neoplasms Detected by Colonoscopy in Patients with Gastric Cancer

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Abstract

Purpose. Our purpose was to study the characteristics of colorectal neoplasms in patients with gastric cancer (GC).

Methods. The study group comprised GC patients who underwent colonoscopy before resection of their GC. We examined the prevalence, site, and histology of colorectal neoplasms, as well as the clinicopathological features and treatment of the patients who had synchronous colorectal cancers (CRC). The logistic regression model was applied to investigate the features of the GC patients with concurrent CRC.

Results. We studied 466 GC patients (mean age 64.5 years; 147 women, 319 men), 143 (31%) of whom had a family history of gastrointestinal cancer. Synchronous colorectal adenoma and cancer were detected in 182 (39%) and 18 (4%) patients, respectively. Among the 18 synchronous CRCs, 11 were in the early stages and 10 of these were resected endoscopically. The other eight required simultaneous open radical surgery. All the GC patients with synchronous CRC were older than 50 years. Statistical analysis did not show a significant difference between the features of the patients with and those without concurrent CRC.

Conclusions. The possibility of synchronous colorectal neoplasms in GC patients cannot be disregarded in clinical practice; however, screening of the large bowel may not be necessary in GC patients younger than 50 years.

Key words Synchronous gastric cancer · Synchronous colorectal cancer · Endoscopy

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Introduction

An aging population and advances in diagnostic imaging techniques have led to an increase in the incidence and rate of detection of multiple primary cancers.[1–3] Multiple primary cancers are more likely to develop in organs of the same system than in those of different systems.[3] In Japan, Italy, and Korea, colorectal cancer (CRC) is the most common synchronous neoplasm associated with gastric cancer (GC).[4–7] The incidence of metachronous CRC has also been reported to increase after gastrectomy or cholecystectomy.[8–10] Moreover, the development of CRC has been linked to adenomas; considered to be precancerous lesions.[11] To the best of our knowledge, the incidence of CRC and adenoma detected through colonoscopy alone in patients with GC has not been discussed earlier. Thus, the aim of this study was to investigate synchronous CRC and adenoma in patients with GC.

Patients and Methods

The study group comprised patients who were admitted to undergo surgical or endoscopic resection of GC at the Department of Surgery, Jichi Medical University Hospital, between 2000 and 2004. The patients underwent colonoscopy before treatment for GC. The patients with concurrent CRC diagnosed by the referring clinicians, those with evidence of distant metastasis, those with serious diseases associated with bleeding or strictures, those who had undergone a colonoscopy or barium enema examination within the preceding year, and those who refused colonoscopy were excluded from the analysis. The patients with advanced CRC were included if it had not been detected by the referring clinician. All patients were informed that the objectives of the colonoscopy were to identify and treat synchronous carcinomas or adenomas, and that endoscopic

examinations and treatments such as polypectomy and endoscopic mucosal resection could cause complications. A written consent was obtained from all patients. The endoscopic resection was indicated for adenomas with a diameter of 5 mm or more[12] and for lesions suspected of being intramucosal carcinomas or carcinomas with submucosal micro-invasion on the basis of colonoscopic findings. All the patients received 2 L polyethylene glycol lavage solution (Niflec, Ajinomoto, Tokyo, Japan) before the colonoscopy, which was performed by experienced endoscopists.

The study variables included the complications of colonoscopy and the prevalence of colorectal neoplasms (namely, adenomas and carcinomas), the tumor sizes and sites of adenomas and colorectal carcinomas, the staging of colorectal carcinomas, the relationship of colorectal neoplasms to the clinicopathological factors of GC, and the family history (limited to that of gastrointestinal cancer among first-degree relatives). Familial adenomatous polyposis (FAP) and hereditary nonpolyposis CRC (HNPCC) were diagnosed according to the General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus.[13] GC and CRC were staged according to the Japanese Classification of Gastric Carcinoma[14] and the General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus.[13] The histological types of GC were classified as the intestinal, diffuse, or mixed type, according to the criteria of Lauren.[15] When two different types of GC were found in one patient, the dominant histology was used for the purpose of the analysis.

Numerical data (age) are expressed as means ± standard deviation, and were compared using Student's *t* test. Concurrent carcinoma in the large intestine was set for the endpoint, and odds ratios were calculated using the logistic regression model. Sex (women, men), age group (<60, 60–79, and 80–99), pathological type of GC (diffuse, mixed, and intestinal), stages of GC (I, II, III, IV), multiplicity of GC, and family history of gastrointestinal cancer were selected as possible confounding factors. All analyses were performed with the statistical software package STATA (version 8.0, SAS Institute, Cary, NC, USA).

Results

Of the 899 patients admitted to undergo GC resection, 433 (mean age 67.1 years; 125 women, 308 men) were excluded on the basis of the exclusion criteria. Thus, 466 patients with GC were enrolled in this study. The characteristics of these 466 patients are shown in Table 1. The mean age was 64.5 ± 11.7 (range 22–89) years, and 143 patients (30.7%) had a family history of gastrointestinal cancer, including 98 GCs, 23 CRCs, 18 esophagopharyngeal cancers, 15 pancreatic cancers, and 6 hepatobiliary tract cancers. Neither FAP nor HNPCC was found. There were 45 patients with two or more GCs at the same time. One squamous-cell carcinoma originating in the stomach was excluded from the analysis. GC was treated by surgery in 443 patients, by endoscopic resection in 13, and by chemotherapy, when it was the only remaining option, in 10.

Table 1. Characteristics of the 466 patients with gastric cancer

	Number	%
Age (year)		
<40	16	3.4
40–59	134	28.8
60–79	283	60.7
80–99	33	7.1
Sex		
Female	147	31.5
Male	319	68.5
FH of GIC		
Present	143	30.7
Absent	323	69.3
Pathological type		
Intestinal	288	55.9
Diffuse	218	42.3
Mixed	9	1.7
Stage		
I (A, B)	287 (225, 62)	61.2
II	50	10.7
III (A, B)	87 (51, 36)	18.7
IV	42	9.0
Multiplicity of GC		
Single	421	90.3
Multiple	45	9.7
Treatment of GC		
Surgery	443	95.1
Endoscopic resection	13	2.8
Chemotherapy	10	2.1

Pathological type: including 515 gastric cancer lesions detected in this series; Stage: classified according to the Japanese Classification of Gastric Carcinoma[14]
FH of GIC, family history of gastrointestinal cancer among first-degree relatives; GC, gastric cancer

Colorectal lesions were diagnosed in 235 (50.5%) patients (Table 2). There were no complications such as perforation or bleeding after colonoscopy or endoscopic polypectomy. There were 182 (39.1%) patients with adenomas; 5–9 mm in size in 86, and 10 mm or larger in 33. CRCs were detected in 18 (3.9%) patients. Table 3 summarizes the clinical characteristics of the 18 patients with synchronous CRCs. The symptoms were abdominal pain or discomfort in eight patients, anemia in two, weight loss in two, hematemesis in one, and none in five. All the patients with synchronous CRC were older than 50 years. Seven (38.9%) patients had a family history of gastrointestinal cancer among first-degree relatives, and only one patient had a family history of CRC. Among

Table 2. Colorectal neoplasms in the patients with gastric cancer

	Non-neoplastic lesion[a]	Adenoma[b]	Carcinoma	None
Patients, *N*	46 (9.9%)	182 (39.1%)	18 (3.9%)	231 (49.5%)
Age ± SD (range)	64.8 ± 12.1 (34–87)	66.9 ± 9.2 (41–87)	68.8 ± 12.2 (50–89)	62.4 ± 13.0 (22–88)
Sex (M/F)	26/20	144/38	15/3	143/88
FH	12 (26.1%)	53 (29.1%)	7 (38.9%)	71 (30.7%)

FH, family history of gastrointestinal cancer among first-degree relatives
[a] Inflammatory or hyperplastic polyps
[b] Including 11 patients who had synchronous colorectal carcinomas

the 18 synchronous CRCs, 11 (61.1%) were in the early stages (Tis: 7, T1: 4), and 10 of these were endoscopically resected. The CRC was resected simultaneously at the time of GC surgery in the other eight patients. The mean age of the eight patients who underwent surgery was 72.8 years, whereas that of the ten patients who underwent endoscopic resection was 65.7 years ($P = 0.2$).

Table 4 summarizes the characteristics of the patients with and those without concurrent CRCs. The difference between the mean ages of the patients with and those without synchronous CRC was not significant ($P = 0.11$). The histological type (mixed or intestinal) was another possible factor, but no significant difference was found ($P = 0.053$), even when the mixed type and the intestinal type were put into the same category. Statistical analysis did not show any significant difference in the features of the patients with concurrent CRC.

Discussion

According to some researchers, patients with GC may be at increased risk of the development of synchronous or metachronous CRC.[4,5,16] However, the incidence of synchronous CRC in patients with GC is reported to be only about 1%.[5,7,16] These data were obtained not only from colonoscopic examinations but also from barium enema examinations, and the frequency of synchronous CRC seems to be higher than that in the general population.[17] This cannot be ignored in clinical practice. In our study, colonoscopy was selected as the screening method, and synchronous CRCs were detected with a much higher prevalence (4%). Although we were not able to establish the fact that GC is directly related to synchronous CRC, because of the lack of control subjects, the high prevalence of synchronous CRCs in this series may imply that patients with GC are at increased risk of synchronous CRC. However, this might be a false assumption because the prevalence of GC in the Japanese population in the 1970s was high,[18] whereas that of CRC was lower than in the western countries.[17,19] If GC was a significant risk factor of CRC, the prevalence of CRC would have been as high as that of GC during the same period. A recent study shows an increasing incidence of CRC in the Japanese population,[17] which could be attributed to environmental changes, including the westernization of lifestyle and dietary habits.[20,21] On the other hand, the incidence of GC is decreasing slightly.[17,22] These facts do not support the consensus that the patients with GC are at increased risk of synchronous CRC. This false assumption might originate from the fact that upper GI endoscopy is a first-priority screening tool in Japan for patients with gastrointestinal symptoms, such as abdominal pain, discomfort, anemia, or body weight loss. These symptoms are occasionally common to both GC and CRC. Indeed, GC was detected before CRC in at least three of our patients who had advanced CRC, even though they did not have symptoms of GC.

Earlier studies have found that 30%–40% of patients with GC or CRC, who have synchronous cancers in other organs, have a family history of cancer among first-degree relatives.[23,24] This finding is consistent with our results (7/18, 39%); however, the frequency of a family history of cancer did not differ between the patients with and those without synchronous CRC. Furthermore, 30% of the recent causes of death in Japanese people are cancer-related, suggesting that genetic factors play a minor role in the development of GC with synchronous CRC.

Patients with GC may have a secondary cancer, which is often a current prevalent malignancy.[25] In Japan, GC is still the most common malignancy,[22] although the incidence of CRC is increasing,[16,26] and even approaching that of GC. Therefore, it is likely that an appreciable number of patients would have GC with synchronous CRC, in accordance with our data (3.9%). This may also be attributed to the fact that GC and CRC share the same risk factors, particularly environmental factors, although we failed to identify any specific risk factors of concurrent CRC in GC patients.

To our knowledge, no other studies have assessed the incidence of colorectal carcinomas and adenomas on the basis of the colonoscopy findings in as large a series

Table 3. Patients with gastric cancer and synchronous colorectal cancer

Sex	Age (years)	Symptom	FH of GIC	Gastric cancer				Synchronous colorectal cancer			
				Site	Multiplicity	Histology	Stage	Site	Depth	Stage	Treatment
M	54	Anemia	–	L, M	Multiple	Both intestinal	IA	Right colon	m	0	ER
M	55	Abdominal pain	+	M	Single	Intestinal	II	Right colon	m	0	ER
M	55	Abdominal pain	–	Both L	Multiple	Both mix	IA	Rectum	m	0	ER
M	66	Abdominal pain	–	L	Single	Diffuse	IIIB	Left colon	m	0	ER
M	72	None	–	U	Single	Intestinal	IB	Right colon	m	0	ER
M	74	None	–	U	Single	Intestinal	IA	Right colon	m	0	ER
M	77	None	+	M	Single	Intestinal	IA	Right colon	m	0	ER
M	50	None	–	U	Single	Diffuse	IIIB	Rectum	sm	I	ER
F	74	Abdominal discomfort	+	M	Single	Intestinal	IA	Rectum	sm	I	ER
M	80	Abdominal pain	+	U	Single	Intestinal	IA	Right colon	sm	I	ER
M	55	Hematemesis	+	UM	Single	Diffuse	II	Rectum	sm	IIIA	Surgery
M	73	Abdominal pain[a]	–	L	Single	Intestinal	IIIA	Left colon	ss	II	Surgery
M	78	Body weight loss[b]	–	L	Single	Diffuse	IA	Left colon	ss	II	Surgery
F	89	Abdominal pain	–	L	Single	Intestinal	IA	Right colon	ss	II	Surgery
M	78	None	+	L	Single	Intestinal	IA	Left colon	ss	IV	Surgery
M	51	Anemia	+	U	Single	Intestinal	IB	Left colon	se	IIIA	Surgery
F	81	Abdominal discomfort[b]	–	L	Single	Intestinal	IA	Both left colon	se, ss	II	Surgery
M	77	Body weight loss	–	M	Single	Intestinal	IB	Rectum	si (bladder)	IIIA	Surgery

FH of GIC, family history of gastrointestinal cancer among first-degree relatives; ER, endoscopic resection
Site and stage of gastric cancer were classified according to the Japanese classification of gastric carcinoma[14]
Stage of colorectal cancer was classified according to the General rules for clinical and pathological studies on cancer of the colon, rectum, and anus[13]
The right colon was defined as the cecum, ascending colon, and the right side of the transverse colon
The left colon was defined as the left side of the transverse colon, the descending colon, and the sigmoid colon
[a] Pain in the left side of the abdomen
[b] These patients seemed to manifest symptoms of colorectal cancer

Table 4. Characteristics of the patients with and those without concurrent colorectal cancer

	Absent	Present	OR (95% CI)
Number	448	18	
Age			
Average (year) ± SD	64.3 ± 11.7	68.8 ± 12.2	
Range	22–88	50–89	
<60	144	6	1.00
60–79	274	9	0.79 (0.28–2.26)
80–99	30	3	2.40 (0.57–10.14)
Sex			
Female	144	3	1.00
Male	304	15	2.37 (0.67–8.31)
FH of GIC			
Absent	312	11	1.00
Present	136	7	1.46 (0.55–3.85)
Pathological type			
Diffuse	207	4	1.00
Mixed	6	1	8.46 (0.82–87.53)
Intestinal	244	13	2.76 (0.89–8.60)
Stage			
I (A, B)	274 (215.59)	13 (10.3)	1.00
II	48	2	0.90 (0.20–4.12)
III (A, B)	84 (50.34)	3 (1.2)	0.76 (0.21–2.71)
IV	42	0	NA
Multiplicity of GC			
Single	405	2	1.00
Multiple	43	16	1.21 (0.27–5.44)
Treatment of GC			
Surgery	426	17	1.00
Endoscopic resection	12	1	2.09 (0.26–17.00)
Chemotherapy	10	0	NA

Pathological type: including 515 gastric cancer lesions
OR, odds ratio calculated with logistic regression model; CI, confidence interval; FH of GIC, family history of gastrointestinal cancer among first-degree relatives; NA, not applicable; GC, gastric cancer

of patients with GC as this (466 patients, after the exclusion of 433 patients whose conditions did not meet the study criteria). We found a high prevalence (3.9%) of concurrent CRC in these patients and we think that our data are clinically meaningful. Of the 18 synchronous CRCs, 11 were in the early stages (Tis 7, T1 4); therefore, the incidence of CRC in the advanced stage was 1.5%, which is consistent with previous data.[5,7,16] This result shows that colonoscopy contributes to a high rate of detection of CRC, especially in the early stages. Thus, we recommend screening colonoscopy, before treatment if possible, for patients with GC.

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