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Original Article

Characteristics and prognosis of Japanese colorectal cancer patients: The BioBank Japan Project

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ABSTRACT

Background: Colorectal cancer is the third most common cancer worldwide, and in Japan, it is estimated that about 10% of men and 8% of women will be diagnosed with colorectal cancer during their lifetime.
Methods: We focused on 5864 participants (3699 men and 2165 women) who had colorectal cancer and were registered with BioBank Japan (BBJ) between April 2003 and March 2008. Characteristics of colon and rectal cancer patients were calculated separately. Among the enrolled patients registered in BBJ within 90 days after diagnosis, we also calculated the 5-year cumulative and relative survival rates, and estimated the effect of lifestyle factors on all-cause mortality.
Results: Our participants included younger men than those in the Patient Survey and the Cancer Registry Japan. In more than 95% of cases the histological type was adenocarcinoma both in colon and rectal cancer. Rectal cancer patients tended to eat more meat and less green leafy vegetables compared with colon cancer patients. The 5-year cumulative survival rate was 73.0% (95% CI; 70.1%–75.7%) and the 5-year relative survival rate was 80.6% (77.4%–83.6%), respectively, for colon cancer. For rectal cancer, the rates were 73.3% (69.1%–77.0%) and 80.9% (76.3%–85.0%), in the same order. Lifestyle factors such as consuming less green leafy vegetables, being underweight, smoking, not consuming alcoholic beverages and being physically inactive were found to be related to poor survival.
Conclusions: We described lifestyle characteristics of colorectal cancer patients in BBJ and examined the impacts on subsequent all-cause mortality.

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Introduction

Colorectal cancer is the third most common cancer worldwide and the fourth most common cause of death.[1] Its known risk factors

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are westernized lifestyles[2] such as alcohol consumption, obesity and eating red and processed meat. For this reason, the incidence and mortality rates of colorectal cancer in Japan have increased, with an especially large increase up until the 1990s. Nowadays, the upward trend has slowed and it is estimated that about 10% of men and 8% of women in Japan will be diagnosed with colorectal cancer during their lifetime.[3]

With early detection by cancer screening and progress in its treatment, the 5-year survival rate of colon and rectal cancer is up to 71.6% and 70.1%, respectively, for those diagnosed between 2006 and 2008.[3] Recently, modifiable lifestyle factors which contributed to the prognosis of colorectal cancer have been examined. Although the evidence from randomized controlled trials is limited, maintaining high levels of physical activity, avoiding high carbohydrate intake and limiting consumption of red and processed meats and sugar-sweetened beverages are recommended for patients diagnosed with colorectal cancer.[4]

The BioBank Japan (BBJ) Project is a large-scale patient-based biobank which aims at the implementation of personalized medicine for common diseases such as cancer and cardiovascular disease.[5] Because of the nationwide scope of patient recruitment and survival survey of BBJ, it might be necessary to describe the lifestyle and clinical characteristics of Japanese colorectal cancer patients in BBJ and to examine their prognoses. The increasing trend in colorectal cancer in Japan nowadays is mostly attributed to colon cancer, thus, we show the results of colon cancer and rectal cancer separately.

Participants and methods

Study design and population

The details of the BBJ Project are described elsewhere.[5,6] In brief, the BBJ Project enrolled patients who had any of 47 targeted common diseases including colorectal cancer at 66 hospitals consisting of 12 cooperating medical institutions nationwide. Clinical information and biological samples of all patients were collected from April 2003 to March 2008 with written informed consent, under the diagnosis of diseases by each attending physician. The BBJ Project then followed up patients who had 32 of the 47 diseases until 2014.[7] Date and cause of death were recorded for deceased participants. The study protocol of the BBJ Project was approved by the Research Ethics Committees of the Institute of Medical Science, the University of Tokyo, RIKEN Yokohama Institute and the 12 cooperating medical institutions.

Data collection

Data were collected through interviews and medical records.[8] The data included age and year of entry, diagnosis, patients' own and family medical history, height, weight, lifestyle at entry such as consumption of meat and green leafy vegetables, smoking status, alcohol intake and physical exercise. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Presence of medical history of type 2 diabetes was evaluated from 2 data sources; disease name registered to BBJ and disease name checked on medical history. Stage of colorectal cancer was classified according to the Japanese Classification of Colorectal Cancer, Sixth edition, 1998. In this paper, histological type was based on the findings from biopsy or cytological sample.

Statistical analysis

In this paper, we focused on 5864 participants (3699 men and 2165 women) who had colorectal cancer with information on their sex, age and duration from diagnosis to registration and were registered to the BBJ Project. The characteristics were described for all colorectal cancer patients, and also for colon and rectal cancer patients separately. Colon cancer included cancers that occurred in the cecum, the ascending colon, the transverse colon, the descending colon and the sigmoid colon, and rectal cancer included cancers that occurred in the rectosigmoid colon, and the rectum. There were 3334 colon cancer patients, 1893 rectal cancer patients and 118 patients were classified to both. The patients with appendiceal or anal cancer were only included in the overall analysis. We also showed the characteristics of 1708 newly diagnosed participants (1018 men and 517 women) who were registered in BBJ within 90 days after their diagnosis. When examining the association between lifestyle factors and subsequent all-cause mortality, 1598 newly diagnosed participants (987 men and 611 women) who consented to the follow-up survey and whose follow-up information was successfully obtained were included in the analysis.

We calculated the 5-year cumulative survival rate using the Kaplan–Meier method. We also calculated the 5-year expected survival rate, using a survival-rate table of reference Japanese cohort from Cancer Registry and Statistics, Cancer Information Service, National Cancer Center, Japan,[9] based on sex- and age-specific mortality rates and Gompertz-Makeham's law in Abridged Life Tables, annually published by the Statistics and Information Department of Ministry of Health, Labour and Welfare, Japan.[10] Relative survival rate was then obtained by dividing cumulative survival rate by sex- and age-adjusted expected survival rate.

To examine the impact of the obtained lifestyle factors on mortality, Cox proportional hazards model was used to estimate the hazard ratios and 95% confidence intervals (CIs) for all-cause mortality. All models were stratified by sex and institutions and adjusted for age and entry year. The statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). All probability values were two-tailed, and the significance level was set at $p < 0.05$.

Results

Characteristics of the colorectal cancer patients in BBJ

The average age at entry of colon and rectal cancer patients was 67.4 years and 65.5 years, respectively. Fig. 1 shows the age distribution of overall colon and rectal cancer patients in BBJ and those of Patient Survey, Japan, 2005, which represented prevalent cases, separated by sex. The ratio of men to women was 1.6 for colon cancer and 2.0 for rectal cancer, while that of Patient Survey was 1.1 and 1.6, revealing that more men tended to be registered in BBJ than women. Also compared with Patient Survey, elderly patients were registered less often in BBJ, for both men and women and both colon and rectal cancer. When restricted to only patients registered within 90 days after diagnosis, the average age at entry was 65.7 for colon cancer and 63.4 for rectal cancer. The sex ratio was 1.4 for colon cancer and 2.2 for rectal cancer in BBJ, and the number was 1.2 and 1.7 in the Cancer Registry in 2005, which represented incident cases, respectively. As shown in Fig. 2, compared with age distribution of patients in the cancer registry, BBJ patients were younger, especially among the women.

Table 1 shows the characteristics of the all colon and rectal cancer patients and those of the newly diagnosed patients. Among all patients, about 20% were diagnosed before the year 2000. About half of the patients were registered within 1 year after diagnosis, and 17% were survivors longer than 5 years after their diagnosis. Information of stage and histology were mainly not registered.

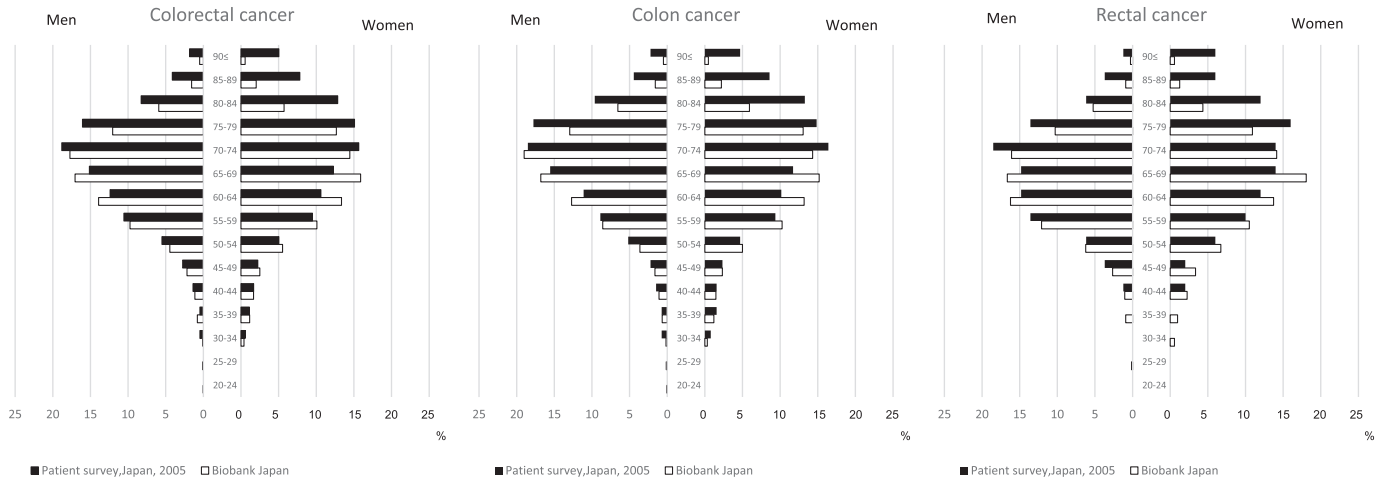

Fig. 1. Age-group distribution of the overall colon and rectal cancer patients in BBJ and in the Patient Survey, Japan, 2005, by sex. White bars represent patients in BBJ and black bars represent patients in the Patient Survey, Japan.

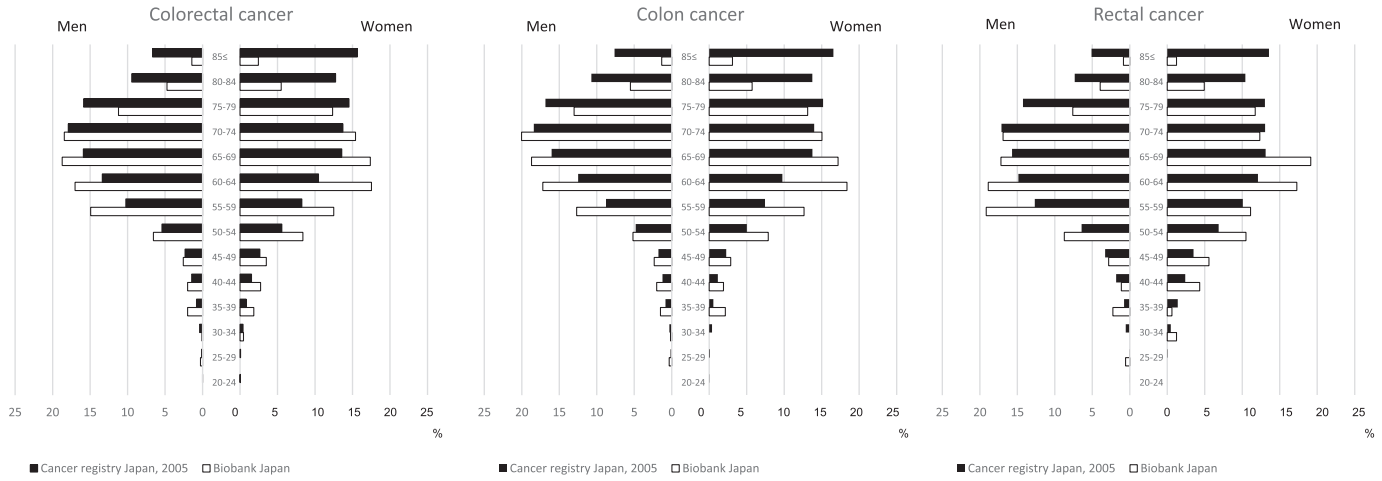

Fig. 2. Age-group distribution of the colon and rectal cancer patients in BBJ who were registered within 90 days after diagnosis and incident patients in the Cancer Registry Japan, 2005, by sex. White bars represent patients in BBJ who were registered within 90 days after diagnosis and black bars represent patients in the Cancer Registry Japan, 2005, respectively.

Among 72% of participants with available information, in more than 95% the histological type was adenocarcinoma both in colon and rectal cancer. About 12% of colon and rectal cancer patients had a medical history of type 2 diabetes and over 13% had a family history of colorectal cancer, even under conditions such that we could not distinguish absence of family history from missing data. For lifestyle factors at entry, rectal cancer patients tended to consume more meat than colon cancer patients (10.8% vs. 9.0% of patients consumed meat almost everyday), while the opposite trend was found for consumption of green leafy vegetables (76.5% vs. 79.6% of patients consumed green leafy vegetables almost everyday). We did not find large differences in BMI distribution between colon and rectal cancer patients, though those registered within 90 days after diagnosis (i.e., newly diagnosed patients) were categorized more to the underweight (BMI < 18.5 kg/m^2) group compared with all patients (14.8% vs. 11.2%). About 45% of patients were never-smokers, and the proportion was higher in colon cancer than in rectal cancer (45.5% vs. 38.1%). Similarly, over 40% were never-drinkers, and the proportion was also higher in colon cancer than rectal cancer (42.6% vs. 39.4%). No large difference was found in habits of physical exercise between the colon and rectal cancer patients (23.0% vs. 21.2% of patients exercised $\geq$3 times/week); however, all patients tended to engage in exercise compared with those registered within 90 days after diagnosis (22.8% vs. 19.2%).

When compared with the distributions of the National Health and Nutrition Survey, Japan, 2005,[11] both colon and rectal cancer patients registered within 90 days tended to be underweight, current drinkers and not having physical exercise habits. They also tended to not be never-smokers except colon cancer patients aged 40–49 years old (Fig. 3, because of small numbers, we omitted to describe the distribution among patients under 40 years old ($n = 12$, 10, 9 and 3 for male colon and rectal cancer, and female colon and rectal cancer patients, respectively)).

Prognosis of participants registered within 90 days after diagnosis

Among 971 and 492 eligible colon and rectal cancer patients, 260 and 130 deceased cases were identified during 5 years of follow-up, respectively. Consequently, the 5-year cumulative survival rate was 73.0% (95% CI, 70.1%–75.7%) and the 5-year relative survival rate was 80.6% (77.4%–83.6%) for colon cancer. For rectal

Table 1
Characteristics of colorectal cancer patients in BBJ.

	Overall patients						Patients registered within 90 days after diagnosis					
	Colorectal cancer		Colon cancer		Rectal cancer		Colorectal cancer		Colon cancer		Rectal cancer	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Total	5864		3334		1893		1708		1018		517	
Sex												
Men	3699	(63.1)	2059	(61.8)	1269	(67.0)	1052	(61.6)	599	(58.8)	355	(68.7)
Women	2165	(36.9)	1275	(38.2)	642	(33.9)	656	(38.4)	419	(41.2)	162	(31.3)
Year of diagnosis												
-2000	1287	(21.9)	691	(20.7)	436	(23.0)	–	–	–	–	–	–
2001	393	(6.7)	225	(6.7)	126	(6.7)	–	–	–	–	–	–
2002	529	(9.0)	300	(9.0)	164	(8.7)	–	–	–	–	–	–
2003	778	(13.3)	444	(13.3)	264	(13.9)	142	(8.3)	90	(8.8)	90	(8.8)
2004	852	(14.5)	508	(15.2)	261	(13.8)	348	(20.4)	218	(21.4)	218	(21.4)
2005	754	(12.9)	429	(12.9)	261	(13.8)	370	(21.7)	208	(20.4)	208	(20.4)
2006	657	(11.2)	387	(11.6)	204	(10.8)	395	(23.1)	245	(24.1)	245	(24.1)
2007	584	(10.0)	331	(9.9)	170	(9.0)	423	(24.8)	238	(23.4)	238	(23.4)
2008	30	(0.5)	19	(0.6)	7	(0.4)	30	(1.8)	19	(1.9)	19	(1.9)
Duration between diagnosis and registration												
-90 days	1708	(29.1)	1018	(30.5)	517	(27.3)	1708	(100.0)	1018	(100.0)	517	(100.0)
-0.5 years	631	(10.8)	347	(10.4)	226	(11.9)	–	–	–	–	–	–
-1 year	616	(10.5)	359	(10.8)	193	(10.2)	–	–	–	–	–	–
-2 years	801	(13.7)	449	(13.5)	270	(14.3)	–	–	–	–	–	–
-3 years	489	(8.3)	282	(8.5)	158	(8.3)	–	–	–	–	–	–
-4 years	348	(5.9)	194	(5.8)	102	(5.4)	–	–	–	–	–	–
-5 years	268	(4.6)	147	(4.4)	91	(4.8)	–	–	–	–	–	–
Longer than 5 years	1003	(17.1)	538	(16.1)	336	(17.7)	–	–	–	–	–	–
Stage												
0	71	(5.1)	46	(5.3)	46	(5.3)	13	(4.1)	9	(4.4)	4	(3.6)
I	256	(18.5)	140	(16.2)	140	(16.2)	62	(19.4)	38	(18.4)	21	(18.8)
II	394	(28.4)	269	(31.1)	269	(31.1)	87	(27.3)	57	(27.7)	31	(27.7)
IIIa	345	(24.9)	209	(24.2)	209	(24.2)	71	(22.3)	46	(22.3)	27	(24.1)
IIIb	108	(7.8)	67	(7.8)	67	(7.8)	17	(5.3)	13	(6.3)	4	(3.6)
IV	213	(15.4)	133	(15.4)	133	(15.4)	69	(21.6)	43	(20.9)	25	(22.3)
No information	4477	–	2470	–	2470	–	1389	–	812	–	405	–
Histology												
Adenocarcinoma	4037	(95.3)	2355	(95.2)	1345	(95.3)	1212	(95.5)	742	(95.6)	385	(95.1)
Adenosquamous carcinoma	15	(0.4)	9	(0.4)	4	(0.3)	6	(0.5)	3	(0.4)	1	(0.2)
Basaloid cell carcinoma	4	(0.1)	1	(0.0)	3	(0.2)	2	(0.2)	1	(0.1)	1	(0.2)
Squamous cell carcinoma	14	(0.3)	2	(0.1)	5	(0.4)	4	(0.3)	1	(0.1)	2	(0.5)
Carcinoid tumor	7	(0.2)	2	(0.1)	5	(0.4)	3	(0.2)	1	(0.1)	3	(0.7)
Malignant melanoma	2	(0.0)	0	(0.0)	2	(0.1)	0	(0.0)	0	(0.0)	0	(0.0)
Non-epithelial tumor	4	(0.1)	2	(0.1)	2	(0.1)	1	(0.1)	0	(0.0)	1	(0.2)
Lymphoma	1	(0.0)	1	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Unclassified tumor	9	(0.2)	7	(0.3)	2	(0.1)	2	(0.2)	0	(0.0)	1	(0.2)
Metastatic tumor	7	(0.2)	5	(0.2)	2	(0.1)	1	(0.1)	1	(0.1)	0	(0.0)
Others	61	(1.4)	41	(1.7)	17	(1.2)	19	(1.5)	14	(1.8)	5	(1.2)
Unknown	77	(1.8)	48	(1.9)	24	(1.7)	19	(1.5)	13	(1.7)	6	(1.5)
No information	1626	–	861	–	482	–	439	–	242	–	112	–
History of Type 2 diabetes												
Absence/No information	5195	–	2946	–	1661	–	1532	–	913	–	459	–
Presence	669	(11.4)	388	(11.6)	232	(12.3)	176	(10.3)	105	(10.3)	58	(11.2)
Family history of colorectal cancer												
Absence/No information	5081	–	2849	–	1643	–	1472	–	868	–	442	–
Presence	783	(13.4)	485	(14.5)	250	(13.2)	236	(13.8)	150	(14.7)	75	(14.5)
Meat consumption												
Almost everyday	509	(9.6)	281	(9.0)	190	(10.8)	177	(11.2)	108	(11.1)	55	(11.2)
3–4 days/week	1678	(31.7)	1006	(32.2)	543	(30.8)	525	(33.3)	318	(32.8)	167	(33.9)
1–2 days/week	2317	(43.8)	1363	(43.7)	781	(44.3)	673	(42.7)	418	(43.1)	210	(42.6)
Almost never	789	(14.9)	472	(15.1)	249	(14.1)	202	(12.8)	125	(12.9)	61	(12.4)
No information	571	–	212	–	130	–	131	–	49	–	24	–
Green leafy vegetable consumption												
Almost everyday	4153	(78.6)	2483	(79.6)	1348	(76.5)	1210	(76.6)	753	(77.5)	365	(73.7)
3–4 days/week	682	(12.9)	387	(12.4)	251	(14.3)	209	(13.2)	124	(12.8)	71	(14.3)
1–2 days/week	334	(6.3)	193	(6.2)	114	(6.5)	116	(7.3)	71	(7.3)	41	(8.3)
Almost never	114	(2.2)	56	(1.8)	48	(2.7)	45	(2.8)	23	(2.4)	18	(3.6)
No information	581	–	215	–	132	–	128	–	47	–	22	–
BMI												
<18.5	621	(11.2)	337	(10.7)	202	(11.4)	245	(14.8)	144	(14.7)	68	(13.5)
18.5–24.9	3813	(69.0)	2176	(69.1)	1216	(68.9)	1135	(68.7)	673	(68.9)	350	(69.6)
25–29.9	985	(17.8)	568	(18.0)	315	(17.8)	242	(14.7)	140	(14.3)	79	(15.7)
≥30	111	(2.0)	68	(2.2)	32	(1.8)	29	(1.8)	20	(2.0)	6	(1.2)
No information	334	–	185	–	128	–	57	–	41	–	14	–

(*continued on next page*)

Table 1 (*continued*)

	Overall patients						Patients registered within 90 days after diagnosis					
	Colorectal cancer		Colon cancer		Rectal cancer		Colorectal cancer		Colon cancer		Rectal cancer	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Smoking status												
Never-smoker	2509	(43.6)	1490	(45.5)	706	(38.1)	724	(42.7)	464	(46.0)	176	(34.4)
Ex-smoker	2090	(36.3)	1201	(36.7)	749	(40.4)	638	(37.7)	367	(36.4)	226	(44.1)
Current smoker	997	(17.3)	558	(17.1)	383	(20.6)	297	(17.5)	171	(16.9)	107	(20.9)
Smoker with unknown status	162	(2.8)	23	(0.7)	17	(0.9)	35	(2.1)	7	(0.7)	3	(0.6)
No information	106	–	62	–	38	–	14	–	9	–	5	–
Alcohol intake												
Never-drinker	2396	(41.7)	1390	(42.6)	729	(39.4)	705	(41.7)	439	(43.7)	199	(38.9)
Ex-drinker	702	(12.2)	415	(12.7)	246	(13.3)	215	(12.7)	133	(13.2)	73	(14.3)
Current drinker consuming 0–15 g alcohol/day	999	(17.4)	611	(18.7)	339	(18.3)	257	(15.2)	157	(15.6)	82	(16.0)
Current drinker consuming 15–30 g alcohol/day	523	(9.1)	292	(9.0)	176	(9.5)	149	(8.8)	85	(8.5)	49	(9.6)
Current drinker consuming ≥30 g alcohol/day	903	(15.7)	509	(15.6)	324	(17.5)	314	(18.6)	182	(18.1)	102	(19.9)
Drinker with unknown status	218	(3.8)	45	(1.4)	36	(1.9)	50	(3.0)	9	(0.9)	7	(1.4)
No information	123	–	72	–	43	–	18	–	13	–	5	–
Physical exercise												
≥3 times/week	1183	(22.8)	704	(23.0)	366	(21.2)	298	(19.2)	182	(19.2)	85	(17.4)
1–2 times/week	229	(4.4)	137	(4.5)	74	(4.3)	54	(3.5)	33	(3.5)	19	(3.9)
No habit	3776	(72.8)	2215	(72.5)	1283	(74.5)	1197	(77.3)	733	(77.3)	384	(78.7)
No information	676	–	278	–	170	–	159	–	70	–	29	–

cancer, they were 73.3% (69.1%–77.0%) and 80.9% (76.3%–85.0%), in the same order.

During 7.4 median years with 6333 and 3233 person-years of follow-up, 350 and 171 deaths occurred among colon and rectal cancer patients, respectively. Table 2 shows the estimated hazard ratios for all-cause mortality. Patients with type 2 diabetes showed elevated risk (HR; 1.31, 95% CI; 1.02–1.67) in all colorectal patients, though we could not distinguish subgroup without information from patients without diabetes among the reference group. Consuming less green leafy vegetables was associated with an increased risk, and almost never-consumers showed 1.87 (1.22–2.88)-, 2.06 (1.10–3.86)- and 1.40 (0.70–2.83)-fold greater risk compared with everyday consumers, among all colorectal, colon and rectal cancer patients, respectively. Being underweight (BMI < 18.5) elevated the risk of all-cause mortality in all colorectal and colon cancer patients, with HRs of 1.40 (1.12–1.76) and 1.46 (1.09–1.95), respectively. Current smoking was also found to elevate the risk of all-cause mortality, showing HRs of 1.38 (1.06–1.81), 1.50 (1.07–2.11) and 1.54 (0.92–2.57) in all colorectal, colon and rectal cancer patients, respectively. In contrast, alcohol

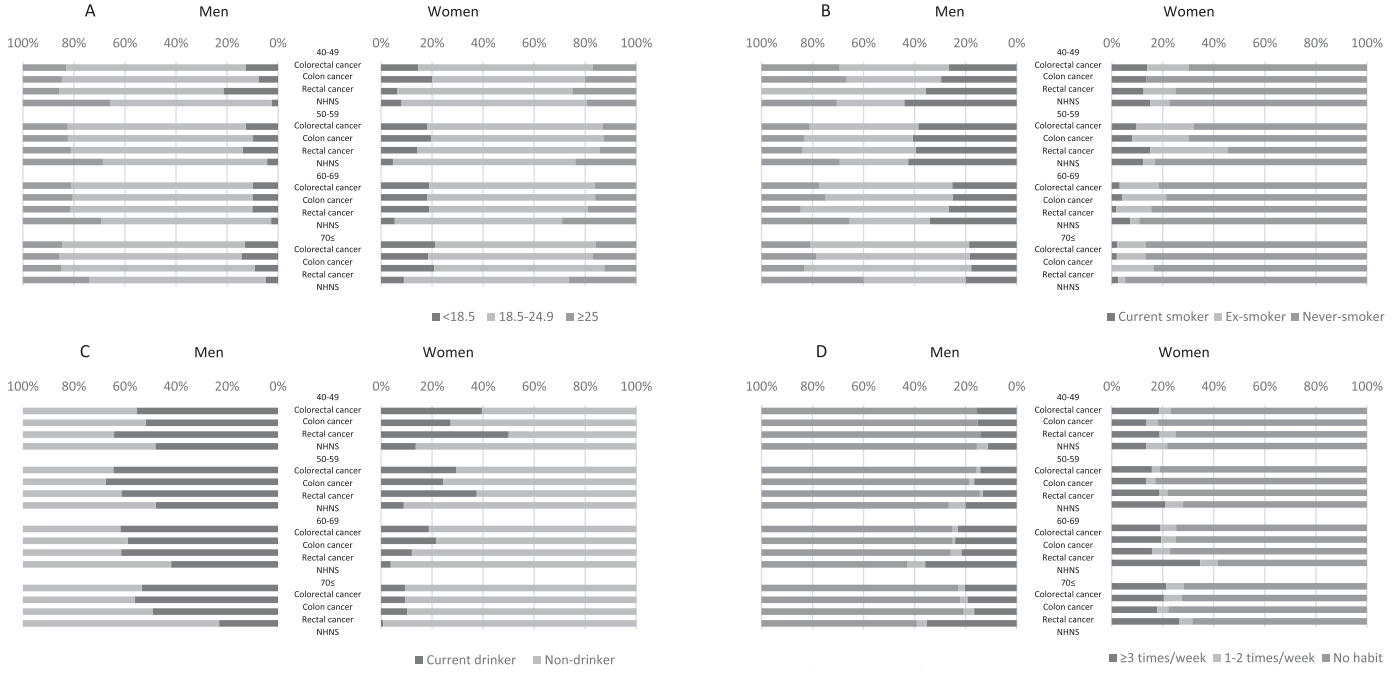

Fig. 3. Distributions of (A) BMI, (B) smoking status, (C) alcohol drinking status and (D) physical exercise status of the colon and rectal cancer patients in BBJ who were registered within 90 days after diagnosis and the general population in the National Health and Nutrition Survey, Japan 2005, according to sex and age group.

Table 2
Age-adjusted hazard ratios for all-cause mortality among colorectal cancer patients registered in BBJ within 90 days after diagnosis.

	Colorectal cancer			Colon cancer			Rectal cancer		
	Person-years	Death	Adjusted HR (95% CI)	Person-years	Death	Adjusted HR (95% CI)	Person-years	Death	Adjusted HR (95% CI)
History of Type 2 diabetes									
Absence/No information	9442.4	484	1.00	5754.1	304	1.00	2904.3	147	1.00
Presence	997.2	75	1.31 (1.02–1.67)	578.4	46	1.32 (0.96–1.81)	328.6	24	1.26 (0.81–1.97)
Family history of colorectal cancer									
Absence/No information	8938.3	487	1.00	5388.4	308	1.00	2764.9	142	1.00
Presence	1501.4	72	0.93 (0.72–1.19)	944.2	42	0.84 (0.61–1.16)	468	29	1.28 (0.86–1.92)
Meat consumption									
Almost everyday	1186.4	55	1.00	729	33	1.00	352.7	21	1.00
3–4 days/week	3346.6	169	1.04 (0.76–1.41)	2031.2	106	1.07 (0.72–1.59)	1054.1	52	0.86 (0.52–1.44)
1–2 days/week	4102.5	229	1.06 (0.78–1.43)	2545.9	145	1.08 (0.73–1.59)	1297.9	70	0.84 (0.51–1.38)
Almost never	1218.6	76	1.21 (0.85–1.71)	737	50	1.33 (0.85–2.07)	362.5	23	0.94 (0.50–1.74)
Green leafy vegetable consumption									
Almost everyday	7797.7	379	1.00	4767.5	251	1.00	2364.7	113	1.00
3–4 days/week	1254.7	78	1.27 (0.99–1.62)	775.1	46	1.20 (0.87–1.66)	423.4	25	1.11 (0.70–1.74)
1–2 days/week	602.9	47	1.61 (1.18–2.20)	408.2	25	1.17 (0.77–1.78)	191.2	19	2.36 (1.42–3.94)
Almost never	227.4	23	1.87 (1.22–2.88)	108.6	11	2.06 (1.10–3.86)	103.1	9	1.40 (0.70–2.83)
BMI									
<18.5	1363.7	97	1.40 (1.12–1.76)	794.8	61	1.46 (1.09–1.95)	430.3	22	1.17 (0.73–1.87)
18.5–24.9	7062.6	359	1.00	4269	225	1.00	2217.1	111	1.00
25–29.9	1576.6	65	0.80 (0.62–1.05)	940.6	40	0.79 (0.56–1.11)	487.2	28	1.20 (0.79–1.84)
≥30	167.5	12	1.54 (0.86–2.76)	126.3	7	1.17 (0.55–2.49)	36.6	3	1.72 (0.49–6.02)
Smoking status									
Never-smoker	4584.8	200	1.00	3061.8	133	1.00	1132.2	47	1.00
Ex-smoker	3868.1	231	1.27 (1.02–1.59)	2180.3	143	1.42 (1.07–1.88)	1371.8	81	1.45 (0.93–2.25)
Current smoker	1780	114	1.38 (1.06–1.81)	1008.5	65	1.50 (1.07–2.11)	658.4	42	1.54 (0.92–2.57)
Alcohol intake									
Never-drinker	4248.2	230	1.00	2658.9	155	1.00	1186.7	71	1.00
Ex-drinker	1189.2	94	1.26 (0.98–1.63)	732.8	60	1.18 (0.86–1.63)	435.4	27	1.01 (0.63–1.62)
Current drinker consuming 0–15 g alcohol/day	1715.1	72	0.73 (0.56–0.97)	1067.9	43	0.65 (0.45–0.92)	530.1	23	0.70 (0.43–1.16)
Current drinker consuming 15–30 g alcohol/day	929.6	46	0.79 (0.57–1.11)	554.3	27	0.69 (0.44–1.07)	293.6	14	0.74 (0.40–1.35)
Current drinker consuming ≥30 g alcohol/day	2083.5	98	0.73 (0.56–0.96)	1196.9	55	0.64 (0.45–0.90)	692.4	34	0.76 (0.49–1.20)
Physical exercise									
≥3 times/week	1946.7	86	1.00	1191.2	49	1.00	560.4	29	1.00
1–2 times/week	361.3	12	0.60 (0.33–1.08)	210.3	10	0.81 (0.42–1.56)	134.9	1	0.14 (0.02–1.00)
No habit	7333.8	418	1.33 (1.05–1.68)	4495.3	265	1.52 (1.12–2.08)	2311	134	1.16 (0.77–1.76)

The hazard ratios were calculated using a Cox proportional hazards regression model stratified by sex and institutions and adjusted for age and entry year.

intake was found to reduce the risk, even in the highest category (30 g and more alcohol/day) compared with non-drinkers. Being physically inactive raised the all-cause mortality risk to 1.33 (1.05–1.68) and 1.52 (1.12–2.08) in all colorectal and colon cancer patients, respectively. Other characteristics showed no association with all-cause mortality in any sites.

Discussion

In this paper, we have described the distribution of lifestyle characteristics of Japanese colorectal cancer patients registered in BBJ between April 2003 and March 2008 and the impact on subsequent mortality. Both the allover patients registered in BBJ and patients who registered within 90 days after diagnosis were obviously younger than the patients of the Patient Survey and of the Cancer Registry, the former represented prevalent cases and the latter represented incident cases in Japan. Among the lifestyles previously reported as risk/preventive factors for development of colorectal cancer, being underweight, current or ex-smoker, current drinker and not having physical exercise habits were apparent among colorectal patients compared with the general public in the National Health and Nutrition Survey. Our rectal cancer patients tended to eat more meat and less green leafy vegetables compared with the colon cancer patients. Also smokers and drinkers were more evident in the rectal cancer patients than the colon cancer patients. We found that lifestyles practices such as consuming less green leafy vegetables, being underweight, smoking, not consuming alcoholic beverages, and being physically inactive increased the subsequent mortality risk.

According to the stage distribution at diagnosis reported by the Japanese Society for Cancer of the Colon and Rectum, the prevalence of 0, I, II, IIIa, IIIb and IV stage between 2000 and 2004 was 5.4%, 19.1%, 28.5%, 19.9%, 9.3% and 17.8% for colon cancer, and 4.9%, 25.3%, 22.4%, 22.2%, 11.9% and 13.2% for rectal cancer.[12] Though most of our patients did not have information about the stage of their cancer, more patients registered within 90 days after diagnosis in our study tended to be in stage IIIa (24.2% and 26.5% for colon and rectal cancer, respectively) compared with the patients reported from the Japanese Society for Cancer of the Colon and Rectum.

From the same registry, the 5-year cumulative survival rate was reported to be 72.8% and 71.3% for colon and rectal cancer,[12] and the values were almost equivalent to our patients. On the other hand, the Japanese Association of Clinical Cancer Centers reported the 5-year relative survival rate of 75.7% and 76.0% in colon and rectal cancer patients who were registered between 2004 and 2007.[13] Our patients showed slightly higher 5-year relative survival rates both in colon and rectal cancer, however the large number of patients without stage information made it difficult to elucidate the reasons for such differences.

Recent meta-analysis or systematic review papers revealed that uncontrolled diabetes,[14] obesity and underweight,[15] smoking,[16] western dietary pattern,[4] and physical inactivity[4] were correlated with poor overall survival. We found that underweight, smoking,

and physically inactivity were all associated with all-cause mortality risk in line with the previous studies. Medical history of type 2 diabetes was also founded to increase the risk of all-cause mortality, however the reference group which was mixed up with patients without diabetes and those without appropriate information made it difficult to interpret this result. In contrast, obesity, and consuming more meat were not associated with all-cause mortality in our study. Consuming green leafy vegetables and moderate alcohol consumption were known to be associated with lower risk of occurrence of colorectal cancer,[2] our results showed that these two lifestyles would also be associated with higher probability of survival.

The strength of the present study is the large-scale enrollment and follow-up of colon and rectal cancer patients nationwide, and the comparison of their characteristics between colon and rectal cancer. The factors associated with disease progression were evaluated among the newly diagnosed participants. However, most of patients registered in BBJ were prevalent cases and the lifestyle information was collected at the registration. Thus, even though we restricted patients to those registered within 90 days after diagnosis to evaluate prognostic factors, there might be some misclassification occurred. Furthermore, we have to exercise caution in interpreting the results because data on some variables including disease stage were missing in the BBJ Project database.

Conflicts of interest

All authors declare no conflicts of interest.

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Appendix

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