ORIGINAL ARTICLE—ALIMENTARY TRACT





Medical costs according to the stages of colorectal cancer: an analysis of health insurance claims in Hachioji, Japan

Takahiro Utsumi¹ [©] · Takahiro Horimatsu² · Yoshitaka Nishikawa³ [®] · Nobuaki Hoshino⁴ · Yoshimitsu Takahashi³ · Rei Goto⁵ · Soichiro Kashihara⁶ · Jun Fukuyoshi⁶ · Takeo Nakayama³ · Hiroshi Seno¹

Received: 1 April 2021 / Accepted: 7 June 2021 © Japanese Society of Gastroenterology 2021

Abstract

Background Although the effect of the early detection of colorectal cancer (CRC) on medical costs needs to be clarified, there are few reports on the actual medical costs of CRC patients in Japan. We aimed to identify medical costs according to CRC stage, using health insurance claims.

Methods This observational study included CRC patients who had received specific treatment for CRC, which was defined by the procedure code and the claim computer processing system code associated with the treatment of CRC. CRC patients who underwent endoscopic or radical surgical treatment were defined as the curable group and those with palliative treatment, including palliative chemotherapy, as the non-curable group. Total medical costs and medical costs of specific treatments for CRC for

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00535-021-01798-9.

Takahiro Utsumi tk_utsumi@kuhp.kyoto-u.ac.jp

- ¹ Department of Gastroenterology and Hepatology, Kyoto University Graduate School of Medicine, 54 Kawaharacho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan
- ² Institute for Advancement of Clinical and Translational Science (iACT), Kyoto University Hospital, Kyoto, Japan
- ³ Department of Health Informatics, Kyoto University School of Public Health, Kyoto, Japan
- ⁴ Department of Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan
- ⁵ Graduate School of Business Administration, Keio University, Yokohama, Japan
- ⁶ Cancerscan, Co., Ltd., Tokyo, Japan

3 years were measured using the claims held by Hachioji City from May 2014 to July 2019.

Results This study included 442 patients in the curable group, including 267 patients who underwent endoscopic treatment, and 175 patients who underwent radical surgical treatment, and 161 patients in the non-curable group. The mean (standard deviation) total medical costs in the curable and non-curable groups were 2,130 (2,494) and 8,279 (5,600) thousand Japanese Yen (JPY), respectively. The mean (standard deviation) medical costs for the specific treatment of CRC in the curable and non-curable groups were 408 (352) and 3,685 (3,479) thousand JPY, respectively.

Conclusions We clarified the actual medical costs of CRC in curable and non-curable groups. These results suggest the effect of early detection of CRC in reducing medical costs.

Keywords Colorectal cancer \cdot Early detection \cdot Health insurance claims \cdot Medical costs

Introduction

The incidence of colorectal cancer (CRC) is increasing in Japan. CRC is the most common cancer and has the second highest mortality rate among all cancers. Screening for CRC using the immunochemical fecal occult blood test (iFOBT), which has been shown to reduce the mortality from CRC [1–7], has been conducted for persons aged 40 years or older as part of the Japan's public health policy. It is necessary to increase the rates of both, cancer screening using iFOBT and subsequent diagnostic investigation using either colonoscopy or flexible sigmoidoscopy in combination with a double-contrast barium

enema for iFOBT-positive patients [7–9]. All of the approximately 1700 municipalities in Japan are responsible for the provision and financing of population-based cancer screening programs to their residents. Local governments are very interested in the budgetary impact of cancer screening, considering both the costs of screening and medical care. However, it is unclear whether the early detection of CRC has led to a reduction in medical costs in Japan. It is important to ascertain the efficacy for reducing medical costs through the early detection of CRC to develop the appropriate strategies for cancer prevention [10, 11].

The medical costs according to stages of CRC should be examined before assessing the efficacy of early CRC detection in reducing them. When claims data are not available, a micro-costing approach is used to estimate medical costs by summing up the products of unit price and the predefined volume of procedures and drugs based on the standard clinical process [12-14]. However, even if patients have CRC of the same stage, different treatments may be recommended to each patient after detailed characterization of CRC. In addition, some patients cannot complete the recommended treatment because of complications or comorbidities. Thus, the actual medical costs incurred from CRC treatment should be determined. Furthermore, for the analysis of all costs related to CRC, we should also consider the total medical costs, including those for the complications caused by CRC and its treatment, and those for the worsening of comorbidities due to CRC. For municipalities, which are considered national health insurers, the reduction of total medical costs would be more important than the costs of specific treatment for CRC. However, in Japan, there are no large-scale reports on the actual total medical costs and medical costs incurred by specific treatments for CRC patients.

In the present study, we aimed to clarify the total medical costs and medical costs for specific treatments of CRC, including endoscopic resection, surgery, radiation, and chemotherapy, in each stage of CRC, to identify the efficacy of reducing medical costs through early detection, using the national health insurance claims data owned by a municipality. This was the first study in Japan to elucidate the actual medical costs of CRC patients at a municipal scale using the national health insurance claims data of the municipality.

Methods

This observational study was conducted in 2020 for the evaluation of actual medical costs according to the stage of CRC, using anonymized national health insurance claims (inpatient, outpatient, dispensing) from May 2014 to July

2019 held by Hachioji City. Hachioji City is located in the west of Tokyo. The city, with a population of approximately 580,000 in 2015, had 12 designated emergency hospitals in 2017, including two academic medical centers. As part of Hachioji City's project, this study group was commissioned for medical cost analysis by the city. The results of this study are already available to citizens on the city's website. The study protocol was approved by the Institutional Review Board of Kyoto University Hospital, Kyoto, Japan (approval number: R2898).

Patients

In this study, we included only patients with the disease named CRC (C18-20) per the Implementation of the International Statistical Classification of Disease and Related Health Problems, 10th Revision between May 2014 and March 2017, and the coding system for the specific treatment of CRC between June 2014 and August 2016. As shown in Table 1, three board-certified gastroenterologists, a board-certified surgeon in gastroenterology, and a claims database researcher/epidemiologist in our study group extracted the procedure codes of the Ministry of Health, Labour and Welfare associated with the specific procedures for CRC, and the claim computer processing system codes of the anticancer agents that are covered by insurance for the treatment of CRC. Based on our previous study, aimed at identifying CRC patients from the claims data (https://mhlw-grants.niph.go.jp/node/ 59785), we used an algorithm that defined the treatment with these codes, including endoscopic treatment, surgery, radiation, and chemotherapy, as the specific treatment for CRC in this study (Online Resource 1). Since it was considered difficult to correctly distinguish cancer in the anus or anal canal from cancer in the rectum based only on the disease name, we also included the disease name of cancer in the anus or anal canal region (C21). The codes for radiotherapy and surgery for cancer of the anus or anal canal were applied to only cases with the name of rectal cancer in the claims data. The name of the disease registered in the health insurance claims data does not necessarily correspond to the name of the diagnosed disease. In some cases, the name of the disease may be continued even when the patients have no current treatment for CRC or be inputted for medical billing in the claims data. Therefore, the claims data with the disease name of CRC would include three groups: a group with CRC that received treatment for CRC, a group with CRC that received no treatment for CRC (for example, very elderly patients or patients with serious comorbidities), and a group without CRC during the study period. Patients with both the disease name of CRC and the code of this specific treatment for CRC can be confirmed as patients with CRC with **Table 1** The codes associatedwith specific procedures forCRC, and the claim computerprocessing system codes of theanticancer agents for CRC

Type of specific treatment for CRC	Procedure code
Endoscopic treatment	
Polypectomy or endoscopic mucosal resection	150285010, 150183410, 190181210, 190181310
	190181410, 190181510
Endoscopic submucosal dissection	150363910
Surgical treatment with resection of primary lesion	
Surgery with colorectomy	150181710, 150181810, 150363810, 150180750
	150180850, 150180950, 150064010, 150181910
	150187010, 150187110, 150187210, 150245310
	150245410, 150297510, 150264010
Laparoscopic surgery with colorectomy	150277810, 150337710, 150324910, 150325210
	150337810, 150337910, 150407210, 150407310
	150407410
Local resection of primary lesion	150183110, 150183510, 150186810, 150186910
	150187010, 150348610, 150364510
	150189050*, 150190310*, 150190710*
Surgical treatment without resection of primary lesion	n
Surgery for stoma	150184510, 150389610, 150367210, 150402470
	150402570, 150186110, 150186210
Intestinal anastomosis	150184110
Surgery for jejunostomy	150184310, 150364010
Lymph node dissection	150322810, 150361110, 150377010
Radiotherapy*	
X-ray therapy	180008810, 180019410
High-energy radiotherapy	180020710, 180020810, 180020910, 180021010
	180021110, 180021210, 180021310, 180021410
	180021510, 180021610, 180021710, 180021810
	180021910, 180022010
Intensity modulated radiation therapy	180031910
Treatment for obstruction	
Stent placement	150364410
Placement of long intestinal tube	140007010
Chemotherapy	
Generic name	Claim computer processing system code
Aflibercept beta	622551801, 622551901
Irinotecan hydrochloride hydrate	620007257, 620007258, 620009516, 620009520
	620009515, 620009519, 620009518, 620009522
	620919501, 620919701, 622019401, 622019501
	622059701, 622059801, 622258901, 622259001
	622236901, 622237001, 622230201, 622230301
	622470401, 622470501
Tegafur, Uracil	620915001, 621929901, 621930001, 621930101
Oxaliplatin	621932201, 621932301, 622189401, 622374801
	622374901, 622371801, 622371901, 622411901
	622371101, 622371201, 622426801, 622373201
	622373301, 622414601, 622385701, 622385801
	622434901, 622437201, 622437301, 622437401
	622389801, 622389901, 622431101, 622388601
	622388701, 622428001, 622393201, 622393301
	622437001, 622460601, 622394701, 622394801

Table 1 continued

Generic nam

Generic name	Claim computer processing system code
	622432401, 622392001, 622392101, 622439101
	622383201, 622383301, 622461701
Tegafur, Gimeracil, Oteracil Potassium	620915501, 620915601, 620009353, 620009354
	622256001, 622256101, 622254901, 622255001
	622243001, 622243101, 622275701, 622275801
	622266701, 622266801, 622294601, 622294701
	622285701, 622285801, 622397301, 622397401
	622397101, 622397201, 622434701, 622434801
	622430801, 622430901, 622487301, 622487401
	622497901, 622498001, 622537501, 622537601
Capecitabine	610470009
Cyclophosphamide hydrate	640453101, 644210037, 620005941, 622181601
Cytarabine	620003714, 620003715, 620003716, 620003717
	620003718
Picibanil	620004740, 620004741, 620004742, 620004743
Cetuximab	620008443
Trifluridine and tipiracil hydrochloride	622336001, 622336101
Tegafur	620004566, 620004748, 644210046, 620004820
	620910101, 620005087
Doxifluridine	614210128, 614210129
Doxorubicin Hydrochloride	621995301, 621995401, 621983201, 621983301
	620003675, 622014001
Nimustine hydrochloride	644210020, 644210021
Panitumumab	621985901, 622086201
Fluorouracil	614210004, 614210003, 622229101, 622047901
	622412501, 622412601
Bevacizumab	620004872, 620004873
Calcium Folinate	620000424, 620000421, 622513001, 622553701
	622535801, 622544201, 622566001, 622561401
	622548801, 622540801, 622552401
Mitomycin C	620000328, 620000329
Ramucirumab	622417901, 622418001
Regorafenib Hydrate	622225801
Calcium Levofolinate Hydrate	620005725, 620005730, 620005722, 620005729
	620005717, 620005728, 620005718, 620005880
	620005720, 620005881, 620005716, 620005879
	620005719, 620008234, 620005723, 620005726
	620008543, 620005721, 620009589, 620005724
	620009590, 620007161, 620007162, 620005715
	620005727, 621813503, 622119703, 621813603

CRC colorectal cancer

*These codes are applied only to cases with the name of rectal cancer in the claims data

confidence. However, patients with a code for the specific treatment of CRC in the claim in May 2014 were excluded because the treatment might have started prior to the study period. Given that it may take some time for the disease name to be confirmed or modified, we included patients with the disease name of CRC by March 2017. Since the national health insurance does not insure people aged 75 years or older, we included only CRC patients under 72 years of age at the start of treatment, who could be followed for 3 years.

Classification of stages according to the treatment for CRC

Based on the specific treatments performed for CRC during this period, patients with CRC were categorized into three groups: endoscopic treatment only group (endoscopic group), radical surgery with or without postoperative adjuvant chemotherapy group (surgical group), and a palliative therapy group (palliative group). Each treatment in the groups corresponds to the treatment recommended for CRC classified as Stage 0/I (T1a), Stage I (T1b, T2)/II/III, and Stage IV according to the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma by the Japanese Society for Cancer of the Colon and Rectum [15, 16]. In the classification, Tis refers to cancer that does not extend beyond the lamina propria regardless of invasion [15, 17]. Radical surgery was defined as treatment that included resection of the primary lesion. Patients who received radical chemoradiation were included in the surgical group. Palliative treatment included chemotherapy with a total duration of more than 1 year or molecular targeted therapy treatment, treatment for distant metastases including resection, radiation, and radiofrequency ablation of metastatic lesions, colostomy without primary tumor resection, and radiation to the primary lesion. Furthermore, CRC patients who underwent endoscopic or radical surgical treatment (endoscopic and surgical group) were defined as the curable group and those with palliative therapy (palliative group), as the non-curable group. Three gastroenterologists, who were accredited by the Japanese Society of Gastroenterology, confirmed the accuracy of the classification based on treatment in each CRC patient by reviewing individual claims data.

Variables

Primary outcome measure

The primary outcome was the total medical costs in the curable (endoscopic and surgical group) and non-curable (palliative group) groups for 3 years after the initial specific treatment for CRC. Since multiple disease names are recorded on the claim, it is not possible to accurately analyze the costs of individual diseases [18]. Therefore, total medical costs were measured in our study to include various costs associated with CRC, including pre- and post-treatment examinations, perioperative management, treatment for complications due to surgery, management of side effects due to chemotherapy, and treatment for symptoms associated with the progression of cancer, especially in the terminal stage. The median survival time for unresectable colorectal cancer is reported to be approximately 30 months [19–21], and therefore, the period was set at

3 years. The total medical costs were calculated by summing the monthly scores of the national health insurance claims. Medical costs were rounded to the nearest thousand.

Secondary outcome measure

The secondary outcome had four measures: (1) the medical costs for CRC-specific treatment in the curable and noncurable groups for 3 years; (2) medical costs for 1 year, 2 years, and 3 years in the endoscopic, surgical, and palliative groups; (3) the total medical costs for each age group (30-39, 40-49, 50-59, 60-69, and 70-71 years old) in the endoscopic, surgical, and palliative groups; and (4) the incidence rate of CRC calculated using the number of patients identified as those with CRC by our algorithm or those with the disease named CRC in the claims data. The medical costs for CRC-specific treatment, which were calculated using the national fee schedule in 2019 in Japan, included the costs of treatment for distal metastasis in addition to the treatment in Table 1. Medical costs for 1 year, 2 years, and 3 years in the endoscopic, surgical, and palliative groups were calculated to evaluate trends over time in medical costs, and the total medical costs for each age group were examined to identify the differences in medical costs according to age. The median value was also calculated to verify the validity of the results. The incidence rate (per 100,000 person-years) was calculated by dividing the number of CRC patients, identified using our algorithm or the disease name found in the claims data, by the sum of observed periods of people insured by the National Health Insurance. However, detailed information regarding the subjects during the study period was unavailable; thus, we assumed that people insured by the National Health Insurance in 2014 were observed from June 2014 to August 2016 when CRC patients were identified by the algorithm, and from May 2014 to March 2017 when identified by the disease name, for the calculation of the sum of observed periods using the person-year method.

Statistical analyses

Continuous variables were described using medians and interquartile ranges (IQR), and categorical variables were described with numbers in the endoscopic, surgical, and palliative groups. Medical costs were assessed using means, standard deviations (SD), medians, and IQR. The Kruskal–Wallis test, or Pearson's chi-square test, was used to assess whether there were significant differences in the age or sex distributions of CRC patients between the endoscopic, surgical, and palliative groups. To evaluate the difference in medical costs between the curable and noncurable groups, the medical costs between the curable and non-curable groups were compared using the Mann–Whitney U test. Patients with missing values were excluded from statistical analysis. All tests were two-sided, and statistical significance was set at P < 0.05. All statistical analyses were performed using IBM SPSS (version 24.0; IBM Corp., Armonk, NY, USA).

Results

Patients

The number of citizens in Hachioji City insured by the National Health Insurance in 2014 was 155,526. Of 2643 claims with the disease name of CRC from May 2014 to March 2017, 889 patients had the codes relating to the specific treatment for CRC described in Table 1 from June 2014 to August 2016. Two patients did not have detailed information for the calculation of medical costs in their claims, and 35 patients were excluded because the treatment defined as specific treatment for CRC may be performed for other diseases, including treatment for cancer of other organs or diverticular perforation. This study excluded 249 patients aged 72 years old or older (including 121 patients in the endoscopic group, 76 patients in the surgical group, and 52 patients in the palliative group), and included 442 patients in the curable group (267 patients in the endoscopic group and 175 patients in the surgical group), and 161 patients in the non-curable group (Fig. 1).

Characteristics

The median age (IQR) in the endoscopic, surgical, and palliative groups was 67 (64–70), 67 (64–69), and 66 (63–68.5), respectively (P = 0.079) (Table. 2). The male-to-female ratios in the endoscopic, surgical, and palliative groups were 1.34, 1.54, and 1.88 (P = 0.268) (Table. 3).

Total medical costs in the curable and non-curable groups

Table 4 shows that the mean (SD) total medical costs in the curable or non-curable group for 3 years was 2130 (2494) or 8279 (5600) thousand Japanese Yen (JPY) (P < 0.001), respectively, and the median (IQR) total medical costs were 1474 (768–2686) or 7083 (3690–11,614) thousand JPY, respectively.

Medical costs for CRC-specific treatment in the curable and non-curable groups

Table 5 shows that the mean (SD) medical costs for CRC-specific treatment in the curable or non-curable group for

3 years were 408 (352) or 3685 (3479) thousand JPY (P < 0.001), and the median (IQR) medical costs were 291 (145–595) or 2361 (862–5537) thousand JPY, respectively.

Medical costs for 1 year, 2 years, and 3 years in endoscopic, surgical, and palliative groups

The total medical costs and medical costs for CRC-specific treatment for 1 year, 2 years, or 3 years are shown in Tables 4 and 5. In the endoscopic group, the mean (SD) total medical costs for 1 year, 2 years, or 3 years were 517 (685), 924 (1299), or 1302 (1853) thousand JPY and mean (SD) medical costs for CRC-specific treatment were 150 (85), 179 (112), and 198 (128) thousand JPY, respectively. In the surgical group, the mean (SD) total medical costs were 2296 (1375), 2905 (2067), or 3393 (2802) thousand JPY, and the mean (SD) medical costs for CRC-specific treatment were 681 (316), 711 (333), and 728 (345) thousand JPY, respectively. In the palliative group, the mean (SD) total medical costs were 4052 (2406), 6636 (4318), or 8279 (5600) thousand JPY, and the mean (SD) medical costs for CRC-specific treatment were 1758 (1441), 2970 (2669), or 3685 (3479) thousand JPY, respectively.

Total medical costs for each age group in endoscopic, surgical, and palliative groups

Table 6 shows the total medical costs for each age group (30–39, 40–49, 50–59, 60–69, and 70–71 years). In each group classified according to the treatment, groups aged 30–39 or 40–49 years old had less than 10 CRC patients. The maximum value of the difference between the mean total medical costs for the 50–59, 60–69, and 70–71 age groups and those for the group including all ages was 660 thousand JPY.

Incidence rate of CRC from the claims data

This study included 603 patients identified as those with CRC by our algorithm from June 2014 to August 2016 and 2643 patients with the disease name of CRC from May 2014 to March 2017 among approximately 155,000 citizens insured by the National Health Insurance in the city. The incidence rate of CRC was approximately 173 and 585 per 100,000 person-years, respectively.

Discussion

In the present study, we clarified the actual medical costs according to CRC stage in Hachioji City. From the insurer's standpoint, we calculated the mean value of the medical costs, which allowed us to estimate the total

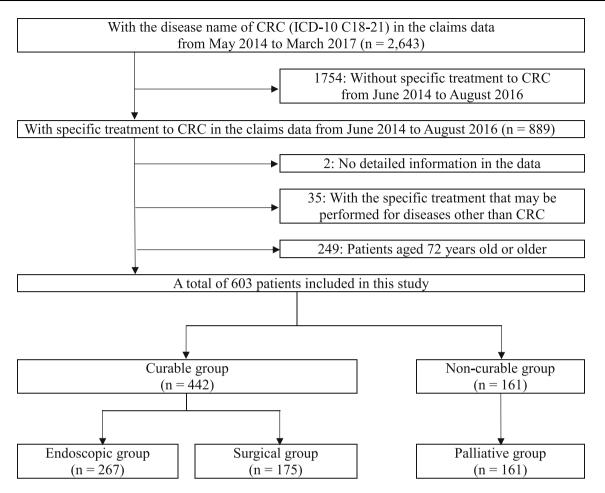


Fig. 1 Flow chart showing details of patient enrollment

Table 2 CRC treat

Age distribution in the atment groups		30–39 years old (<i>n</i>)	40–49 years old (<i>n</i>)	50–59 years old (<i>n</i>)	60–69 years old (<i>n</i>)	70–71 years old (<i>n</i>)	Median age (IQR) [years old]
	Endoscopic group* (n = 267)	1	8	22	169	67	67 (64–70) †
	Surgical group* $(n = 175)$	1	8	14	115	37	67 (64–69) †
	Palliative group* $(n = 161)$	2	6	19	105	29	66 (63–68.5) [†]

*According to the treatment performed in the study, patients with colorectal cancer were categorized into three groups: a group with only endoscopic treatment (endoscopic group), a group with radical surgery (surgical group), and a group with palliative therapy (palliative group)

 $^{\dagger}p = 0.079$

CRC colorectal cancer, IQR interquartile range

medical costs insured by the municipality. The differences in mean total medical costs and medical costs for CRCspecific treatment between the curable and non-curable groups were 6,149 and 3,277 thousand JPY, respectively. These results suggest that early detection of CRC can lead to a considerable reduction in medical costs. Prior to our study, there were no reports that calculated the actual medical costs of CRC patients with the information of all medical procedures performed in Japan [11, 22–24]. While databases linking tumor registries and health insurance

Table 3 Sex distribution in the CRC treatment groups

	Male (<i>n</i>)	Female (<i>n</i>)	P value
Endoscopic group ($n = 267$)	153	114	
Surgical group $(n = 175)$	106	69	0.268
Palliative group $(n = 161)$	105	56	

CRC colorectal cancer

claims data have already been established in the West [25–27], no database has been established in Japan. In the absence of sharing claims data from each hospital, the costs of medical procedures across multiple hospitals cannot be evaluated. Patients with cancer may be transferred to a different hospital depending on their condition or receive emergency care for complications at a different hospital. This is a major problem when considering the medical costs in Japan. By using the health insurance claims data provided by the insurer, such as municipality data, we were able to estimate all medical treatments.

The strength of our study was that three board-certified gastroenterologists, performing medical treatment in clinical situations, confirmed the accuracy of the algorithm by reviewing the claims data, in addition to the use of the algorithm developed for the identification of CRC patients. It has been an issue that the names of diseases registered in the health insurance claims data may differ from the names of diseases actually diagnosed, and include no detailed information, including position and stage of cancer, in the claims data [18, 28, 29]. In the previous simple calculation using the health insurance claims data of Hachioji City from 2012 to 2016, the difference between the total medical cost of CRC patients for 3 years with and without the name of early stage cancer in the claims data was calculated to be approximately 1870 thousand JPY, which was clearly different from those estimated from the present result. Diseases recorded in claims data do not always meet the diagnostic criteria for the disease. By selecting CRC patients from the claims data using only the disease name of CRC, we may extract more CRC patients than the actual cases [28]. In our study, the incidence rate of CRC calculated when CRC patients were defined as those with the disease name of CRC in the claims data was higher than that for men aged 85 and older in 2016 according to the Cancer Registry and Statistics by Cancer Information Service, National Cancer Center, Japan (Ministry of Health, Labour and Welfare, National Cancer Registry). On the other hand, the incidence rate of CRC using the number of patients identified as those with CRC by our algorithm was similar to that in all the subjects reported by

Table 4	Trends in th	e total medical	costs in the	CRC tre	atment groups
---------	--------------	-----------------	--------------	---------	---------------

	Total medical costs for 1 year*	Total medical costs for 2 years*	Total medical costs for 3 years*
		Mean value (SD) [1000 JPY]	
Curable group			2130 (2494) [†]
Endoscopic group	517 (685)	924 (1299)	1302 (1853)
Surgical group	2296 (1375)	2905 (2067)	3393 (2802)
Non-curable group			8279 (5600) [†]
Palliative group	4052 (2406)	6636 (4318)	8279 (5600)
Difference between the	curable and non-curable $\operatorname{groups}^{\ddagger}$		6149
		Median value (IQR) [1000 JPY]	
Curable group			1474 (768–2686)
Endoscopic group	371 (254–573)	647 (438–981)	943 (577–1382)
Surgical group	1923 (1535–2565)	2385 (1795–3012)	2709 (2070–3590)
Non-curable group			7083 (3690–11,614)
Palliative group	4066 (1949–5629)	5987 (2812–9487)	7083 (3690–11,614)
Difference between the	curable and non-curable groups [‡]		5609

CRC colorectal cancer, IQR interquartile range, SD Standard deviation

*Total medical costs for 1 year, 2 years, and 3 years after the initial specific treatments for CRC were evaluated

 $^{\dagger}p < 0.001$

[‡]The differences in the mean and median values of the total medical costs for 3 years between the curable and non-curable groups

	1	e i	
	Medical costs for 1 year*	Medical costs for 2 years*	Medical costs for 3 years*
		Mean value (SD) [1000 JPY]	
Curable group			408 (352) †
Endoscopic group	150 (85)	179 (112)	198 (128)
Surgical group	681 (316)	711 (333)	728 (345)
Non-curable group			3685 (3479) [†]
Palliative group	1758 (1441)	2970 (2669)	3685 (3479)
Difference between the cu	rable and non-curable groups [‡]		3277
		Median value (IQR) [1000 JPY]	
Curable group			291 (145–595)
Endoscopic group	145 (100–181)	145 (100–231)	145 (120–291)
Surgical group	595 (429-839)	601 (495-842)	645 (502-886)
Non-curable group			2361 (862–5537)
Palliative group	1330 (615–2763)	1943 (811–4888)	2361 (862–5537)
Difference between the cu	rable and non-curable $\operatorname{groups}^{\ddagger}$		2070

Table 5 Trends in the medical costs for CRC specific treatments in the CRC treatment groups

CRC colorectal cancer, IQR interquartile range, SD Standard deviation

*The medical costs for CRC specific treatment for 1 year, 2 years, and 3 years after the initial specific treatment for CRC were evaluated $^{\dagger}p < 0.001$

[‡]The differences in the mean and median values of the medical costs for CRC specific treatments for 3 years between the curable and non-curable groups

Table 6 Distribution in the total medical costs for each age group	able 6	ble 6 Distribution in	the total	medical costs	for each	age group)
--	--------	-----------------------	-----------	---------------	----------	-----------	---

	Mean value of total medical costs (SD) [1000 JPY]							
	30-39 years old	40-49 years old	50-59 years old	60-69 years old	70-71 years old	Total		
Endoscopic group $(n = 267)$	938	614 (397)	879 (749)	1362 (2237)	1376 (879)	1302 (1853)		
Surgical group $(n = 175)$	2444	2834 (2102)	2847 (843)	3590 (3114)	3132 (2391)	3393 (2802)		
Palliative group $(n = 161)$	5984 (5684)	7735 (8133)	8648 (6410)	8468 (5449)	7619 (5334)	8279 (5600)		
	Median value of	total medical costs (IQ	R) [1000 JPY]					
Endoscopic group $(n = 267)$	938	512 (283–940)	596 (263–1402)	851 (551–1283)	1230 (920–1602)	943 (577–1382)		
Surgical group $(n = 175)$	2444	1642 (1402–4703)	2789 (2103–3417)	2801 (2070–3597)	2669 (2198–3052)	2709 (2070–3590)		
Palliative group $(n = 161)$	5984	4868 (3132–11,558)	6606 (2923–15,660)	7466 (4427–11,742)	6168 (3529–10,735)	7083 (3690–11,614)		

CRC colorectal cancer, IQR interquartile range, SD Standard deviation

the Cancer Registry and Statistics by Cancer Information Service, National Cancer Center, Japan and another cohort study [30]. Thus, our algorithm and confirmation by boardcertified clinicians would be valuable. We calculated two types of medical costs in our study: total medical costs and medical costs of CRC-specific treatment that could be confirmed to be performed for CRC. The medical costs of CRC-specific treatment in our study were the minimum calculation as direct medical costs for CRC treatment. On the other hand, the total medical costs were the total calculation of all medical costs from the beginning of CRC treatment, and may include costs that are not related to colorectal cancer depending on comorbidities. We could show a range of medical costs related to CRC by presenting both total medical costs and medical costs of CRC-specific treatment. In the palliative group, total medical costs tended to rise more clearly than in the other groups in the second and third years. Although in the palliative group, the total medical costs in the second year were 2584 thousand JPY and 1643 thousand JPY in the third year, the medical costs of CRC-specific treatments, including anticancer agents, were 1212 thousand JPY in the second year and 715 thousand JPY in the third year, which was less than half of the total medical costs (Online Resources 2 and 3). This suggests that medical costs other than the costs of ongoing specific treatment for CRC account for a large portion of the high total medical costs in the palliative group. It is important to compare the total medical costs, especially when considering the medical costs of the non-curable group. This range of medical costs, shown by total medical costs and medical costs of CRC-specific treatment, would be helpful for both patients and insurers. Furthermore, in this study, there was no significant difference in total medical costs according to age in each treatment group. Our data may lead to further recommendations for cancer screening over a wide range of ages.

Further research that shows the accuracy of this algorithm for identifying patients with CRC is required. There are CRC patients with no CRC treatment due to older age or severe comorbidities. Although there were probably few in the age groups included in this study, it was difficult to find CRC patients without treatment for CRC from the claims data, even after a detailed review of the data in our study. Cancer registries and health insurance claims data in Japan should be linked. This may also allow us to clarify the efficacy of CRC screening programs on medical costs. In general, CRC patients with no symptoms have an earlier stage of CRC than those detected with symptoms. This asymptomatic group includes not only patients detected by CRC screening but also those that are incidentally detected during follow-up of other diseases and post-polypectomy colonoscopic surveillance. Cancer registries in Japan, which include information on the process of detection, such as screening and follow-up for other diseases, are expected to make it possible to clarify the effect of cancer screening itself on medical costs.

Our study had some limitations. First, the subjects of this study were limited to those insured by the National Health Insurance, in which the insurer is the municipality. Those insured by insurance do not include persons aged 75 years or older, who are insured by the medical care system for the advanced elderly. Elderly patients may not receive the recommended treatment for CRC, or may require treatment for various complications or comorbidities, which could lead to different results from the present study. Similar studies should be conducted using claims data from other insurance systems. Second, the treatment recommended according to cancer stage may not always match the treatment actually performed for cancer. Some patients may not receive the recommended treatment due to comorbidities. In this study, this limitation mainly caused the classification of the curable group into the non-curable group. This misclassification may lead to a decrease in the difference in medical costs between the curable and noncurable groups. Finally, we calculated the medical costs of patients diagnosed with CRC between 2014 and 2016. With the prolonged prognosis of CRC patients associated with advances in chemotherapy, including the recent introduction of expensive drugs related to immunotherapy, medical costs in the non-curable group are expected to increase further [31]. In the future, our results pertaining to medical costs will require updating.

In conclusion, we clarified the actual medical costs of CRC using the health insurance claims data of Hachioji City. The mean total medical costs in the curable group were 6,149 thousand JPY lower than in the non-curable group, and medical costs for CRC-specific treatment were 3,277 thousand JPY lower. This result suggests the efficacy of the early detection of CRC in reducing medical costs. We hope that our results will be used as fundamental data for the recommendation of CRC screening.

Acknowledgements We are grateful to everyone at Hachioji City involved in this study.

Author contributions Conception and design: TU, TH, YN, YT, JF, TN, and HS. Analysis and interpretation of the data: TU, TH, YN, NH, YT, RG, SK, JF, TN, and HS. Drafting of the article: TU, TH, and YN. Critical revision of the article for important intellectual content: NH, YT, RG, SK, JF, TN, and HS.Final approval of the article: TU, TH, YN, NH, YT, RG, SK, JF, TN, and HS.

Declarations

Conflict of interest Jun Fukuyoshi is the founder of Cancerscan Co. Ltd. Soichiro Kashihara is a member of Cancerscan Co. Ltd. The other authors declare that they have no competing interests.

References

- Saito H. Colorectal cancer screening using immunochemical faecal occult blood testing in Japan. J Med Screen. 2006;13(Suppl 1):S6-7.
- 2. Nakajima M, Saito H, Soma Y, et al. Prevention of advanced colorectal cancer by screening using the immunochemical faecal

occult blood test: a case-control study. Br J Cancer. 2003;89:23-8.

- Saito H, Soma Y, Nakajima M, et al. A case-control study evaluating occult blood screening for colorectal cancer with hemoccult test and an immunochemical hemagglutination test. Oncol Rep. 2000;7:815–9.
- Lee KJ, Inoue M, Otani T, et al. Japan Public Health Centerbased Prospective Study. Colorectal cancer screening using fecal occult blood test and subsequent risk of colorectal cancer: a prospective cohort study in Japan. Cancer Detect Prev. 2007;31:3–11.
- van Rossum LG, van Rijn AF, Laheij RJ, et al. Random comparison of guaiac and immunochemical fecal occult blood tests for colorectal cancer in a screening population. Gastroenterology. 2008;135:82–90.
- Chiu HM, Chen SL, Yen AM, et al. Effectiveness of fecal immunochemical testing in reducing colorectal cancer mortality from the One Million Taiwanese Screening Program. Cancer. 2015;121:3221–9.
- 7. Sano Y, Byeon JS, Li XB, et al. Colorectal cancer screening of the general population in East Asia. Dig Endosc. 2016;28:243–9.
- Brown JP, Wooldrage K, Kralj-Hans I, et al. Effect of once-only flexible sigmoidoscopy screening on the outcomes of subsequent faecal occult blood test screening. J Med Screen. 2019;26:11–8.
- Nishihara R, Wu K, Lochhead P, et al. Long-term colorectalcancer incidence and mortality after lower endoscopy. N Engl J Med. 2013;369:1095–105.
- 10. Saltz LB. The value of considering cost, and the cost of not considering value. J Clin Oncol. 2016;34:659–60.
- Takata K, Fujita KI, Kubota Y, et al. Cost-minimization analysis of adjuvant chemotherapy regimens given to patients with colorectal cancer in Japan. J Pharm Health Care Sci. 2016;2:30.
- Sekiguchi M, Igarashi A, Sakamoto T, et al. Cost-effectiveness analysis of colorectal cancer screening using colonoscopy, fecal immunochemical test, and risk score. J Gastroenterol Hepatol. 2020;35:1555–61.
- Sekiguchi M, Igarashi A, Matsuda T, et al. Optimal use of colonoscopy and fecal immunochemical test for population-based colorectal cancer screening: a cost-effectiveness analysis using Japanese data. Jpn J Clin Oncol. 2016;46:116–25.
- Sekiguchi M, Igarashi A, Sakamoto T, et al. Cost-effectiveness analysis of postpolypectomy colonoscopy surveillance using Japanese data. Dig Endosc. 2019;31:40–50.
- Japanese Society for Cancer of the Colon and Rectum. Japanese classification of colorectal, appendiceal, and anal carcinoma: the d Secondary. J Anus Rectum Colon. 2019;3:175–95.
- Hashiguchi Y, Muro K, Saito Y, et al. Japanese Society for Cancer of the Colon and Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines for the treatment of colorectal cancer. Int J Clin Oncol. 2020;25:1–42.
- Yao T, Shiono S. Differences in the pathological diagnosis of colorectal neoplasia between the East and the West: present status and future perspectives from Japan. Dig Endosc. 2016;28:306–11.
- Kimura S, Sato T, Ikeda S, et al. Development of a database of health insurance claims: standardization of disease classifications and anonymous record linkage. J Epidemiol. 2010;20:413–9.

- Yamada Y, Takahari D, Matsumoto H, et al. Leucovorin, fluorouracil, and oxaliplatin plus bevacizumab versus S-1 and oxaliplatin plus bevacizumab in patients with metastatic colorectal cancer (SOFT): an open-label, non-inferiority, randomised phase 3 trial. Lancet Oncol. 2013;14:1278–86.
- 20. Yamazaki K, Nagase M, Tamagawa H, et al. Randomized phase III study of bevacizumab plus FOLFIRI and bevacizumab plus mFOLFOX6 as first-line treatment for patients with metastatic colorectal cancer (WJOG4407G). Ann Oncol. 2016;27:1539–46.
- Loupakis F, Cremolini C, Masi G, et al. Initial therapy with FOLFOXIRI and bevacizumab for metastatic colorectal cancer. N Engl J Med. 2014;371:1609–18.
- 22. Yajima S, Shimizu H, Sakamaki H, et al. Real-world cost analysis of chemotherapy for colorectal cancer in Japan: detailed costs of various regimens during the entire course of chemotherapy. BMC Health Serv Res. 2016;16:2.
- Shiroiwa T, Fukuda T, Tsutani K. Cost-effectiveness analysis of bevacizumab combined with chemotherapy for the treatment of metastatic colorectal cancer in Japan. Clin Ther. 2007;29:2256–67.
- 24. Miyazaki Y, Harada T, Akase T, et al. Cost-minimization analysis of sequence changes between FOLFIRI and FOLFOX6 therapy for advanced colorectal cancer in Japan. Clin Ther. 2009;31:2433–41.
- Lang K, Lines LM, Lee DW, et al. Lifetime and treatment-phase costs associated with colorectal cancer: evidence from SEER-Medicare data. Clin Gastroenterol Hepatol. 2009;7:198–204.
- Tramontano AC, Chen Y, Watson TR, et al. Racial/ethnic disparities in colorectal cancer treatment utilization and phasespecific costs, 2000–2014. PLoS ONE. 2020;15:e0231599.
- Laudicella M, Walsh B, Burns E, et al. Cost of care for cancer patients in England: evidence from population-based patient-level data. Br J Cancer. 2016;114:1286–92.
- Ogino M, Kawachi I, Otake K, et al. Current treatment status and medical cost for multiple sclerosis based on analysis of a Japanese claims database. Clin Exp Neuroimmunol. 2016;7:158–67.
- 29. Nakayama T, Imanaka Y, Okuno Y, et al. Analysis of the evidence-practice gap to facilitate proper medical care for the elderly: investigation, using databases, of utilization measures for National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB). Environ Health Prev Med. 2017;22:51.
- Fujii T, Ohisa M, Sako T, et al. Incidence and risk factors of colorectal cancer based on 56 324 health checkups: a 7-year retrospective cohort study. J Gastroenterol Hepatol. 2018;33:855–62.
- Verma V, Sprave T, Haque W, et al. A systematic review of the cost and cost-effectiveness studies of immune checkpoint inhibitors. J Immunother Cancer. 2018;6:128.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.