Original Research Article

Prognostic Significance of the Number of Teeth in Patients with Colorectal Cancer

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Abstract

Objectives: *Fusobacterium nucleatum*, which is the predominant subgingival microbial species found in chronic periodontitis, has been recently proposed as a risk factor for both the initiation and progression of colorectal cancer. We evaluated whether the number of teeth, which represents oral health, is a marker for the prognosis of patients with colorectal cancer.

Methods: This retrospective single-center study recruited 179 patients who underwent primary colorectal cancer resection with curative intent between 2015 and 2017. The baseline characteristics and survival were analyzed according to the number of teeth observed in dental panoramic radiographs taken before surgical resection as a part of the perioperative surveillance for oral function and hygiene.

Results: The median number of teeth was 20 (interquartile range: 6-25), including 28 patients with no teeth. Patients with 20 or more teeth had better overall survival ($p = 0.002$) and colorectal cancer-specific survival ($p = 0.032$) than those with less than 20 teeth. Multivariate analyses confirmed that the number of teeth was a significant prognostic factor for overall survival ($p = 0.045$) but not for colorectal cancer-specific survival ($p = 0.258$). We also took a propensity score-weighting approach using inverse probability weighting, and the *p*-values of the number of teeth were 0.032 for overall survival and 0.180 for colorectal cancer-specific survival.

Conclusions: A low number of teeth, which can be easily and noninvasively assessed, has been a poor prognostic factor for overall survival in colorectal cancer patients who underwent surgery with curative intent.

Keywords

tooth number, colorectal cancer, prognostic factor, *Fusobacterium nucleatum*, periodontitis

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Introduction

Colorectal cancer (CRC) is the most common cancer and the second leading cause of cancer-related death in Japan[1]. The incidence of CRC is increasing, and this may be explained by the westernization of dietary habits and the increase in the elderly population[2,3]. However, the underly-

ing mechanisms have not been elucidated. CRC develops through the accumulation of genetic and epigenetic alterations that might be influenced by microbial and other environmental exposures[4,5]. Both ends of the orodigestive tract of humans have abundant microbiota dominated by anaerobic bacteria[6]. The same bacterial genera can be found in oral and colonic samples. *Fusobacterium nucleatum* (FN),
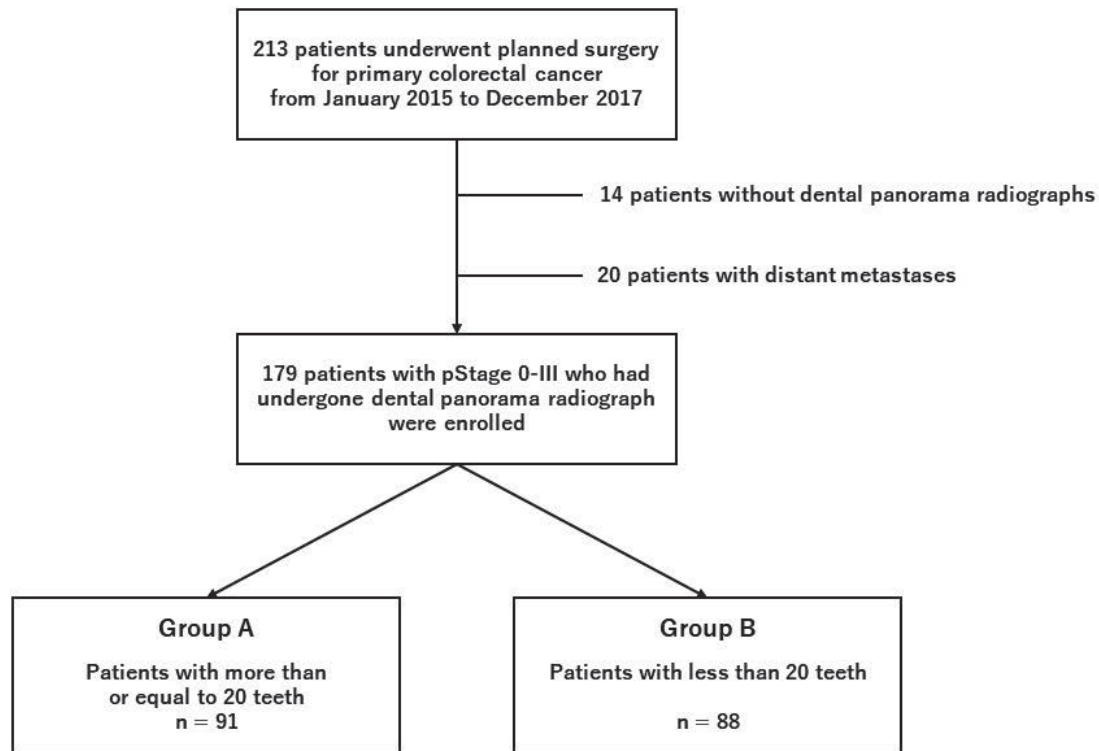
Figure 1. Flow chart showing the cohort of the current study.

which is the predominant subgingival microbial species found in chronic periodontitis, was reported to be associated with non-colitis-associated CRC in 2012[7,8].

The number of teeth is adversely affected by intraoral conditions such as chronic periodontitis, and the number of teeth is well known to be associated with quality of life and life expectancy[9]. Some studies have reported an association between tooth loss or periodontitis and the incidence of CRC or CRC mortality risk[10,11]. However, to the best of our knowledge, the association between the number of teeth and the prognosis of CRC patients has not been elucidated. Therefore, we aimed to investigate whether the number of teeth, which might be affected by periodontitis mainly due to FN, could be a marker for the prognosis of patients with CRC.

Methods

This was a retrospective single-center study that evaluated the prognostic impact of the number of teeth in patients who underwent primary CRC resection with curative intent from January 2015 to December 2017. A perioperative intervention for the optimization of oral function and hygiene has been covered by the Japanese health insurance since 2012. As routine screening for assessment, dental panoramic radiographs were taken before elective surgical resection at our hospital. The number of teeth was retrospectively counted from these dental radiographs.

Patients

All patients who underwent a dental panoramic radiograph before the primary CRC resection with curative intent were included. The baseline characteristics included demographic data such as age at primary cancer resection, sex, body mass index, smoking habit, Eastern Cooperative Oncology Group Performance Status (ECOG PS), and Charlson comorbidity index (CCI). Serum albumin level, serum carcinoembryonic antigen (CEA) level, and serum carbohydrate antigen 19-9 (CA19-9) level were surveyed. We extracted oncological factors such as sidedness of the primary cancer site, TNM (tumor, nodal, metastasis) classification according to the Union for International Cancer Control 8th edition, *RAS* status, and introduction of postoperative adjuvant chemotherapy. The cause of death was categorized into CRC mortality and others, including unknown causes. Overall survival (OS) was defined as the time from primary cancer resection until the date of death or the date of last follow-up (censored). Colorectal cancer-specific survival (CCS) was the time from primary cancer resection until the date of death attributable to CRC. This study was approved by the medical ethics committee of Tottori University Hospital. All the study participants provided informed consent to participate.

Statistical analysis

There is evidence that the number of lost teeth increases

Table 1. Patient and Tumor Characteristics According to the Number of Teeth.

	Number of teeth		
	Group A ≥20 (n = 91)	Group B <20 (n = 88)	p-value
Age (median, range, years)	67 (39–89)	78 (56–92)	0.000*
Sex			0.495
Male	45 (49.5%)	48 (54.5%)	
Female	46 (50.5%)	40 (45.5%)	
BMI (median, IQR, kg/m²)	22.7 (21.1-25.3)	21.5 (19.5-24.2)	0.193
ECOG PS			0.000*
0 or 1	78 (85.7%)	47 (53.4%)	
2–4	13 (14.3%)	41 (46.6%)	
Smoking (missing = 4)			0.296
Never	59 (67.8%)	53 (60.2%)	
Once or current	28 (32.2%)	35 (39.8%)	
Charlson comorbidity index (mean)	2.58	2.83	0.253
Serum albumin level (median, IQR, g/dL)	4.1 (3.8-4.4)	3.9 (3.5-4.1)	0.000*
Serum CEA level (missing = 12. Median, IQR, ng/mL)	3.0 (1.9-5.8)	3.3 (2.2-6.7)	0.392
Serum CA19-9 level (missing =14. Median, IQR, U/mL)	13.0 (8.8-25.0)	14.0 (8.0-25.0)	0.543
Primary tumor sidedness			0.525
Right	31 (34.1%)	34 (38.6%)	
Left (including rectum)	60 (65.9%)	54 (61.4%)	
T stage			0.059
0–2	37 (40.7%)	24 (27.3%)	
3–4	54 (59.3%)	64 (72.7%)	
Nodal metastases			0.248
Negative	60 (65.9%)	65 (73.9%)	
Positive	31 (34.1%)	23 (26.1%)	
Stage			0.139
0	8 (8.8%)	5 (5.7%)	
I	24 (26.4%)	18 (20.5%)	
II	28 (30.8%)	42 (47.7%)	
III	31 (34.1%)	23 (26.1%)	
RAS status (missing = 23)			0.450
Wild type	39 (52.0%)	47 (58.0%)	
Mutated	36 (48.0%)	34 (42.0%)	
Adjuvant chemotherapy			0.530
No	58 (63.7%)	60 (68.2%)	
Yes	33 (36.3%)	28 (31.8%)	

BMI = body mass index; IQR = interquartile range; ECOG PS = Eastern Cooperative Oncology Group Performance Status;

CEA = carcinoembryonic antigen; CA19-9 = carbohydrate antigen

*$p < 0.05$

with age[12]. Pearson's correlation analysis was conducted to verify this association in the study population. To assess the clinical impact of the remaining number of teeth on prognosis, the study population was categorized into two groups: patients with more than or equal to 20 teeth as Group A and those with less than 20 teeth as Group B. Patient characteristics and tumor clinicopathological features were presented as numbers and associated percentages for categorical data and as medians and interquartile ranges (IQRs) for continuous variables. Significant differences between the two groups were analyzed using the chi-square test or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Survival curves were plotted using the Kaplan-Meier method, and survival differences were calculated using the log-rank test. To identify predictors of OS and CCS, univariable analysis was performed using the Cox proportional hazards model to determine the hazard ratio (HR) with 95% confidence interval (CI). Continuous variables from blood samples were divided into categorical variables by its reference range during univariable analysis. Multivariable analyses of OS and CCS with factors, which were significantly different in the patient
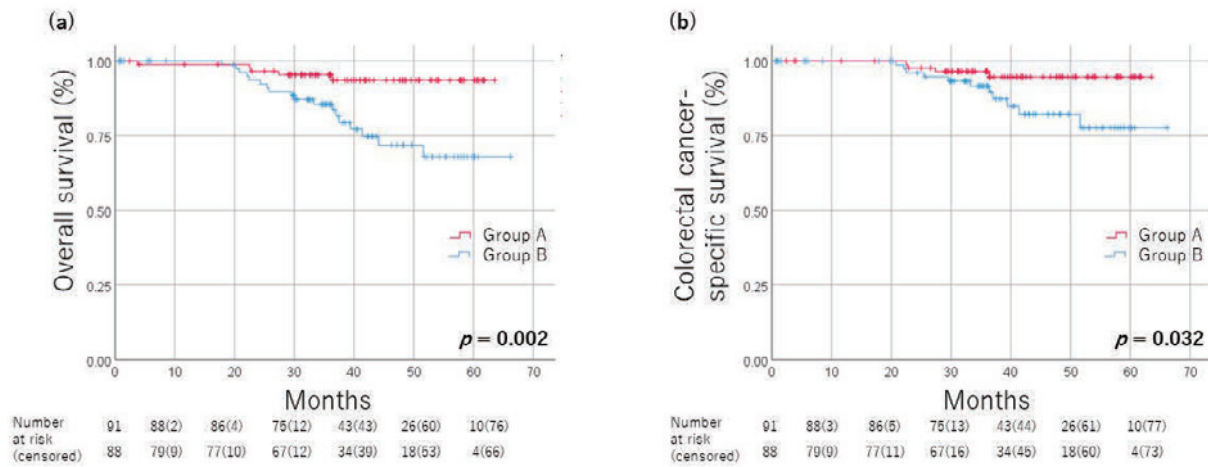
Figure 2. Survival according to the number of teeth.
(a) Overall survival (n = 179; *p* = 0.002); (b) CRC-specific survival (n = 179; *p* = 0.032) in patients who underwent primary tumor resection with curative intent.

characteristics according to the number of teeth, were planned to exclude confounding variables. A two-sided *p*-value of less than 0.05 was considered to be statistically significant in all the tests. These statistical analyses were conducted using IBM SPSS (version 24.0; IBM Inc., Chicago, IL, USA).

Because of the small sample size and the number of events, the number of explanatory variables to use was limited. Thus, we took a propensity score-weighting approach to reduce the influence of confounding factors. The propensity score was defined as the probability of the number of teeth factor conditional on specified covariates. Each case was weighted according to the inverse propensity score for the number of teeth factor. Inverse probability weighting (IPW) has been shown to be an effective means of balancing covariates and has superior performance to propensity score matching, particularly with small sample sizes[13,14]. Age, sex, ECOG PS, smoking habit, CCI, serum albumin level, serum CEA level, serum CA19-9 level, primary tumor sidedness, T stage, nodal metastases, and introduction of postoperative adjuvant chemotherapy were included in the propensity score calculation. The balance between the groups before and after IPW was assessed using the standardized mean difference (SMD) between the groups. An absolute value of SMD of greater than 0.1 is usually considered to indicate a significant imbalance[15]. Our propensity score-weighting analysis was conducted using R 3.5.3.

Results

In total, 213 patients underwent planned surgery for primary CRC between January 2015 and December 2017. Dental panoramic radiographs were taken in 199 out of 213 patients before surgery. Of these, 20 patients were diagnosed with Stage IV CRC. Finally, 179 patients without distant metastasis who underwent dental panoramic radiography before surgery were enrolled in this study (Figure 1). Of them, 10 received preoperative chemotherapy and/or irradiation against CRC. Sixty-one patients received adjuvant chemotherapy after surgery. Regarding the selected regimens, 45 patients received a course of fluorinated pyrimidines and 16 received a doublet regimen such as CAPOX and mFOLFOX 6. The completion rate for adjuvant chemotherapy at 6 months was 80.3% (49 out of 61 patients). The median follow-up period from the date of primary cancer resection was 36.5 months (IQR: 30.3-49.5 months). Overall death and CRC-specific death occurred in 23 and 15 patients during follow-up, respectively. The median number of teeth was 20 (IQR: 6-25), including 28 patients with no teeth. Therefore, the patients were classified into two groups. Group A and Group B included 91 patients with more than or equal to 20 teeth and 88 patients with less than 20 teeth, respectively. The patient and tumor characteristics according to these groups are shown in Table 1. There were significant differences in age (*p* = 0.000), ECOG PS (*p* = 0.000), and serum albumin levels (*p* = 0.000) between the two groups, and these covariates were invested in the multivariable analysis.

Kaplan-Meier survival curves are shown in Figure 2. Patients in Group A had significantly better OS (*p* = 0.002) and CCS (*p* = 0.032) than those in Group B. The results of univariable analyses for OS and CCS are presented in Table 2. Age, sex, ECOG PS, CCI, number of teeth, serum albumin level, serum CEA level, and T stage were significant prognostic factors for OS. Age, sex, ECOG PS, number of teeth, and serum CEA level showed significant differences for CCS.

Figure 3 shows the scatter diagram between the number

Table 2. Factors Associated with Overall Survival and Cancer-Specific Survival after Primary Tumor Resection.

	Univariable					
	Overall survival			Colorectal cancer-specific survival		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Age (years)						
<70		Ref.			Ref.	
≥70	2.597	1.022–6.579	0.045*	3.731	1.053-13.333	0.041*
Sex						
Male		Ref.			Ref.	
Female	0.234	0.079-0.687	0.008*	0.280	0.079-0.992	0.049*
ECOG PS						
0 or 1		Ref.			Ref.	
2–4	4.831	2.096-11.111	0.000*	4.367	1.567-12.195	0.005*
Smoking						
Never		Ref.			Ref.	
Once or current	1.527	0.673-3.460	0.311	0.602	0.192-1.894	0.386
Charlson comorbidity index						
<4		Ref.			Ref.	
≥4	3.401	1.326-8.696	0.011*	2.597	0.726-9.346	0.142
Number of teeth						
≥20 (Group A)		Ref.			Ref.	
<20 (Group B)	4.227	1.569-11.388	0.004*	3.253	1.036-10.219	0.043*
Serum albumin level (g/dL)						
≥4.1		Ref.			Ref.	
<4.1	3.961	1.347-11.644	0.012*	3.341	0.943-11.840	0.062
Serum CEA level (ng/mL)						
<5.0		Ref.			Ref.	
≥5.0	2.439	1.025-5.814	0.044*	3.215	1.074-9.615	0.037*
Serum CA19-9 level (U/mL)						
≤37.0		Ref.			Ref	
>37.0	1.764	0.639-4.854	0.274	2.058	0.642-6.579	0.225
Primary tumor sidedness						
Left (including rectum)		Ref.			Ref.	
Right	1.421	0.622-3.243	0.404	2.114	0.765-5.837	0.149
T stage						
0–2		Ref.			Ref.	
3–4	12.987	1.745-100.000	0.012*	41.667	0.543-∞	0.092
Nodal metastases						
Negative		Ref.			Ref.	
Positive	2.070	0.912-4.695	0.082	1.980	0.717-5.464	0.187
Adjuvant chemotherapy						
No		Ref.			Ref.	
Yes	0.635	0.262-1.536	0.313	0.370	0.048-2.841	0.339

ECOG PS = Eastern Cooperative Oncology Group Performance Status; CEA = carcinoembryonic antigen; CA19-9 = carbohydrate antigen; HR = hazard ratio; CI = confidence interval; Ref. = reference
*$p < 0.05$

of teeth and age. Pearson's correlation coefficient and the coefficient of determination were −0.542 and 0.294 (*p* = 0.000), respectively. We performed subgroup analyses for OS between Groups A and B (Figure 4). The forest plot was constructed in the log scale. All point estimations of covariates were favorable in Group A. OS was significantly better in Group A than in Group B in subgroups such as male, smoker or ex-smoker, CCI less than 4, serum albumin level less than 4.1 g/dL, serum CA19-9 level less than 37.0 U/mL, left tumor sidedness, T stage 3 or 4, negative or positive lymph node metastasis, wild-type *RAS*, and no adjuvant chemotherapy. In the multivariable analysis of the covari-
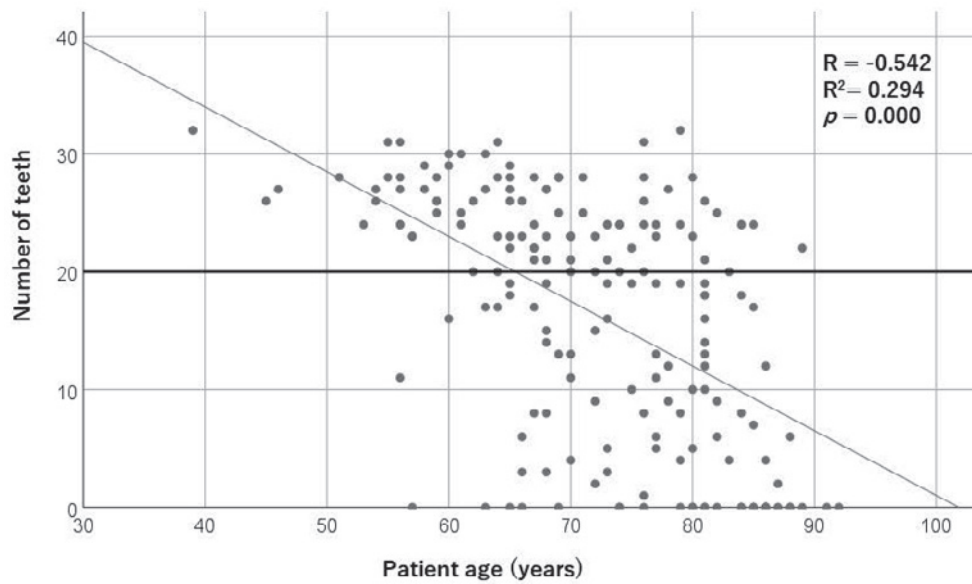
Figure 3. Scatter diagram comparing patient age and the number of teeth.
Pearson's correlation coefficient and the coefficient of determination were −0.542 and 0.294 (*p* = 0.000), respectively.

Characteristics			n	HR	95% CI
Age	years	< 70	76	2.828	0.571-14.022
		≥ 70	103	4.157	0.950-18.192
Sex		male	93	3.084	1.108-8.580*
		female	86	84.312	NA
ECOG PS		0-1	125	2.303	0.648-8.179
		2-4	54	5.622	0.722-43.849
Smoking		never	112	2.591	0.779-8.618
		once or current	67	10.718	1.371-83.775*
CCI		< 4	153	4.175	1.361-12.807*
		≥ 4	26	2.099	0.244-18.060
Serum albumin level	g/dl	< 4.1	103	3.427	1.136-10.340*
		≥ 4.1	76	4.796	0.499-46.113
Serum CEA level	ng/ml	< 5	110	4.765	0.988-22.972
		≥ 5	58	2.779	0.752-10.272
Serum CA19-9 level	U/ml	< 37	11	6.830	1.541-30.269*
		≥ 37	25	3.303	0.551-19.809
Tumour sidedness		right	65	3.973	0.842-18.735
		left	114	4.135	1.137-15.036*
T stage		0-2	61	119.107	NA
		3-4	118	3.419	1.260-9.273*
Lymph node metastasis		negative	125	5.298	1.161-24.183*
		positive	54	3.855	1.020-14.570*
RAS status		wild	86	8.325	1.054-65.727*
		mutant	70	2.205	0.645-7.535
Adjuvant chemotherapy		no	118	3.601	1.174-11.047*
		Yes	61	7.434	0.895-61.764

ECOG PS = Eastern Cooperative Oncology Group Performance Status; CEA = carcinoembryonic antigen; CA19-9 = carbohydrate antigen; HR = hazard ratio; CI = confidence interval; NA = not available
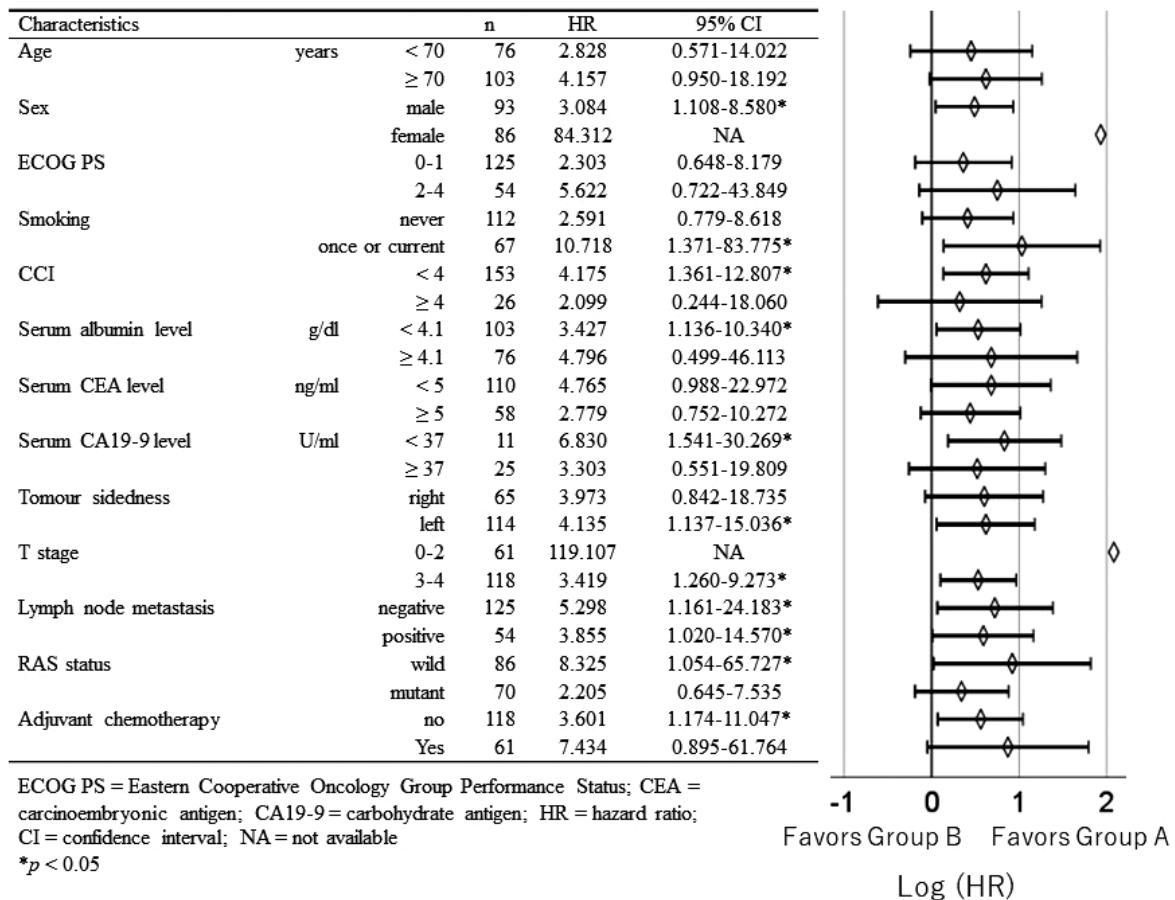*p < 0.05

Log (HR)

Figure 4. Subgroup analyses for overall survival.
HR = hazard ratio; CI = confidence interval; ECOG PS = Eastern Cooperative Oncology Group Performance Status; CCI = Charlson comorbidity index; CEA = carcinoembryonic antigen; CA19-9 = carbohydrate antigen; NA = not available

Table 3. Multivariable Analysis of Factors that Were Significantly Different in the Patient Characteristics According to the Number of Teeth for Overall Survival and Colorectal Cancer-Specific Survival.

| | Multivariable | | | | | |
| | Overall survival | | | Colorectal cancer-specific survival | | |
	HR	95% CI	p-value	HR	95% CI	p-value
Age (years)						
<70		Ref.			Ref.	
≥70	1.590	0.431–5.869	0.487	1.435	0.302-6.803	0.649
ECOG PS						
0 or 1		Ref.			Ref.	
2–4	3.984	1.267-12.500	0.018*	2.639	0.772-9.009	0.122
Number of teeth						
≥20 (Group A)		Ref.			Ref.	
<20 (Group B)	2.983	1.025-8.681	0.045*	2.029	0.596-6.907	0.258
Serum albumin level (g/dL)						
≥4.1		Ref.			Ref.	
<4.1	2.836	0.941-8.546	0.064	2.379	0.654-8.661	0.189

ECOG PS = Eastern Cooperative Oncology Group Performance Status; HR = hazard ratio; CI = confidence interval; Ref. = reference

*$p < 0.05$

ates, which were found to be significantly different between Group A and Group B, ECOG PS and the number of teeth were significant prognostic factors for OS (Table 3, p = 0.018 and 0.045, respectively). However, none of these covariates was significant for CCS.

Using IPW of covariates, patient characteristics, including patient age, sex, ECOG PS, smoking habit, CCI, serum albumin level, serum CEA level, primary tumor sidedness, T stage, and introduction of adjuvant chemotherapy, could be well adjusted between the two groups (Table 4). The results of univariable analysis after IPW of the number of teeth showed p-values of 0.032 and 0.180 in OS and CCS, respectively (Table 5). The absolute value of the SMD of nodal metastases was still greater than 0.1 (SMD = 0.1021); however, it could be acceptable in comparison with those before IPW adjustment. Group A did not demonstrate a significant difference in CCS after IPW. However, point estimations of Group B against Group A for CCS remained as high as 2.323.

Discussion

In this study, several characteristics, which are known prognostic indicators of CRC including age, ECOG PS, and serum albumin levels, were favorable prognostic indicators for patients in Group A. As expected, the number of teeth was inversely proportional to age (p = 0.000), although Pearson's correlation coefficient and the coefficient of determination were low (R = −0.542, R^2 = 0.294). Patients in Group B were older than those in Group A (median ages;

78 years vs 67 years, p = 0.000), and ECOG PS of Group B was worse than that of Group A (percentage of ECOG PS 2-4; 46.6% vs 14.3%, p = 0.000). The study enrolled only patients who could tolerate surgery. ECOG PS 2-4 in Group B included only one patient of ECOG PS 4, three patients of ECOG PS 3, and the rest were ECOG PS 2. This selection might reflect that there was no significant difference in CCI between the two groups even though the percentage of ECOG PS 2-4 was significantly higher in Group B. The serum albumin level of Group A was superior to that of Group B (p = 0.000). The number of teeth is associated with age, which is also associated with ECOG PS and serum albumin level. Multivariable analysis of these covariates showed that the number of teeth and ECOG PS, but neither age nor serum albumin level, were independent prognostic factors for OS (p = 0.045, 0.018, 0.487, and 0.064, respectively). This result supports the idea that the number of teeth has a stronger effect on the OS of CRC patients than age and serum albumin level, although there may have been some degree of confounding. In the univariable analysis, there were several factors that showed a significant difference for OS and CCS other than age, ECOG PS, number of teeth, and serum albumin level. Because of the small sample size of this study and the limited number of events, the number of covariates to invest in the multivariable analysis should be limited to a few. Thus, we took another approach using IPW for further exploration. After IPW for the number of teeth factor, we could find well-balanced covariates. Only OS showed a significant difference in the univariable analysis after IPW. The dataset in our study consisted of 179 pa-

Table 4. Patient and Tumor Characteristics According to the Number of Teeth before and after IPW.

	Before IPW			After IPW		
	Percentage		SMD	Percentage		SMD
	Group A (≥20)	Group B (<20)		Group A (≥20)	Group B (<20)	
Age (years)			−0.8548*			0.0096
<70	61.5	22.7		41.6	42.1	
≥70	38.5	77.3		58.4	57.9	
Sex			0.1021*			0.0466
Male	49.5	54.5		49.8	52.1	
Female	50.5	45.5		50.2	47.9	
ECOG PS			-0.7498*			0.0630
0 or 1	85.7	53.4		66.4	69.3	
2–4	14.3	46.6		33.6	30.7	
Smoking			-0.1586*			-0.0280
Never	67.8	60.2		63.8	62.4	
Once or current	32.2	39.8		36.2	37.6	
Charlson comorbidity index			-0.3347*			-0.0019
<4	91.2	79.5		85.6	85.5	
≥4	8.8	20.5		14.4	14.5	
Serum albumin level (g/dL)			-0.3853*			-0.0663
≥4.1	51.6	33.0		43.8	40.5	
<4.1	48.4	67.0		56.2	59.5	
Serum CEA level (ng/mL)			-0.1855*			0.0688
<5.0	69.8	61.0		64.4	67.7	
≥5.0	30.2	39.0		35.6	32.3	
Serum CA19-9 level (U/mL)			0.1665*			-0.0803
≤37.0	83.1	88.9		85.9	83.0	–
>37.0	16.9	11.1		14.1	17.0	
Primary tumor sidedness			0.0951			-0.0263
Left (including rectum)	65.9	61.4		64.5	65.7	
Right	34.1	38.6		35.5	34.3	
T stage			0.2855*			0.0745
0–2	40.7	27.3		31.6	35.1	
3–4	59.3	72.7		68.4	64.9	
Nodal metastases			0.1735*			0.1021*
Negative	65.9	73.9		66.6	71.4	
Positive	34.1	26.1		33.4	28.6	
Adjuvant chemotherapy			0.0939			-0.0270
No	53.7	58.2		67.5	66.3	
Yes	36.3	31.8		32.5	33.7	

IPW = inverse probability weighting; SMD = standardized mean difference; ECOG PS = Eastern Cooperative Oncology Group Performance Status; CEA = carcinoembryonic antigen; CA19-9 = carbohydrate antigen
*|standardized mean difference| > 0.1

Table 5. Univariable Analysis of the Number of Teeth for Overall Survival and Colorectal Cancer-Specific Survival after IPW.

	Overall survival			Colorectal cancer-specific survival		
	HR	95% CI	p-value	HR	95% CI	p-value
Number of teeth						
≥20 (Group A)		Ref.			Ref.	
<20 (Group B)	3.297	1.107–9.823	0.032	2.323	0.677–7.968	0.180

HR = hazard ratio; CI = confidence interval; Ref. = reference

tients, with a median follow-up period of 36.5 months. The number of CRC-specific deaths was only 15. Further analytical and clinical validations in studies consisting of larger sample sizes and longer follow-up periods are required to estimate whether the number of teeth is an independent prognostic factor for CCS.

According to the subgroup analysis in Figure 4, we saw that all point estimations of covariates were favorable in Group A. This result may also emphasize our hypothesis that the number of teeth indicates the prognosis of CRC patients. The HRs of unfavorable characteristics, such as older age (≥ 70 years), ECOG PS 2-4, smoker or ex-smoker, and hypoalbuminemia (< 4.1 g/dL), tended to be higher than those of favorable characteristics. The number of teeth is more likely to indicate the prognosis of the unfavorable population with greater significance than that of the favorable population. The number of teeth can be easily assessed with or without a dental radiograph almost noninvasively. With an increasing life expectancy and an increase in the elderly population, the number of teeth of CRC patients should be considered as one of the prognostic factors that affect OS more than patient age. Additionally, perioperative oral management has succeeded in reducing the risk of surgical site infection or postoperative pneumonia in CRC[16].

Nodal metastases should be a strong prognostic factor for the survival of CRC patients. However, the univariate analysis in our study did not show significant differences for OS or CSS ($p = 0.082$ and 0.187, respectively). The survival of patients with incurable metastases has increased by more than 30 months with remarkable advances in chemotherapy in this century[17]; hence, our study may be immature, with a median follow-up period of 36.5 months. Chemotherapy after diagnosis of recurrence evidently influences the prognosis of CRC patients. Because this was a retrospective cohort study, various regimens of chemotherapy had been administered at the doctor's discretion; hence, these therapeutic interventions were not taken into consideration, except adjuvant chemotherapy. A larger sample size is required to consider the influence of chemotherapeutics in the analysis.

Several studies have reported the correlation between the number of teeth and the incidence of CRC or CRC mortality risk[18-20] and have concluded a causal relationship between CRC and systemic chronic inflammation due to periodontitis[21]. As one of the mechanisms, lipopolysaccharide is a known risk factor for both cardiovascular disease and CRC progression and acts through the Toll-like receptor 4 and NF-κB[22]. The modified Glasgow prognostic score (mGPS), which is based on serum C-reactive protein and albumin, is already known to indicate the prognosis of CRC patients[23]. Our study did not consider any inflammatory index in exploring the correlation between periodontitis and systemic chronic inflammation. There are intraindividual diversities and similarities in the salivary and fecal microbiota[24]. Moreover, gastrectomy causes marked changes in oral and gut microbiota[25]. Recent studies also showed that FN initiates CRC cell growth and promotes tumor multiplicity[26,27]. Collectively, these findings suggest that the translocation of FN from the oral cavity to the gut may play a role in the initiation and promotion of CRC. However, neither the amount of FN in the oral cavity nor colorectal carcinoma of patients was quantified in our study. Thus, whether the correlation between the number of teeth and the prognosis of CRC patients is a direct result of the change in the gut microbiota due to FN in the oral cavity or due to systemic inflammation resulting from periodontitis[28,29] remains an unresolved concern.

Our study may provide a scope for future research on whether changes in the intestinal microbiota are the cause or the result of carcinogenesis and whether microbiota in the oral cavity contribute to cancer progression.

Conclusion

A low number of teeth was a poor prognostic factor for OS in CRC patients who underwent surgery with curative intent. The number of teeth can be easily assessed with or without a dental radiograph almost noninvasively. With an increasing life expectancy and an increase in the elderly population, the number of teeth of CRC patients should be considered as one of the prognostic factors. Further analytical and clinical validations in studies consisting of larger sample sizes and longer follow-up periods are required to estimate whether the number of teeth is an independent prognostic factor for CCS.

Conflicts of Interest
There are no conflicts of interest.

Author Contributions
Study conception and design: K. Kihara and M. Yamamoto; acquisition of data: K. Kihara, K. Hara, K. Sugezawa, C. Uejima, A. Tanio, and Y. Tada; analysis and interpretation of data: K. Kihara, H. Noma, and N. Tokuyasu; drafting of the manuscript: K. Kihara; critical revision of the manuscript: T. Sakamoto, S. Honjo, and Y. Fujiwara.

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