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Effect of perioperative oral management on the prevention of surgical site infection after colorectal cancer surgery

A multicenter retrospective analysis of 698 patients via analysis of covariance using propensity score

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Abstract

Surgical site infection (SSI) is 1 of the frequent postoperative complications after colorectal cancer surgery. Oral health care has been reported to reduce the risk of SSI or postoperative pneumonia in oral, esophageal, and lung cancer surgeries. The purpose of the study was to investigate the preventive effect of perioperative oral management on the development of SSI after a major colorectal cancer surgery.

The medical records of 698 patients who underwent colorectal cancer surgery at 2 hospitals in Japan were reviewed. Among these patients, 563 patients received perioperative oral management (oral management group) and 135 did not (control group). Various demographic, cancer-related, and treatment-related variables including perioperative oral management intervention and the occurrence of SSI were investigated. The relationship between each variable and the occurrence of SSI was examined via univariate and multivariate analyses using Fisher exact test, 1-way analysis of variance (ANOVA), and logistic regression. The occurrence of SSI in the 2 groups was evaluated via logistic regression using propensity score as a covariate. The difference in mean postoperative hospital stay between the oral management and control groups was analyzed using Student's t test.

SSI occurred in 68 (9.7%) of the 698 patients. Multivariate analysis showed that operation time, blood loss, and perioperative oral management were significantly correlated with the development of SSI. However, after the propensity score analysis, not receiving perioperative oral management also became a significant risk factor for SSI. The odds ratio of the oral management group was 0.484 ($P = .014$; 95% confidence interval: 0.272–0.862). Mean postoperative hospital stay was significantly shorter in the oral management group than in the control group.

Perioperative oral management reduces the risk of SSI after colorectal cancer surgery and shortens postoperative hospital stay.

Abbreviations: ALT = alanine aminotransferase, BMI = body mass index, CDC = Centers for Disease Control and Prevention, CRP = C-reactive protein, ERAS = enhanced recovery after surgery, SSI = surgical site infection.

Keywords: colorectal cancer surgery, oral management, propensity score, surgical site infection

1. Introduction

Perioperative oral management has been performed in patients undergoing cancer surgery as perioperative management using a team approach involving nutrition management, medicines management, and rehabilitation teams. Some investigators have reported the preventive effect of perioperative oral management on postoperative pneumonia and surgical site infection (SSI) after esophageal, cardiac, and oral cancer surgeries and thoracic surgery.[1–7] However, there are only a few studies with high evidence level; therefore, the recommendations of the Centers for Disease Control and Prevention (CDC) Guideline[8] and enhanced recovery after surgery (ERAS) program[9] do not contain the description of oral management.

Although the fasting period after digestive surgery has recently been shortened due to the introduction of the ERAS program, digestive surgery is still longer than other types of surgery; thus, there is an increase in oral bacteria after surgery. Therefore, perioperative oral management is considered especially important in patients who are to undergo digestive surgery, but there have been only a few reports regarding the appropriate oral

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management methods and their effectiveness in the prevention of postoperative complications.

SSI is 1 of the most frequent postoperative complications after major gastrointestinal surgeries,[10] especially after colorectal cancer surgery; its occurrence and severity are generally known to be relatively high.[11,12] SSI leads to a longer hospital stay, decrease in quality of life, increased medical cost, as well as mortality of patients; therefore, recommendations have been proposed for its prevention.[13,14] According to the CDC Guideline, it is recommended to whenever possible, identify and treat all infections remote to the surgical site before elective operation and postpone elective operations on patients with remote site infections until the infection has resolved.[8] One of the most frequent remote infections is an intraoral infectious lesion such as periodontal disease of periapical periodontitis.

We previously reported that perioperative oral management reduced the occurrence of postoperative pneumonia in patients who underwent esophageal cancer surgery.[1,2] The purpose of the current study was to investigate whether perioperative oral management can prevent SSI after colorectal cancer surgery using a multicenter retrospective study with a large sample size.

2. Materials and methods

2.1. Patients

This retrospective cohort study included all patients who underwent colorectal cancer surgery with curative intent at Hiroshima Prefectural Hospital or Nagasaki University Hospital between 2014 and 2016. The exclusion criteria were palliative surgery, transanal endoscopic surgery, and emergency surgery. After excluding patients with inadequate or unknown information, the remaining 698 patients were eligible for inclusion.

The standard infection control methods were performed according to the recommendation of CDC Guideline.[8] Patients received administration of antibiotics such as cefmetazole, flomoxef, or cefazolin plus metronidazole during surgery and for 24 to 48 hours postoperatively.

2.2. Oral management intervention

Among a total of 698 patients, 563 received perioperative oral management by dentists and dental hygienists immediately after their referral to the dentistry department. The oral management consisted of instructions regarding self-care, extraction of infected teeth, removal of dental plaques and calculus (scaling), professional mechanical teeth cleaning, removal of tongue coating, and cleaning of dentures. Self-care instructions included teeth brushing, interdental brushing, dental flossing, tongue brushing, denture brushing, and gargling. A total of 335 patients received professional oral management 2 or more times before surgery, and 228 patients received it once. The remaining 135 patients did not receive the perioperative oral management intervention.

2.3. Variables

The following variables were examined using the patients' medical records;

1) age,
2) gender,
3) body mass index (BMI),
4) general complications (diabetes, hypertension, and heart disease),
5) serum laboratory data before surgery (albumin, alanine aminotransferase [ALT], creatinine, and C-reactive protein (CRP)),
6) site of cancer (colon/rectum),
7) operation time,
8) blood loss,
9) method of surgery (laparoscopic surgery versus laparotomy),
10) occurrence of SSI, and
11) postoperative hospital stay.

2.4. Statistical analysis

Statistical analyses were performed using software (SPSS version 24.0; Japan IBM Co., Tokyo, Japan). First, the correlation between each variable and SSI occurrence in the 698 patients was analyzed using Fisher exact test and 1-way analysis of variance (ANOVA), followed by multivariate logistic regression analysis using stepwise selection. Mean hospital stay in the oral management and control groups was compared using Student *t* test. In all the analyses, a 2-tailed *P* value $<.05$ was considered statistically significant.

Subsequently, propensity score analysis was performed to reduce the selection bias associated with retrospective data. A propensity score was calculated for each patient using logistic regression with the following variables: age, gender, BMI, diabetes, hypertension, heart disease, serum albumin, ALT, creatinine, CRP, operation time, blood loss, tumor site, and operation method. The oral management group was compared to the control group using logistic regression analysis with propensity score as a covariate.

2.5. Ethics

This study was approved by the institutional review board of Nagasaki University Hospital (N0. 17082139). This was a retrospective study, and therefore we published research plan and guaranteed opt-out opportunity by the homepage of our hospital according to instruction of the institutional review board.

3. Results

Table 1 shows the background data of the 563 patients in the oral management group and the 135 patients in the control group. There was some bias between the 2 groups regarding heart disease, albumin, creatinine, CRP, and surgical method. More patients in the oral management group underwent laparotomy than in the control group. The mean operation time and blood loss did not differ significantly between the groups.

SSI occurred in 68 (9.7%) of the 698 patients. Using univariate analysis, operation time, blood loss, and oral management intervention were significantly correlated with the occurrence of SSI (Table 2). Multivariate analysis showed that operation time, blood loss, and oral management intervention were significantly correlated with SSI (Table 3). The odds ratio of the patients who received oral management was 0.428 ($P=.003$; 95% confidence interval [CI]: 0.244–0.749). Further, from the propensity score analysis, oral management intervention significantly reduced the risk of SSI (Table 4). The odds ratio of the oral management group was 0.484 ($P=.014$; 95% CI: 0.272–0.862).

Regarding the relationship between the frequency of oral care and SSI prevention, patients who received 2 or more oral management sessions had a lower frequency of SSI and

Table 1

Demographic characteristics of the oral management and control groups (698 patients).

Variable		Oral management group (n = 563)	Control group (n = 135)	*P* value
Age	(years)	68.3 ± 11.6	69.9 ± 11.5	.166
Gender	male	305	77	.565
	female	258	58	
BMI	(kg/m^2)	22.4 ± 3.46	22.2 ± 3.45	.446
Diabetes	(-)	450	104	.478
	(+)	113	31	
Hypertension	(-)	308	74	.478
	(+)	255	61	
Heart disease	(-)	534	112	<.001*
	(+)	29	23	
Albumin	(g/dL)	3.91 ± 0.505	3.80 ± 0.661	.024*
ALT	(U/L)	19.9 ± 17.4	19.6 ± 14.6	.831
Creatinine	(mg/dL)	0.862 ± 0.700	1.08 ± 1.29	.007*
CRP	(mg/dL)	0.620 ± 1.44	0.940 ± 2.16	.037*
Operation time	(minute)	280 ± 98.4	297 ± 114	.081
Blood loss	(g)	158 ± 259	150 ± 235	.724
Site	colon	376	91	.919
	rectum	187	44	
Operation method	laparoscopic surgery	340	107	<.001*
	laparotomy	223	28	

ALT = alanine aminotransferase, BMI = body mass index, CRP = C-reactive protein.
* significant values are expressed as means ± standard deviation or number.

significantly shorter postoperative hospital stay than those who received only 1 oral management session (Table 5).

4. Discussion

The oral cavity has been recognized as a significant reservoir of pathogenic microorganisms, which cause the infection of multiple organs[15–17]; therefore, quantitative and qualitative control of oral bacteria via oral health care is considered important for the prevention of infectious diseases. Oral bacteria are known to influence various general diseases, such as pneumonia,[18] cardiovascular[19] and cerebrovascular disease,[20] rheumatoid arthritis,[21] preterm birth or low-weight birth,[22] and carcinogenic[23] and non-alcoholic steatohepatitis.[24] Some investigators reported that *Fusobacterium nucleatum*, 1 of the periodontal pathogens, or deep periodontal pockets might influence the development of colon cancer.[25–27]

Regarding the mechanism by which oral bacteria affect general disease, 4 factors have been considered. First, direct transfer of oral bacteria may cause SSI after head and neck cancer surgery,

Table 2

Univariate analysis of the relationship between each variable and the occurrence of surgical site infection.

Variable		SSI (-)	SSI (+)	*P* value
Age	(years)	68.8 ± 11.4	67.3 ± 12.8	.324
Sex	male	341	41	.370
	female	289	27	
BMI	(kg/m^2)	22.4 ± 3.43	22.0 ± 3.68	.404
Diabetes	(-)	498	56	.636
	(+)	132	12	
Hypertension	(-)	342	40	.523
	(+)	288	28	
Heart disease	(-)	584	62	.627
	(+)	46	6	
Albumin	(g/dL)	3.90 ± 0.538	3.79 ± 0.559	.098
ALT	(U/L)	19.9 ± 17.2	19.7 ± 13.5	.942
Creatinine	(mg/dL)	0.888 ± 0.775	1.06 ± 1.37	.115
CRP	(mg/dL)	0.684 ± 1.63	0.663 ± 1.38	.917
Operation time	(minute)	278 ± 97.2	334 ± 128	<.001*
Blood loss	(g)	141 ± 225	303 ± 420	<.001*
Site	colon	429	38	.057
	rectum	201	30	
Operation method	laparoscopic surgery	406	41	.508
	laparotomy	224	27	
Oral management intervention	(−)	112	23	.003*
	(+)	518	45	

ALT = alanine aminotransferase, BMI = body mass index, CRP = C-reactive protein, SSI = surgical site infection.
* significant values are expressed as means ± standard deviation or number.

Table 3

Multivariate analysis of the variables related to surgical site infections in the 698 patients.

Variable		*P* value	Odds ratio	95% CI
Operation time	(minute)	.030*	1.003	1.000–1.005
Blood loss	(g)	.002*	1.001	1.000–1.002
Oral management intervention	(+) vs. (−)	.003*	0.428	0.244–0.749

CI = confidence interval.
* significant stepwise selection.

Table 4

Propensity score analysis of the association between oral management intervention and the development of surgical site infection.

Oral management group versus control group	*P* value	Odds ratio	95% CI
Univariate analysis (baseline)	.002	0.423	0.246–0.728
Multivariate analysis (baseline)	.003	0.428	0.244–0.749
After adjustment using propensity score analysis	.014	0.484	0.272–0.862

CI = confidence interval.

Table 5

Differences in preventive effect based on the number of perioperative oral management sessions.

Number of oral management	Occurrence of surgical site infection			Postoperative hospital stay		
0	23/135 (17.0%)	]0.031*	] 0.002*	15.7 days	]0.13	] <0.001*
1	21/228 (9.21%)	]0.429		14.1 days	]0.001*	
2 or more	24/335 (7.16%)			10.7 days		

* significant values are expressed as means±standard deviation or number.

SSI after upper digestive tract cancer surgery, and postoperative aspiration pneumonia. Second, intravascular invasion of odontogenic bacteremia and transition to remote organs by blood vessel or lymph duct may cause SSI of various sites of surgeries. Third, blood transfer of endotoxin or inflammatory cytokine by oral bacteria may influence to remote organs. And fourth, swallowing pathogenic microorganism of the oral cavity may change of intestinal flora and disorder of intestinal barrier function. Among them, we believe odontogenic bacteremia, which could cause infection after colorectal cancer surgery is especially important. Moreover, it is known that transient bacteremia often occurs in patients with severe periodontal disease.[28] The CDC Guideline for the prevention of SSI[8] describes that preoperative infectious lesions in a remote site became a risk factor for SSI; therefore, these lesions should be treated before surgery. Although urinary tract or respiratory tract infections are frequently problematic as remote infections, there are oral infectious lesions such as in periodontal disease that is more problematic than these remote infections.

The current study indicates that not receiving perioperative oral management is 1 of the risk factors associated with the development of SSI. Furthermore, it shows that receiving 2 or more oral management sessions is more effective than receiving only 1 management session. This is possibly because the effect of preventing periodontal inflammation and enhancing self-care capacity using 2 or more oral interventions is high compared to a single intervention. These findings suggest that perioperative oral management should be started not just before surgery but as soon as surgery is decided.

In digestive surgery, the prevention of postoperative complications has advanced due to the spread of minimally invasive surgeries such as laparoscopic surgery and progression in perioperative management. However, factors that increase postoperative complications such as the expansion of the indication for surgery to elderly patients with various general diseases and increase in drug-resistant bacteria. Perioperative oral management, which controls the bacterial flora in the mouth and reduces oral infectious lesions from the significance of treatment of remote infection before surgery, may play an important role in perioperative management. We believe further investigation is necessary to standardize oral management methods and verify their effectiveness.

In the current study, multivariate analysis revealed that operation time, blood loss, and oral management intervention were independent risk factors for SSI. Because of the retrospective nature of the study, it was necessary to align background factors between the 2 groups. Therefore, we applied propensity score matching analysis. However, since there was a large difference in sample size between the non-intervention and intervention groups many subjects were excluded, and the decrease in the generalizability of the findings became a problem. To solve these problems, we observed the onset of SSI using a model containing a propensity score, calculated as the oral management intervention, as a covariate in the multivariate analysis (binomial logistic regression analysis), and it was shown that when oral care was administered, SSI onset reduced by 0.484 times with a significant probability of 0.014.

However, this study had several weaknesses. First, because it was retrospective, there was the possibility of unknown confounding factors despite the propensity matching analysis. Specific dental indicators such as periodontal indexes (probing depth), caries indexes (DMFS; Number of decayed, missing, or filled surfaces), alveolar bone loss, and indexes of oral hygiene (plaque score) could not examined because it is a retrospective study and such information was not described in the medical records. Second, since the 2 hospitals do not have a unified oral care protocol, it is not clear which of the procedures was effective in the prevention of SSI. Perioperative oral management has been included in the Japanese medical insurance system since 2012, and most Japanese patients now receive oral management before cancer surgery. Thus, it would be challenging to conduct a randomized controlled trial on the protective effect of perioperative oral management. We believe that based on the results of this study, it can be concluded that perioperative oral management may reduce the risk of SSI after colorectal cancer surgery.

In summary, our retrospective investigation of 698 patients with colorectal cancer undergoing surgery suggested the effects of perioperative oral management on prevention of SSI.

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