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ORIGINAL ARTICLE

Clinical impact of periodontal disease on postoperative complications in gastrointestinal cancer patients

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Abstract

Background The effectiveness of perioperative oral management in gastrointestinal surgery remains unclear. To elucidate the clinical significance of oral care, we investigated the relationship between the oral environment and postoperative infectious complications (POICs) in patients undergoing gastrointestinal surgery.

Methods This was a single-institute and historical cohort study of 341 patients. The participants were isolated from consecutive patients undergoing planned radical resection for gastrointestinal carcinoma from January 2016 to June 2017. Dentists assessed the oral environment for periodontal disease, hygiene status, dry mouth, fur on tongue, and tooth stumps. All patients received scaling and tooth brushing instructions. A stepwise logistic regression analysis was conducted to identify risk factors for POICs among the different oral statuses.

Results The surgical procedures performed were gastrectomy in 123 (36.1%), colorectal resection in 185 (54.2%), and pancreatoduodenectomy or others in 38 (11.1%). POICs occurred in 48 patients (14.1%), including deep organ space infection in 20, surgical site infection in 11, anastomotic leakage in 5, urinary tract infection in 4, pneumonia in 2, and others in 6. After adjusting for confounding factors, periodontal disease was isolated as an independent risk factor for POICs (odds ratio 2.091, $p = 0.037$, 95% confidence interval 1.045–4.183). Other variables of oral environment such as hygiene status, dry mouth, fur on tongue, and tooth stumps did not have a significant impact on POICs.

Conclusions Periodontal disease is a risk factor for infectious complications after gastrointestinal surgery.

Keywords Oncological surgery · Infectious complication · Periodontal disease · Perioperative oral management

Introduction

Perioperative oral management has been adopted in many fields of surgery recently [1–4]. Surgeons have recognized that a poor oral environment can increase the risk of postoperative infectious complications (POICs) associated with perioperative ventilator management or contamination due to surgical manipulation in the oral cavity, laryngopharynx, esophagus, or airway. One of the purposes of oral care is to reduce the direct exposure of oral bacteria to the surgical fields or airway [5]. Indeed, several previous reports have demonstrated the preventive effect of oral care against POICs, such as postoperative pneumonia or wound infection, in esophageal or head and neck cancer surgery [3, 6–8].

Improving the chronic inflammatory status of patients with severe periodontal disease may be one way to prevent POICs via blood stream infection or bacteremia [9, 10]. For example, the incidence of infective endocarditis is known to be higher in patients with a poor oral environment than in those with a better oral environment [11–13]. Therefore, dental evaluations and treatments are required for perioperative patients scheduled to receive heart valve-replacement surgery [14, 15].

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If chronic inflammatory conditions in the oral cavity can cause POICs following either bacteremia or a bloodstream infection, then oral care is an important intervention for preventing POICs in not only esophagectomy patients, but also gastrointestinal surgery patients. More intensive oral care might be needed for more severe periodontal disease patients with chronic inflammation in the gingiva. However, type II diabetes mellitus (DM) [9, 16, 17], atherosclerosis [9, 18, 19], fatty liver [9, 20], and other systemic diseases [9, 21, 22] are known to be related to periodontal disease. These comorbidities might be potential confounding factors, so the preventive effect of oral care for POICs has not been established in patients scheduled to undergo gastrointestinal surgery.

We conducted this historical cohort study to investigate the relationship between the oral environment and POICs in patients who have undergone gastrointestinal surgery, with adjustment for measurable confounding factors. Our hypothesis is that periodontal disease is an independent risk factor for POICs in gastrointestinal surgery.

Patients and methods

Study design and participants

The design is a single-institute, historical cohort study. Patients with histologically confirmed carcinoma were identified from the institutional cancer database as eligible cases from January 2016 to June 2017. All patients underwent radical resection for gastric, colorectal, or biliopancreatic cancer and reconstruction, including gastrointestinal anastomosis. Before surgery, dentists assessed the oral cavity condition in all patients and performed initial periodontal treatment, such as scaling and tooth brushing instruction. None of the patients had received dental surgery in this study. The prophylactic antibiotic cefazolin sodium (1.0 g) was routinely administered immediately before operation. All emergency cases were excluded from this study. All procedures were conducted in accordance with the ethical standards of the respective committees on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. The patient's consent was obtained by the opt-out method in this retrospective observational study. The study protocol was approved by the Institutional Review Board of Southern TOHOKU General Hospital.

The assessment of the oral environment

Dentists evaluated the following items for enrolled patients: periodontal disease, hygiene status, dry mouth, fur on tongue, and tooth stumps. Specifically, they measured the probing pocket depth (PPD) of all teeth in the patients. The degree of periodontal disease was divided into three categories according to the deepest PPD as follows: mild (PPD < 4 mm), intermediate (4 mm ≤ PPD < 6 mm), or severe (PPD ≥ 6 mm) [23]. The hygiene status was classified according to the presence of plaque, with a plaque index [24] of 0–1 indicating a good status and that of 2–3 a poor status. Dry mouth was diagnosed by two findings: dry tongue mucosa or high viscosity of saliva. Fur on the tongue was based on the Miyazaki classification [25], with a score of 0 for no fur on the tongue and 1–3 for fur on the tongue. Tooth stumps were assessed using orthopantomography.

Outcomes and data collection

The primary outcome is the incidence of POICs, and the severity was described according to the Clavien–Dindo classification [26]. To investigate the relationship between the oral environment and the outcome, other clinical data that might be potential confounding factors were collected from electronic medical records, including the basic patient profile, smoking habit, DM, other comorbidities, surgical approach, performance status (Eastern Cooperative Oncology Group [ECOG]) [27], and TNM stage according to the seventh UICC classification [28]. The smoking habit was assessed based on the pack-years: number of cigarettes smoked per day/20 × number of years smoked. Patients were classified into three smoking habit categories [29].

Statistical analyses

We evaluated the oral environment variables and the incidence of POICs. A stepwise logistic regression analysis was performed to assess the influence of other confounding factors, with the incidence of POICs considered to be the dependent variable and the items surveyed that had a possibility of being confounding factors were identified by the univariate analysis. The Chi-square test for dichotomous variables and the *t* test for continuous variables were performed for the univariate analysis. All statistical analyses were performed with the STATA software program, version 14.

Results

Among the 382 patients who met the inclusion criteria during the period, 41 who did not receive an oral evaluation before surgery were excluded, leaving 341 patients enrolled in the analysis. Table 1 shows the patients' characteristics and oral status.

Table 1 Patients' characteristics

	Total ($n=341$)		%
Age	Median [IQR]	68 [61–75]	
Sex	Male	208	61.0
	Female	133	39.0
BMI (kg/m^2)	Mean (SD)	22.7 (3.52)	
Performance status (ECOG)	0	295	86.5
	1	35	10.3
	2	11	3.2
Smoking	Non/mild (< 5PY)	170	49.9
	Intermediate (≥ 5, < 50PY)	129	37.8
	Heavy (≥ 50PY)	42	12.3
Comorbidities	Diabetes	79	23.2
	Hypertension	105	30.8
	COPD	11	3.2
	Cerebrovascular disease	10	2.9
	Rheumatoid arthritis	3	0.9
	Myocardial infarction	2	0.6
	Hemodialysis	1	0.3
	Use of corticosteroid	1	0.3
Site of carcinoma (overlapping)	Stomach	133	39.0
	Colon	134	39.3
	Rectal	64	18.8
	Biliary–pancreas	15	4.4
Surgery (overlapping)	Total gastrectomy	34	10.0
	Distal gastrectomy	89	26.1
	Right hemicolectomy	55	16.1
	Left hemicolectomy	58	17.0
	Anterior resection	72	21.1
	Pancreatoduodenectomy	15	4.4
	Others	23	6.7
Operating time (minutes)	Mean (SD)	247 (96.4)	
Amount of bleeding (mL)	Mean (SD)	117.9 (238.0)	
Serum albumin (g/dL)	< 3.0	25	7.3
	≥ 3.0	316	92.7
Periodontal disease	Mild	36	10.6
	Intermediate	180	52.8
	Severe	82	24.0
	Edentulous	43	12.6
Hygiene status	Good	152	44.6
	Poor	170	49.9
	Missing	19	5.6
Tooth stump	Non-tooth stump	281	82.4
	Tooth stump	60	17.6
Dry mouth	Non-dry mouth	336	98.5
	Dry mouth	5	1.5
Fur on tongue	Non-fur on tongue	319	93.5
	Fur on tongue	22	6.5

IQR inter quadrant range, *PY* pack-years, *SD* standard deviation, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *ECOG* Eastern Cooperative Oncology Group

Outcomes and identification of risk factors

Table 2 shows the POICs and their severity. POICs occurred in 48 patients (14.1%), with superficial surgical site infection (SSI), deep organ space SSI, and anastomotic leakage found in 11/48 (22.9%), 20/48 (41.7%), and 5/48 (10.4%) cases, respectively. Table 3 shows the relationship between the oral environment and POICs. To identify the potential confounding factors, the associations between POICs and other clinical characteristics were assessed, as shown in Table 4. A logistic regression analysis identified periodontal disease as an independent risk factor for POICs (Table 5), and the odds ratio was 2.091 ($p = 0.037$, 95% confidence interval 1.045–4.183).

Table 2 Kinds of infectious complications and severity

Infectious complications	Total ($n = 48$, overlapping)	%
Superficial SSI	11	22.9
Deep organ space SSI	20	41.7
Anastomotic leakage	5	10.4
Urinary tract infection	4	8.3
Pneumonia	2	4.2
Others	6	12.5
Clavien–Dindo classification		
Grade I	7	14.6
Grade II	12	25.0
Grade IIIa	24	50.0
Grade IIIb	5	10.4

Discussion

Our results suggest that periodontal disease is an independent risk factor for POICs in patients who have undergone gastrointestinal surgery including an anastomotic procedure. Among patients with mild periodontal disease (PPD < 4 mm), POICs were evident in only one case (2.9%). Interestingly, other oral findings, such as the hygiene status, dry mouth, fur on tongue, and tooth stumps, were not associated with POICs.

Several previous studies have reported on the preventive effect of perioperative oral management for SSI or pneumonia in the fields of oral, pharynx, larynx, and esophageal cancer surgery. Our results suggest the possibility that oral chronic inflammation may increase the risk for POICs via bloodstream infection, as well as through direct bacterial contamination in patients with severe periodontal disease. The CDC guidelines emphasize the importance of controlling bacterial contamination at both the surgical site and distant organs to prevent postoperative infection [30]. Severe periodontal disease is associated with a wide area of chronic inflammation, and periodontitis bacteria can invade the blood stream via the oral cavity by tooth extraction, brushing, or chewing [9, 10, 22, 31, 32], as the gingiva swells and capillary vessels grow in patients with severe periodontal disease [9, 10, 31]. Such a compromised status might increase the risk of infectious complications after gastrointestinal surgery.

Severe periodontal disease might also be regarded as a surrogate marker of the patient's general condition. Therefore, in our study, we investigated confounding factors such as DM, other comorbidities, smoking habit, and surgical procedures to clarify the causal relationship between the severity of periodontal disease and the risk

Table 3 Infectious complications and oral environment

		Number of patients	Infectious complication	%	*p* value
Periodontal disease	Mild	36	1	2.8	0.022
	Intermediate	180	19	10.6	
	Severe	82	16	19.5	
	Edentulous	43	12	27.9	
Hygiene status	Good	152	16	10.5	0.410
	Poor	170	23	13.5	
	Missing	19	9	47.4	
Tooth stumps	Non-tooth stump	281	34	12.1	0.539
	Tooth stump	60	9	15	
Dry mouth	Non-dry mouth	336	41	12.2	0.063
	Dry mouth	5	2	40	
Fur on tongue	Non-fur on tongue	319	40	12.5	0.881
	Fur on tongue	22	3	13.6	

Table 4 Comorbidities and incidence of infectious complications

		Non-POICs ($n=293$)	POICs ($n=43$)	%	p value
Age	≤ 75	223	34	15.2	0.705
	> 75	75	9	12.0	
Sex	Male	174	34	19.5	0.011
	Female	124	9	7.3	
BMI (kg/m^2)	< 18	16	2	12.5	0.927
	≥ 18, < 25	166	23	13.9	
	≥ 25	116	18	15.5	
Performance status (ECOG)	0	262	33	12.6	0.123
	1	27	8	29.6	
	2	9	2	22.2	
Smoking	Non / mild (< 5PY)	150	20	13.3	0.06
	Intermediate (5–50PY)	116	13	11.2	
	Heavy (≥ 50PY)	32	10	31.3	
Diabetes	Non-diabetes	238	24	10.1	0.002
	Diabetes	60	19	31.7	
Site of carcinoma (overlapping)	Stomach	114	17	14.9	0.241
	Colon	172	22	13.4	
	Biliary–pancreas	11	4	36.4	
Approach	Open surgery	77	24	31.2	< 0.001
	Laparoscopic surgery	221	19	8.6	
Operating time (minutes)	Mean (SD)	245 (6.1)	261 (15.6)	–	0.364
Amount of bleeding (mL)	Mean (SD)	101 (13.3)	229 (57.0)	–	< 0.001
Serum albumin (g/dL)	< 3.0	25	5	20.0	0.278
	≥ 3.0	278	38	11.9	

BMI body mass index, *ECOG* Eastern Cooperative Oncology Group, *PY* pack-years

Table 5 Risk factors for infectious complications in logistic regression model

Variables (reference)	Odds ratio	SE	p value	95% CI
Severe PD (mild/intermediate PD)	2.091	0.740	0.037	1.045–4.183
Female (male)	0.503	0.276	0.211	0.171–1.476
Diabetes (non-diabetes)	3.363	1.450	0.005	1.444–7.832
Smoking ≥ 5PY (smoking < 5PY)	1.477	0.755	0.445	0.542–4.025
Laparoscopic surgery (open)	0.378	0.172	0.033	0.154–0.924
Blood loss ≥ 500 mL (blood loss < 500 mL)	1.128	0.777	0.861	0.292–4.350

CI confidence interval, *PD* periodontal disease, *PY* pack-years, *SE* standard error

of POICs. We identified periodontal disease as an independent risk predictor for infectious complications after abdominal surgery. The purpose of oral management was to reduce the number of bacteria and toxicity due to changes in the kinds of bacteria in the oral cavity [33–35]. All patients received preoperative oral management in our study, therefore oral condition might have improved before surgery. Consequently, the importance of oral care could not be denied, although oral hygiene and tongue fur were not significantly related with the incidence of POICs. The most important variable was the depth of the periodontal pocket. Therefore, more intensive oral management and careful postoperative management might be necessary for patients with a deep periodontal pocket.

The incidence of periodontal disease has increased recently. According to a Japanese survey, the estimated prevalence of periodontal disease is 70% and 90% among subjects 20 and 60 years of age, respectively [36]. Having dentists assess the oral environment may be important in surgical practice to determine the risk of POICs before operation.

Two limitations associated with the present study warrant mention. First, some oral condition variables, such as hygiene, dry mouth, and furred tongue, were assessed

subjectively by each dentist. Second, we were unable to determine the pathophysiological mechanism, although we suspected that the chronic inflammatory status and bacterial translocation via the blood stream contributed to the incidence of POICs. We plan to conduct further studies to determine the routes and the pathogen of POICs using bacterial culture specimens obtained from periodontal pockets and infection sites in patients who develop POICs.

In conclusion, periodontal disease is an independent risk factor for infectious complications after gastrointestinal surgery. Measuring the depth of the periodontal pocket may therefore be a clinically useful predictive factor.

Compliance with ethical standards

Conflict of interest No author has any conflict of interest.

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