Abstract

Background: Extensive resection and free-flap reconstruction surgery has become the standard treatment for locally advanced head and neck cancer. Surgical site infection (SSI) is one of the serious complications of this treatment. This study aimed to investigate the risk factor for onset of SSI, particularly focusing on whether preoperative professional oral health care in cooperation with general dental clinics is effective in reducing the occurrence of SSI.

Methods: From March 2003 to August 2011, 183 patients who underwent head and neck free-flap reconstructive surgery by the same plastic surgeon at Miyagi Cancer Center for Head and Neck Surgery were investigated retrospectively.

Results: Of the 183 patients, 135 and 48 were men and women, respectively, with a mean age of 62 (range, 29–82) years. The tumor was located in the oral cavity (n = 76), hypopharynx (n = 55), oropharynx (n = 28), and others (n = 24). Clinical stages were stage I/II in 18, stage III/IV in 164 patients, and benign tumor in one patient, based on UICC classification. SSI occurred in 66 patients (36.1%). Based on multivariate analysis, professional oral health care \( P = 0.0076 \), odds ratio (OR) = 0.39 and radiation therapy history \( P = 0.0214 \), OR = 2.820 were shown as factors that are significantly related to SSI.

Conclusion: This study identified history of radiation therapy as a significant risk factor for SSI from univariate and multivariate analysis and revealed that patients receiving preoperative professional oral health care at general dental clinics reduce the risk of SSI. Preoperative professional oral health care in cooperation with general dental clinics has been shown to reduce SSI of head and neck free-flap reconstructive surgery.

Key words: Head and neck tumor, free-flap reconstructive surgery, Surgical site infection, Professional oral health care, Medical collaboration, general dental clinic
skin, mouth, and pharynx, classified as class II (clean-contaminated wound area) in the surgical wound classification of the CDC guidelines [6]. SSI causes discomfort and psychological stress, resulting in longer hospital stay and increasing medical expenses. In addition, deterioration of the general condition of the patient, such as nutritional status, not only significantly impairs the patient's quality of life but also delays the start of additional treatment and affects the survival rate [7].

Many risk factors for SSI during head and neck tumor surgery have been reported. Based on the CDC guidelines, risk factors include American Society of Anesthesiologists' Association (ASA) scores, age, nutritional status, smoking, and diabetes [6]. Based on previous multiparameter studies, many risk factors for SSI, such as cervical metastasis, albumin level, hemoglobin level, and oral hygiene status, have been found determined [8,9,10,11,12]. However, comparing these definitions for SSI is difficult because in these studies, and the characteristics of patients (e.g., proportion of cases of free-flap reconstructive surgery) are different.

The oral bacterial count has also been reported to be suppressed by oral health care performed by dental practitioners preoperatively, and it is effective in reducing the incidence of SSI in patients undergoing head and neck cancer reconstructive surgery [13]. During the study period, there was no dental department in our hospital; the head and neck surgery department provided preoperative oral care in cooperation with the general dental clinics in the area for patients undergoing head and neck tumor free-flap reconstruction surgeries from March 2005 onward.

The purpose of this study was to clarify the most important risk factor for SSI after head and neck reconstruction and to identify effective strategy for preventing SSI. In particular, we focused on whether preoperative professional oral care in cooperation with the general dental clinics in the area is effective in reducing the occurrence of SSI.

**Patients and methods**

### Patient

From March 2003 to August 2011, 183 patients with head and neck tumor who underwent free-flap reconstructive surgery by the same plastic surgeon at Miyagi Cancer Center Head and Neck Surgery (Natori City, Miyagi Prefecture) were retrospectively investigated. This survey was conducted in accordance with the Declaration of Helsinki with the approval of the Miyagi Cancer Center Ethics Review Committee.

### SSI strategy and diagnostic method

For all patients, the following methods were used:

- Cefazolin or Ampicillin-sulbactam was started 30–60 min before incision and continued for 3 days postoperatively as prophylactic antibacterial treatment.
- The surgical field was disinfected with povidone-iodine.
- After the skin and oropharynx was separated with a flap, the site is washed with ≥1000 mL of physiological saline.
- Sealed drainage was performed.
- After washing the surgical field with physiological saline, the mandibular reconstruction plate or artificial instruments were used.

SSI was judged based on the CDC guidelines [6]. SSI is defined as the presence of at least one of the following symptoms within 30 days postoperatively:

- purulent effluent from superficial incisional wound
- separation of microorganisms from aseptically collected liquid or tissue culture from superficial incision
- if there is at least one sign or symptom of infection, such as pain or tenderness, local swelling, redness, or fever, the surgeon carefully opens the incision surface and the culture of the incision is positive
- the surgeon or assistant doctor judges that the incision surface has SSI
- fistulas defined as the presence of oral or pharyngeal leakage are regarded as SSI regardless of origin.

### Factors that were reviewed

Clinical data were recorded; SSI, patient age, sex, tumor location, clinical stage, life history, medical history, and general condition were recorded. Preoperative intervention included preoperative tracheotomy, head and neck surgery, radiotherapy (defined as a dose of >40 Gy in the surgical field), and chemotherapy. Pre- and postoperative factors included mandibular resection, reconstruction, duration of surgery, bleeding volume, and blood transfusion.

The presence of diabetes mellitus was defined as a preoperative diagnosis of borderline or more severe diabetes mellitus. The general conditions were as follows: anemia was defined as a hemoglobin concentration of <8.5 g/dl; hypoalbuminemia was defined as a serum albumin level of <4.0 mg/dl;

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diabetes mellitus was defined as a fasting blood glucose level of \( \geq 200 \text{ mg/dl} \); and poor performance status was defined as an American Society of Anesthesiologists Physical Status score \( \geq 3 \).

**Professional Oral health care**

All patients received an explanation about the necessity of professional oral care from doctors and nurses at the visit to the hospital head and neck surgical outpatient and recommended dental examination within a week from the day of surgery. Based on self-determination, patients who visited a general dental clinic underwent oral examination, dental plaque and dental calculus removal, and professional mechanical tooth cleaning, and severe periodontitis and severe caries were extracted. Furthermore, it was guided by dentists and dental hygienists regarding the necessity of oral cleaning and self-care method.

Patients in both groups brushed their teeth and performed self-oral cleaning preoperatively; the oral cavity was cleaned thrice a day by a nurse using a sponge brush immediately postoperatively until oral feeding was resumed. We gradually increased self-care after starting oral feeding.

Statistical analysis was performed using SAS version 9.3 (Cary, NC, USA). We examined the relationship between each variable and SSI using univariate analysis. Categorical data and continuous variables were tested using Fisher exact test and Wilcoxon signed rank test, respectively. Variables with \( P < 0.05 \) in the univariate analysis were subjected to multivariate logistic regression analysis for identifying variables that are independent of SSI. \( P < 0.05 \) was considered to be statistically significant.

**Results**

**Patient characteristics**

Table 1 shows the characteristics of patients. The mean age of patients was 62 (range, 29–82) years. Of the 183 patients, 135 and 48 were men and women, respectively. In total, 66 patients received professional oral health care at the general dental clinic, whereas 117 patients did not. Tumor locations include the oral cavity (n = 76), hypopharynx (n = 55), oropharynx (n = 28), cervical esophagus (n = 7), maxilla (n = 6), salivary gland (n = 6), larynx (n = 4), thyroid (n = 1), and others (n = 24). Clinical stages were stage I/II in 18 patients, stage III/IV in 164 patients, and benign tumor in one patient, according to the UICC classification. The tumor recurred in 10 patients. Free abdominal femoral (n = 23), free fibular (n = 6), free forearm (n = 9), free abdominal (n = 80), free jejunial (n = 63), Latissimus Myocutaneous (n = 1), and Scapular (n = 1) flaps were constructed.

| Characteristic | Patients (%) |
|---------------|-------------|
| Age <65 years | 103 56.3    |
| Age \( \geq 65 \text{ years} \) | 80 43.7 |
| Sex Male     | 135 73.8    |
| Sex Female   | 48 26.2     |
| Location Oral cavity | 76 41.5 |
| Location Hypopharynx | 55 30.1 |
| Location Mesopharynx | 28 15.3 |
| Location Cervical esophagus | 7 3.8 |
| Location Maxilla | 6 3.3 |
| Location Salivary gland | 6 3.3 |
| Location Larynx | 4 2.2 |
| Location Thyroid | 1 0.5 |
| Performance status 1 | 56 30.6 |
| Performance status 2 | 102 55.7 |
| Performance status 3 | 24 13.1 |
| Performance status 4 | 1 0.5 |
| Clinical stage 0/x/benign | 4 2.2 |
| Clinical stage I | 1 0.5 |
| Clinical stage II | 17 9.3 |
| Clinical stage III | 30 16.4 |
| Clinical stage IV | 134 73.2 |

**Relationship between risk factor and SSI**

SSI occurred in 66 patients (36.1%). The incidence of SSI in the group receiving professional oral health care was 24.2% (16/66), whereas that in the non-receiving group was 43.6% (51/117). Univariate analysis showed significant differences in terms of professional oral health care (\( P = 0.011 \)) and radiotherapy history (\( P = 0.042 \)) (Table 2). Multivariate analysis revealed that radiotherapy history increased the risk factor [\( P = 0.0214, \text{OR} = 2.820 \)], and professional oral health care reduced the risk factor [\( P = 0.0076, \text{OR} = 0.39 \)] (Table 3).

The median duration of surgery and blood loss were 596 (range, 284–1094) min and 390 (range, 50–1900) mL. Surgical time and blood loss were not significantly associated with SSI (Table 4).

**Discussion**

Head and neck surgery, particularly head and neck tumor surgery with microvascular free-flap reconstruction, is the most invasive surgery, and the incidence of SSI is high (range, 36.4%–50%) [5, 9, 10]. In our study, the incidence of SSI was 36.1%. Majority of our patients have T3 and T4 disease (89.6%, 164/183) and have more advanced cancer than that reported in other studies. However, the incidence of SSI was similar to that reported in other recent research [3-5, 9, 10]. In our study, univariate analysis and multivariate analysis revealed that a history of radiation therapy increased the risk of SSI, and it was identified that professional oral health care at general dental clinics is a factor that reduces the risk of SSI.
Table 2. Univariate analysis of preoperative and perioperative risk factors

| Variable                        | Cases (%) | Surgical site infection (%) | P value |
|---------------------------------|-----------|----------------------------|---------|
| Sex Male                        | 73.8      | 35.6                       | 0.8617  |
| Age ≥ 65 years                  | 43.7      | 38.8                       | 0.5372  |
| Poor ASA ≥ 1-PS (≥2)           | 13.7      | 44.0                       | 0.3791  |
| BMI (kg/m2) ≥ 25               | 15.9      | 31.0                       | 0.6743  |
| Albumin < 4.0 mg/dl             | 30.6      | 35.7                       | 1.0000  |
| Diabetes mellitus               | 11.5      | 33.3                       | 1.0000  |
| Smoking                         | 68.3      | 36.0                       | 1.0000  |
| Alcohol                         | 36.1      | 68.2                       | 0.2225  |
| T-stage (T3+T4)                 | 73.2      | 38.8                       | 0.2270  |
| Clinical stages III + IV        | 89.1      | 37.4                       | 0.3311  |
| Previous cervical operation     | 10.4      | 42.1                       | 0.6172  |
| Previous chemotherapy           | 16.9      | 45.2                       | 0.3052  |
| Previous radiotherapy           | 13.7      | 56.0                       | 0.0417* |
| Professional oral health care   | 36.6      | 23.9                       | 0.0106* |
| Mandibulotomy                   | 31.7      | 39.7                       | 0.5116  |
| Maxillectomy                    | 7.1       | 53.8                       | 0.2300  |
| Bone reconstruction             | 4.9       | 33.3                       | 1.0000  |
| Bone surgery                    | 36.1      | 39.4                       | 0.5231  |
| Surgery time (>10h)             | 51.9      | 33.7                       | 0.5390  |
| Blood loss (>600 ml)            | 10.4      | 42.1                       | 0.6172  |
| Blood transfer                  | 4.9       | 55.6                       | 0.2872  |
| Tracheotomy                     | 95.4      | 36.8                       | 0.5414  |

* P < 0.05

Table 3. Results of multiple logistic regression analysis of wound infection

| Variables                        | Odds ratio | 95% confidence interval | P value |
|----------------------------------|------------|-------------------------|---------|
| Professional oral health care    | 0.39       | 0.20-0.78               | 0.0076* |
| Previous radiotherapy            | 2.82       | 1.17-6.82               | 0.0214* |

* P < 0.05

Table 4. Relationship between patient characteristics and risk of surgical site infection (continuous data)

| Factor                     | Overall Average | Average with SSI | Average without SSI | P value |
|----------------------------|-----------------|------------------|---------------------|---------|
| Body mass index (kg/m2)    | 21.57 ± 3.49    | 22.04 ± 3.46     | 21.26 ± 3.44        | 0.1502  |
| Duration of surgery (min)  | 600 ± 108       | 615 ± 107        | 592 ± 108           | 0.166   |
| Blood loss (ml)            | 332.9 ± 292.7   | 371.2 ± 338.9    | 311.4 ± 262.3       | 0.184   |

±Standard deviation.

Microorganisms in the oral cavity are sources of SSI pathogens [14]. Preoperative professional oral health program significantly reduces wound infection after oral cancer surgery [15]. The results of this study were supported by these reports. There are two features of this research. First, the effectiveness of professional oral health care was proven to be applicable to oral cancer surgery as well as head and neck tumor free-flap reconstruction surgeries. Second, professional oral health care is not performed only by dentists in the general hospital, but by medical collaboration with the community dental clinic. This is a beneficial result for a hospital with head and neck surgery without dentistry. It is also beneficial for patients to access a local dental office for consultation for treatment to be effective.

The reason why SSI is alleviated by professional oral health care administered preoperatively at the dental clinic is considered to be due to the following features of the oral cavity and pharyngeal region. The oropharynx has complicated structures and organs that are not anatomically uniform. Particularly, the oral cavity has a surface area of approximately 220 cm² with many niches (tooth, buccal mucosa, tongue, mouth cavity, gums, etc.), and the surface is covered by a biofilm. More than 700 kinds of bacteria inhabit the oral cavity, but only 54% can be cultured [16]. Bacterial harvesting in the oropharynx requires testing sticks of the surface of the tongue (dorsal tongue), accounting for 12% of the intraoral area [17]. Therefore, only species of bacterial flora in the oral cavity can be evaluated. This may be one reason for the deviation between the result of bacterial culture of the SSI Wound Department and the result of the oral bacteria test. Saliva covering the oral mucosa contains 10⁸ bacteria per mL [18]. The tooth covers 20% of the oral area, and the biofilm (dental plaque) attached to the surface contains 1 billion bacteria/mg [19]. Generally, pathogenic bacteria are detected at clinically low levels [20, 21]. However, the number and proportion of pathogenic bacteria increases in pathological conditions [18]. Oral diseases are speculated to occur because of harmful changes in the natural balance of microorganisms [22, 23]. A biofilm is formed several minutes after tooth surface cleaning, and bacterial flora changes as time passes. Oral streptococcus is the main facultative anaerobic bacteria present in the oral cavity. However, without self-care and professional oral health care, it becomes a complex biofilm containing many anaerobic bacteria after 7 days, such as gram-negative bacillus spirchoete [24]. They are diffused into the saliva and are speculated to be reservoirs for oropharyngeal region/upper respiratory tract infection. Pathologically increasing oral streptococci will also break down salivary pellicles on the mucosal surface and thereby produce enzymes that expose adhesion receptors to pathogenic bacteria [25, 26].

Oral biofilm (dental plaque/dental calculus) removal is impossible with antibiotics [27]. Mechanical destruction and elimination by removal of dental calculus and professional mechanical tooth surface cleaning are the only methods to remove these diseased biofilms [28]. Immediately after 1 or 2 weeks of treatment with this method, the total number of subgingival organisms decreased 10- to 100-fold and the proportions of culturable gram-negative organisms and anaerobic organisms decreased 3- to 4-fold or more. [29]. These previous findings support
the rationality of the present study, which demonstrated significantly reduced occurrence of SSI by performing self-care daily and professional oral health care at general dental clinics once every 1 to 7 days before surgery [15].

In this study, radiation therapy history was identified as a risk factor for SSI in univariate and multivariate analyses. In multivariate analysis by Lee et al., radiation therapy history [10] was a risk factor for SSI after head and neck surgeries (OR, 2.85). Radiation has been shown to have pathophysiological effect, poor wound healing, and delayed infection [30], which are consistent with our results.

Hypoalbuminemia is the evaluation item that determines whether the nutritional state is a risk factor. Nutritional status is believed to be related to poor healing of tissues, decreased collagen synthesis, and granuloma formation on surgical wounds. In this study, no significant relationship was found between albumin and hemoglobin levels. Accurately determining the nutritional status was impossible because the examination was performed 1–14 days preoperatively, with the half-life of blood albumin at 14–20 days, and dehydration due to difficulty in oral ingestion.

This research has limitations. First, it is an observational research conducted at a single facility. In addition, the preoperative dental condition is not included in the evaluation items. This is because information on the dental condition from the requested dental medical institution could not be obtained. The presence of tooth defects, such as dentures [15], has been reported to be a risk factor for SSI in univariate analysis, but the preoperative dental condition of patients with head and neck tumor is not a serious risk factor for SSI [31]. Therefore, we speculate that quantitatively evaluating and analyzing the condition of the patient's teeth are difficult because each patient may show various dental conditions. Currently, there are methods for quantitatively evaluating various oral hygiene/dental conditions (e.g., OAG [32] and OHAT [33], serum levels of blood-related periodontal disease bacteria [34], and antibody titer). Considering cost effectiveness, prospectively considering whether these are effective as evaluation items is necessary.

In conclusion, this study indicated that preoperative professional oral health care in cooperation with general dental clinics reduces the SSI of head and neck free-flap reconstructive surgery.

Competing Interests

The authors have declared that no competing interest exists.

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