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Determination of the Duration of Preoperative Smoking Cessation to Improve Wound Healing after Head and Neck Surgery

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Background: **Preoperative smoking cessation has been suggested to be effective in reducing various postoperative complications. However, the optimal duration of preoperative smoking cessation for reducing wound complications is unclear.**

Methods: **One hundred eighty-eight consecutive patients who underwent reconstructive head and neck surgery at the authors' institution were included in this retrospective study. Information on preoperative smoking habits was obtained from the patients' medical records. Smokers were defined as having smoked within 7 days before surgery. Late, intermediate, and early quitters were defined as patients whose duration of abstinence from smoking was 8–21, 22–42, and 43 days or longer before the operation, respectively. Patients who required postoperative debridement, resuture, or reconstruction of their flap before hospital discharge were defined as having had impaired wound healing.**

Results: **The incidences (95% confidence intervals) of impaired wound healing among the late, intermediate, and early quitters and nonsmokers were 67.6% (52–83%), 55.0% (33–77%), 59.1% (47–71%), and 47.5% (32–63%), respectively, and the incidence of impaired wound healing was significantly lower among the intermediate quitters, early quitters, and nonsmokers than among the smokers (85.7% [73–97%]). After controlling for sex, age, American Society of Anesthesiologists physical status, operation time, history of diabetes mellitus, chemotherapy, radiation therapy, and the type of flap, the odds ratios (95% confidence intervals) for development of impaired wound healing in the late, intermediate, early quitters, and nonsmokers were 0.31 (0.08–1.24), 0.17 (0.04–0.75), 0.17 (0.05–0.60), and 0.11 (0.03–0.51), respectively, compared with the smokers.**

Conclusions: **Preoperative smoking abstinence of longer than 3 weeks reduces the incidence of impaired wound healing among patients who have undergone reconstructive head and neck surgery.**

CLINICAL studies have revealed that smokers have a higher incidence of perioperative respiratory[1–3] and cardiovascular[4,5] complications than nonsmokers. Recently, many clinical studies found that smoking has adverse effects on wound healing[6–8] and that smoking cessation has been suggested to be effective to reduce wound complications of various types of invasive surgeries.[9] However, the minimum duration of the smoke-free period before surgery needed to improve postoperative wound healing has not been well documented.

Head and neck carcinoma is a smoking-related cancer. Radical resection with wide surgical incisions and free flap reconstruction are often performed, and impaired wound healing of various degrees is often observed. Because impaired wound healing is associated with poor surgical outcome and increased duration of hospital stay,[10–12] it is important to prevent the occurrence of impaired wound healing. The aim of this study was to assess the duration of preoperative smoking cessation that reduces the incidence of impaired wound healing in patients who undergo reconstructive head and neck surgery that would reduce the rate of postoperative complications. If there is a clinically useful, relatively shorter smoke-free duration in preoperative smoking patients that reduces the risk of postoperative complications, such information could be conveyed to patients with a smoking habit and could encourage them to quit smoking.

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Materials and Methods

Design/Subjects

The study subjects were 188 consecutive patients who underwent removal of nasal, oral, pharyngeal, laryngeal, or cervical esophageal cancer and reconstruction requiring a free flap with a vascular pedicle at our institution between January 1996 and December 2001. By reviewing their medical records, we ascertained the preoperative and intraoperative details and determined whether any impaired wound healing occurred during the hospital admission. This retrospective cohort study was approved by the Ethical Committee of Osaka Medical Center for Cancer and Cardiovascular Diseases (Osaka, Japan).

Assessment of Preoperative Factors and Smoking Behavior

We collected the following information from the medical records of each patient: sex, age at the time of surgery, height, weight, American Society of Anesthesiologists physical status, presence of diabetes mellitus or

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chronic obstructive pulmonary disease if the patient was noted to have diabetes mellitus or chronic obstructive pulmonary disease in his or her medical record, serum albumin concentration, history of steroid use if it was written in the medical record that a steroid was prescribed for the patient during the study period, and whether chemotherapy or radiation therapy had been administered before surgery. Information on the smoking habit was obtained from (1) the routine self-administered questionnaire about the health status of the patient at the first visit, (2) the interview at admission by nurses, and (3) the preoperative interview by the anesthesiologist 1 or 2 days before the surgery. If these three data were conflicting, we chose the shortest duration of smoking cessation.

The patients were divided into five groups based on their smoking habits. Smokers were defined as those who had smoked within 7 days before the operation (n = 28). Ex-smokers were divided into three groups according to the duration of the smoke-free period before the surgery to elucidate whether there is a clinically useful duration of preoperative smoking cessation that reduces the incidence of impaired wound healing. The late, intermediate, and early quitters were defined as patients whose smoke-free duration was between 8 and 21 days (n = 34), between 22 and 42 days (n = 20), and more than 43 days (n = 66) before the operation, respectively. We divided the ex-smokers into three groups according to these cutoff points because the average interval from the first visit to the surgery and average interval from admission to the surgery among head and neck cancer patients at our hospital were approximately 6 and 3 weeks, respectively. Nonsmokers were defined as those who had never smoked (n = 40). During the period conveyed by our study, smoking was strictly prohibited in our hospital, and no patient in our study restarted smoking after the operation up to the time of discharge. Also, any smokers in the patients' families could not smoke around the patient preoperatively or postoperatively; therefore, patients had minimum exposure to environmental tobacco smoking in the hospital.

Assessment of Surgical Procedures

From the surgical records, we obtained information on the type and duration of the surgical procedure that was performed in each patient. The surgeries were divided into four categories according to the type of flap: forearm flap (n = 83), rectus abdominis muscle flap (n = 60), free jejunum (n = 33), and other (n = 12).

Assessment of Postoperative Course

One anesthesiologist, who was unaware of the subjects' smoking histories, reviewed the medical records of all subjects to determine the occurrence of impaired wound healing up to the time of hospital discharge. The determination was based on what kind of interventions for the wound was performed by the surgeons. Spontaneous healing was defined as healing without postoperative intervention. The patients with impaired wound healing were divided into three groups based on their postoperative intervention: (1) debridement or resuture in the ward; (2) debridement or resuture in the operating room; and (3) removal and reconstruction of the flap in the operating room. The wound healing had been assessed and treated by the surgeons at our hospital before we started this investigation.

Statistical Analyses

Frequency distributions were determined for discriminate variables and categorized by smoking habit. The chi-square test was used to compare the distribution of sex, American Society of Anesthesiologists physical status, preoperative coexisting disease, adjuvant therapy, and surgical procedure between groups. Continuous data are presented as mean ± SD according to smoking habit. The Bonferroni multiple comparison technique after analysis of variance was performed to compare age, body mass index, smoking consumption, preoperative serum albumin concentration, and duration of surgery in the subjects by smoking habit. The correlation between stepwise improvement of smoking habit and degree of impaired wound healing was examined by calculating the Spearman correlation coefficient by ranks. Logistic regression analysis was performed to estimate the odds ratios of impaired wound healing as a result of smoking habit and controlling for potential confounders. In these analyses, a P value less than 0.05 was considered statistically significant. The statistical analyses were performed using SPSS software (version 12.0J; SPSS Inc., Tokyo, Japan).

Because the numbers of subjects belonging to each week of abstinence duration were small and the variation in the incidence of impaired wound healing each week was large, the moving average was used to smooth such large variation. The 4-week moving average was calculated to observe the relation between the duration of the preoperative smoke-free period and the incidence of impaired wound healing.

Results

The 188 subjects with head and neck carcinoma were divided into five groups according to the interval of time between smoking cessation and the surgery. In the five groups, female patients comprised the majority only among the nonsmokers. The late quitters were significantly younger than the early quitters. The other baseline characteristics of the five groups were similar (table 1).

The incidences (95% confidence intervals [CIs]) of impaired wound healing among the smokers, late quitters, intermediate quitters, early quitters, and nonsmok-

Table 1. Demographic Data and Clinical Characteristics for Patients by Smoking Status

	Smokers (n = 28)	Late Quitters (n = 34)	Intermediate Quitters (n = 20)	Early Quitters (n = 66)	Nonsmokers (n = 40)
Sex, %					
Male	27 (96.4)	32 (94.1)	19 (95.0)	59 (89.4)	13 (32.5)
Female	1 (3.6)	2 (5.9)	1 (5.0)	7 (10.6)	27* (67.5)
Mean age, yr	58.3 ± 9.0	54.7 ± 9.4†	58.8 ± 8.6	62.9 ± 10.6†	57.1 ± 13.2
BMI, kg/m^2	20.4 ± 3.10	20.8 ± 3.43	20.8 ± 3.06	20.7 ± 3.00	22.3 ± 4.71
Smoking habit, pack-years	61.0 ± 21.9	41.8 ± 22.5	48.1 ± 28.1	50.6 ± 35.2	0
ASA PS, %					
I	8 (28.6)	17 (50.0)	7 (35.0)	10 (15.2)	13 (32.5)
II	20 (71.4)	17 (50.0)	13 (65.0)	55 (83.3)	26 (65.0)
III	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (2.5)
Preoperative coexisting disease, %					
DM	5 (17.9)	5 (14.7)	2 (10.0)	12 (18.2)	5 (12.5)
COPD	2 (7.1)	4 (11.8)	3 (15.0)	4 (6.1)	0 (0)
Preoperative serum albumin concentration, g/dl	4.4 ± 0.4	4.4 ± 0.5	4.4 ± 0.5	4.3 ± 0.4	4.4 ± 0.5
Preoperative therapy, %					
Administration of steroids	1 (3.6)	1 (2.9)	0 (0)	2 (3)	3 (7.5)
Chemotherapy	3 (10.7)	3 (8.8)	0 (0)	11 (16.7)	5 (12.5)
Radiation therapy	4 (14.3)	5 (14.7)	3 (15.0)	22 (33.3)	8 (20.0)
Flap, %					
Forearm	10 (35.7)	19 (55.9)	9 (45.0)	25 (37.9)	20 (50.0)
Rectus abdominal muscle	12 (42.9)	11 (32.4)	7 (35.0)	21 (31.8)	9 (22.5)
Free jejunum	4 (14.3)	3 (8.8)	4 (20.0)	16 (24.2)	6 (15.0)
Others	2 (7.1)	1 (2.9)	0 (0)	4 (6.1)	5 (12.5)
Surgery duration, min	610.2 ± 145.8	603.8 ± 109.7	611.5 ± 97.5	597.5 ± 130.8	537.3 ± 101.3

Discriminate variables were analyzed using chi-square test and continuous numbers were summarized mean ± SD and analyzed using analysis of variance.

* Female patients comprised the majority only among nonsmokers. † Early quitters were older than late quitters.

ASA PS = American Society of Anesthesiologists physical status; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus.

ers were 85.7% (73–97%), 67.6% (52–83%), 55.0% (33–77%), 59.1% (47–71%), and 47.5% (32–63%), respectively. The incidence of impaired wound healing was significantly lower in the intermediate quitters, early quitters, and nonsmokers than in the smokers ($P < 0.05$ each); however, the incidence of impaired wound healing did not significantly differ between the late quitters and the smokers. There was a significant correlation between the stepwise improvement of smoking habit and the degree of impaired wound healing (Spearman correlation coefficient by ranks, −0.233; $P = 0.001$; table 2).

Many factors have been reported to increase the incidence of impaired wound healing; therefore, univariate analysis was performed to evaluate the effect of each factor on the development of impaired wound healing. The odds ratios (ORs) of possible risk factors and their 95% CIs (lower limit–upper limit) are shown in table 3. Age at the time of surgery of more than 40 yr, longer duration of surgery, flap other than forearm flap, and smoking cessation less than 3 weeks before the surgery were identified as risk factors for development of impaired wound healing.

On multivariate analysis, longer operation time remained a significant risk factor (table 3). Compared with the smokers, the intermediate quitters (OR, 0.17; 95% CI, 0.04–0.75), early quitters (OR, 0.17; 95% CI, 0.05–0.60), and nonsmokers (OR, 0.11; 95% CI, 0.03–0.51) had a significantly lower risk of development of impaired wound healing. The late quitters tended to have a lower risk of impaired wound healing than the smokers (OR, 0.31; 95% CI, 0.08–1.24).

When we factored in the total amount of cigarette consumption (pack-years) in the multivariate model,

Table 2. Smoking Status and Incidence of Impaired Wound Healing

	Smokers (n = 28)	Late Quitters (n = 34)	Intermediate Quitters (n = 20)	Early Quitters (n = 66)	Nonsmokers (n = 40)
Spontaneous healing, %	4 (14.3)	11 (32.4)	9 (45.0)	27 (40.9)	21 (52.5)
Impaired wound healing, %	24 (85.7)	23 (67.6)	11 (55.0*)	39 (59.1*)	19 (47.5*)
Wound treatment in the ward	12 (42.9)	15 (44.1)	4 (20)	20 (30.3)	13 (32.5)
Wound treatment in the operating room	7 (25.0)	3 (8.8)	7 (35.0)	12 (18.2)	6 (15.0)
Removal and reconstruction of the flap	5 (17.9)	5 (14.7)	0 (0.0)	7 (10.6)	0 (0.0)

There was a significant correlation between the stepwise improvement of smoking habit and the degree of impaired wound healing. Spearman correlation coefficient by ranks, −0.233; $P = 0.001$.

* $P < 0.05$ lower than current smoker.

Table 3. Factors Associated with the Development of Impaired Wound Healing in Patients Who Underwent Head and Neck Surgery According to Univariate and Multivariate Logistic Regression Analyses

Variable	Reference	Value	Odds Ratio			
			Univariate	95% CI	Multivariate	95% CI
Sex	Female	Male	1.22	0.59–2.52	0.47	0.16–1.39
Age	≤ 40 yr	> 40 yr	4.05	1.01–16.22	3.91	0.73–21.10
ASA-PS	1	2 or 3	1.23	0.65–2.34	0.95	0.43–2.09
Surgery duration		For every additional 1 min	1.01	1.00–1.01	1.01	1.00–1.01
DM	−	+	2.17	0.88–5.39	2.06	0.73–5.79
Chemotherapy	−	+	2.30	0.81–6.54	3.30	0.76–14.32
Radiation therapy	−	+	1.32	0.64–2.71	1.06	0.39–2.93
Flap	Forearm	Others	0.39	0.21–0.71	0.63	0.31–1.28
Smoking habit	Smokers	Late quitters	0.35	0.10–1.25	0.31	0.08–1.24
		Intermediate quitters	0.20	0.05–0.81	0.17	0.04–0.75
		Early quitters	0.24	0.08–0.77	0.17	0.05–0.60
		Nonsmokers	0.15	0.04–0.51	0.11	0.03–0.51

CI = confidence interval; DM = diabetes mellitus.

there was no significant change in the OR for the development of impaired wound healing (intermediate quitters: OR, 0.16; 95% CI, 0.03–0.87; early quitters: OR, 0.13; 95% CI, 0.03–0.56). Therefore, the total amount of cigarette consumption (pack-years) did not have a significant effect on the relation between smoking cessation and impaired wound healing.

Moving average analysis indicated that the risk of development of impaired wound healing started to decrease in patients who stopped smoking 1–4 weeks before the surgery. The declining trend continued in those whose preoperative smoke-free periods were 5–8 weeks (fig. 1).

Discussion

Many clinical studies have found that smoking is an independent risk factor for impaired wound healing.[13–15] However, the optimal duration of smoking cessation that reduces the risk of impaired wound healing has not been defined.

Limited information about the optimal timing of smoking cessation before surgery to reduce the incidence of impaired wound healing is available. Three studies examined the effects of preoperative smoking cessation on postoperative wound healing. Smoking cessation 2 weeks before colorectal surgery did not reduce the incidence of postoperative wound complications,[16] although smoking cessation 6–8 weeks before hip or knee alloplasty did so.[6] Moreover, 4-week abstinence from smoking led to reduced incisional wound infections in an experimental setting.[17]

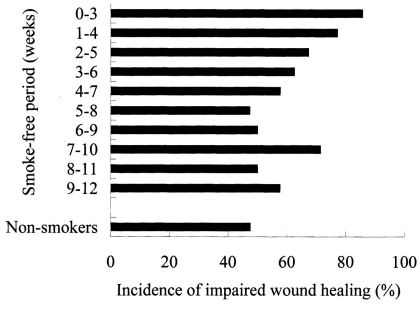

Fig. 1. Moving average of impaired wound healing among smokers and ex-smokers. The risk of development of impaired wound healing started to decrease in patients who stopped smoking 1–4 weeks before surgery. The declining trend continued in those whose preoperative smoke-free periods were 5–8 weeks.

The current study revealed that a 3ee-week smoke-free period reduced the incidence of impaired wound healing among patients who underwent reconstructive head and neck surgery to the incidence among nonsmokers. Although the effect was not significant, a 1- to 3-week smoke-free period tended to reduce the incidence of impaired wound healing. In this study, we considered that the number of late quitters and smokers was too small to make a definitive conclusion about whether a preoperative smoke-free interval of less than 3 weeks decrease the incidence of impaired wound healing. Therefore, we strongly recommend that smoking patients who are going to undergo reconstructive head and neck surgery quit smoking as soon as possible.

Among patients who underwent breast cancer surgery, an increase in smoking consumption had a detrimental effect on wound healing after the surgery.[7] However, after controlling for smoking consumption, we found that the level of smoking consumption had no influence on the beneficial effect of smoking cessation on wound healing. That is, our data suggest that smoking cessation for longer than 3 weeks before reconstructive head and neck surgery is beneficial for all smokers, regardless of their level of smoking consumption.

Cigarette smoke contains more than 4,000 toxic compounds, some of which cause impaired wound healing. Nicotine, carbon monoxide, and hydrogen cyanide combine to reduce the amount of utilizable oxygen and other

substances required for healing.[18] In addition, the synthesis of subcutaneous collagen is impeded in smokers.[19] However, the time course of the reversal of these negative effects of smoking after cessation has not been examined, except for the relation between nicotine and tissue hypoxia.[20] Therefore, further research is needed to explain how smoking cessation improves wound healing and to examine whether the less than 3 weeks of preoperative smoking cessation can improve wound healing.

One limitation of this study is that we did not confirm the smoking status of the patients using biologic monitoring techniques such as monitoring of the expired carbon monoxide concentration or nicotine metabolite monitoring. Some smokers and ex-smokers may have underreported their smoking habit, resulting in misclassification in our study. However, we believe that this misclassification would have overestimated the risk for impaired wound healing among late and intermediate quitters and underestimated the effect of preoperative smoking cessation on the incidence of impaired wound healing in the current analysis. Another limitation was our definition of impaired wound healing. We obtained information on the interventions for the patients' wounds only from their medical records. There may have been the inconsistency in the assessment of impaired wound healing that had been judged by surgeons. However, such inconsistency would reveal the nondifferential misclassifications among the group of smoking status. Therefore, these misclassifications would have underestimated the effect of the duration of the preoperative smoking cessation on the incidence of impaired wound healing in the current analysis.

In conclusion, our retrospective study indicated that among patients who undergo reconstructive head and neck surgery, smoking cessation for 3 weeks or longer before the surgery lowers the risk of impaired wound healing. Therefore, to obtain the necessary duration of smoking abstinence, this information should be disseminated to primary physicians who refer patients with head and neck carcinoma to surgeons as well as to surgeons.

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