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Original Article

Factors influencing delayed referral of oral cancer patients from family dentists to the core hospital

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KEYWORDS

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Abstract *Background/purpose:* Most oral cancer (OC) cases are identified by family dentists in Japan. However, a significant number of patients with OC in Japan are referred to core hospitals at advanced stages. Therefore, identifying the factors that contribute to delayed referrals from family dentists to core hospitals is crucial for detecting OC in its earlier stages. The aim of this retrospective study was to identify the risk factors for referral delays from family dentists to core hospitals.

Materials and methods: The study included 63 patients with OC who were referred by family dentists to the Yamagata University Hospital between 2010 and 2022. The clinical parameters related to referral delays were retrospectively investigated using letters of reference provided by the family dentists and patient charts. Backward multiple regression analysis was performed to identify the relationships between the length of referral delay and potential risk factors. Additionally, backward multivariate logistic regression analysis was performed to examine the independent association between referral delays of >4 weeks and several clinical parameters.

Results: Multiple regression analysis revealed that misdiagnosis of malignant lesions by family dentists ($P = 0.047$) was significantly associated with longer referral delays. Additionally, misdiagnosis of malignant lesions by family dentists was also an independent risk factor for referral delays of >4 weeks (odds ratio, 10.387; $P = 0.006$).

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Conclusion: Misdiagnosis of malignant lesions by family dentists was a significant risk factor for referral delays from family dentists to core hospitals. Our results will motivate family dentists to improve their ability to diagnose OC.

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Introduction

Oral cancer (OC) occurs in different sites of the oral cavity, such as the tongue, gingiva, oral floor, buccal mucosa, palate, and lips. OC occurs commonly worldwide,^{1–4} and its incidence has been increasing.^{5,6} The increasing incidence of OC is compounded by the low survival rate associated with the disease. Despite improvements in the effectiveness of surgery, radiation, and chemotherapy, the survival rate for OC has not improved significantly.^{6–8} The survival rate for advanced-stage OC is extremely low, whereas for OC diagnosed in the initial stage is relatively higher.^{3,4,7,8} The low quality of life (QOL) after surgery is another disadvantage.^{6,9–11} The oral cavity plays important functional and aesthetic roles in daily activities, such as eating and speaking and maintaining the constitution of the face, which are necessary for maintaining a high QOL.^{6,9,10} In advanced-stage OC, wide local resection leads to oral dysfunction and aesthetic dissatisfaction.¹⁰ Therefore, as with cancers at other sites, detection of OC at an early stage is desirable, and referring patients to a core hospital and beginning treatment as early as possible are essential.^{11–14}

OC is evaluated by visual examinations.¹² Although the detection of OC is often assumed to be simple, it is not, especially in the initial stage, since initial-stage OC generally presents with no pain, bleeding, or hypesthesia.^{15,16} Therefore, most patients with initial-stage OC do not notice malignant lesions in the oral cavity by themselves. Furthermore, OC in the initial stage may mimic benign lesions.^{17,18} Unfortunately, even general dental practitioners and family dentists may find it difficult to distinguish early-stage OC from benign lesions.^{11,12} Most family dentists in Japan see only a very limited number of OC cases over the course of their careers. Therefore, approximately 38.5% of patients with OC in Japan are referred to core hospitals at advanced stages, such as stage III or IV.¹⁹

Majority of the cases of OC are identified by family dentists in Japan, who then refer these patients to core hospitals for the treatment of OC. Therefore, the relevant factors related to family dentists should be thoroughly understood to ensure early detection of OC in patients in Japan. Thus, a survey of the risk factors for delayed referral of patients with OC by family dentists to core hospitals will facilitate early OC detection by family dentists.

Therefore, we conducted a retrospective study to identify the risk factors for referral delays by family dentists. We hypothesized that referral delays are influenced by family dentists' diagnostic errors, tumor size, and the site of occurrence of OC. Although investigations on the effect of these factors on diagnosis and referral delays have

been performed in other countries,^{20–22} to our knowledge, no previous study has surveyed the risk factors for referral delays in Japan.

Materials and methods

Study design and participants

This study was approved by the Ethics Committee of Yamagata University School of Medicine (No. 2022-283). All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

The present investigation was a retrospective study conducted using chart data. Consent was obtained through an online opt-out method, and none of the patients withdrew participation. The study participants included 189 patients with OC recruited from the Department of Dentistry, Oral and Maxillofacial Surgery, Yamagata University Hospital, between April 2010 and July 2022. Among the 189 patients, 94 were excluded, as they were not referred by family dentists. Furthermore, 32 patients were excluded because of insufficient information in the referral letters, such as missing information on the diagnosis by the family dentist or the date of the first visit to the family dentist. Thus, 63 patients with OC were finally included in our statistical analyses.

Measurements

Age, sex, diagnosis by family dentists, cancer site, T-classification, year of medical examination, and the duration of the consultation were evaluated in relation to referral delays. The duration of consultation was defined as the number of days from the day of the patient's visit to the family dentist to the day when they were referred to our hospital by the family dentist.

Statistical analyses

The Mann–Whitney U and chi-squared test were conducted to evaluate the distribution of characteristics quantitatively and qualitatively, respectively. Backward multiple regression analysis was performed to investigate the relationship between the length of the referral delay and the potential risk factors. First, a univariate regression analysis was performed to identify the potential risk factors for longer referral delays. Variables with *P*-values <0.25 in the univariate analysis were selected as representative variables, and backward multiple regression analysis was

Table 1 Characteristics of the participants.

		Duration to be referred from the family dentist				P-value [†]
		<4 weeks		≥4 weeks		
		Median (min-max)	S.E	Median (min-max)	S.E	
Age (years)		73 (23–94)	2.0	78 (38–90)	5.4	0.609
		n	%	n	%	
Sex	Male	29	53.7	4	44.4	0.725
	Female	25	46.3	5	55.6	
Diagnosis in referral	Tumor	44	81.5	3	33.3	0.006*
	Other than tumor	10	18.5	6	66.7	
Site of oral cancer	Gingiva	18	33.3	5	55.6	0.267
	Other	36	66.7	4	44.4	
T-classification	0-II	40	74.1	4	44.4	0.114
	III-IV	14	25.9	5	55.6	
Year of medical examination	2010–2016	21	38.9	2	22.2	0.467
	2017–2022	33	61.1	7	77.8	

[†] P-value according to Student's t-test.

* Statistically significant ($P < 0.05$).

Note: SE, standard error.

performed with the representative variables for longer referral delays. To examine the independent association between referral delays of >4 weeks and several clinical parameters, we also performed backward multivariate logistic regression analysis to estimate the adjusted odds ratios (ORs) and 95% confidence intervals (CIs). The multivariate logistic regression analysis included representative variables with $P < 0.25$ in the univariate logistic analysis. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using SPSS version 25.0 (IBM, Armonk, NY, USA).

Results

Table 1 presents the distribution of the characteristics of the participants divided by the duration of consultation (<4 weeks and ≥ 4 weeks). The distribution of diagnoses by family dentists differed significantly between the two groups.

Fig. 1 shows the year-wise distribution of 63 patients with OC. The minimum was zero patients in 2010 and 2011, and the maximum was nine patients in 2017 and 2019. The median was six cases of OC.

Table 2 summarizes the results of the univariate and multiple regression analyses performed to determine the effects of each parameter on the length of referral delay. Univariate regression analysis revealed three variables with P -values <0.25 , including misdiagnosis by family dentists, gingival site, and lower T-classifications such as 0, 1, and 2. Furthermore, multivariate logistic regression analysis with these three representative factors revealed that misdiagnosis of malignant lesions by family dentists ($P = 0.047$, $\beta = 0.251$) was significantly associated with a longer referral delay. The adjusted coefficient of determination (R^2) for this model was 0.048.

Table 3 also lists the significant variables in the multivariate logistic regression analysis using the variables with

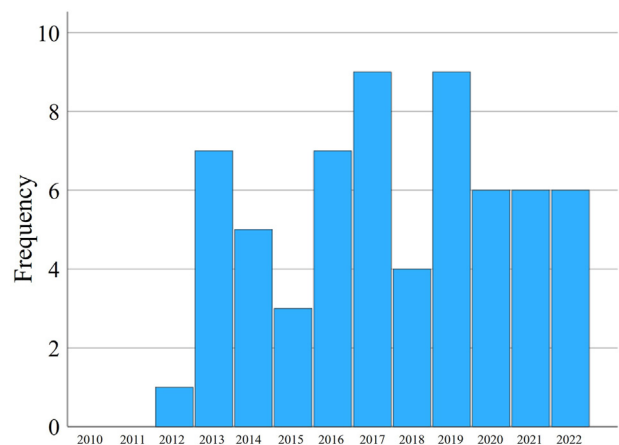


Figure 1 Year-wise distribution of 63 patients with oral cancer.

$P < 0.25$ in the univariate analysis. The independent risk factor for referral delay of >4 weeks was the misdiagnosis of malignant lesions by family dentists (OR, 10.387; 95% CI, 1.977–54.571; $P = 0.006$). Lower T-classifications such as 0, 1, and 2 were not significant risk factors (OR, 4.556; 95% CI, 0.872–23.810; $P = 0.072$); however, this variable was selected in the final logistic model to explain the risk of referral delay.

Discussion

In the present study, we surveyed the risk factors for delayed referral of patients with OC from family dentists to core hospitals and showed that misdiagnosis of malignant lesions by family dentists was a significant risk factor for prolonged referral delays. The present results may give the impression of being the natural result for dentists. Furthermore, most dentists may have recognized our

Table 2 Backward multiple regression analysis of the risk factors for referral delay.

Variable	Univariate					Multivariate				
	B	S.E	β	t	P-value	B	S.E	β	t	P-value
Age (years)	0.002	0.220	0.001	0.010	0.992					
Sex (female vs. male)	-4.879	6.388	-0.097	-0.764	0.448					
Diagnosis in referral (except tumor vs. tumor)	14.433	7.129	0.251	2.025	0.047*	14.433	7.129	0.251	2.025	0.047*
Site of oral cancer (gingiva vs. except gingiva)	9.248	6.552	0.178	1.411	0.163					
T-classification (0-II vs. III, IV)	10.672	6.850	0.196	1.558	0.124					
Year of medical examination (2017–2022 vs. 2010–2016)	5.543	6.620	0.107	0.837	0.406					

*Statistically significant ($P < 0.05$).

Note: SE, standard error.

Adjusted for representative variables that were marginally significant in univariate analysis ($P < 0.25$).**Table 3** Crude and adjusted odds ratios and 95% confidence intervals for the risk for referral delay of more than 4 weeks.

Variable	Crude OR	(95% CI)	P-value	Adjusted OR	(95% CI)	P-value
Age (years) (per 1-year increase)	1.010	(0.960–1.063)	0.701			
Sex (female vs. male)	1.450	(0.351–5.995)	0.608			
Diagnosis in referral (except tumor vs. tumor)	8.800	(1.874–41.323)	0.006*	10.387	(1.977–54.571)	0.006*
Site of oral cancer (gingiva vs. except gingiva)	2.500	(0.597–10.461)	0.210			
T-classification (0-II vs III, IV)	3.571	(0.839–15.207)	0.085	4.556	(0.872–23.810)	0.072
Year of medical examination (2017–2022 vs. 2010–2016)	2.227	(0.422–11.761)	0.346			

*Statistically significant ($P < 0.05$).

Note: OR, odds ratio. CI, confidence interval.

Adjusted for representative variables that were marginally significant in univariate analysis ($P < 0.25$).

results clinically and intuitively, as several reports have already identified insufficient knowledge of OC among general dental practitioners.^{23,24} However, to our knowledge, no scientific study has comprehensively surveyed the risk factors for referral delays in Japan, and our study represents the first attempt to confirm significant risk factors for referral delays in Japan. These factors highlight the relevance of our findings.

In the present study, a low T-classification was not a statistically significant risk factor for prolonged referral delays; however, it showed a slight significance in the final logistic models ($P = 0.072$). This result will also be clinically and intuitively accepted by most dentists. Larger lesions, which indicate higher T-classifications, are very easy to detect by visualization assessments. In general, OC with a higher T-classification, especially more than T3, shows several notable clinical features, such as remarkable ulceration and lumps.¹⁶ Thus, even if the family dentist has no experience in diagnosing OC clinically, they will be able to recognize the lesion and refer the patient to a core hospital. In contrast, smaller OC lesions may be difficult to recognize for family dentists with no specialization in oral surgery, as these smaller lesions generally mimic the characteristics of benign lesions.^{17,18,25,26} Moreover, patients with smaller OC lesions generally do not experience any symptoms,¹⁶ and patients with OC may have little knowledge of the disease.^{27,28} Thus, patients with smaller OC lesions may not present with any complaints. Thus, although T-classification was not statistically significant in

this study, it remains clinically important, and family dentists should especially consider patients with small lesions.

We hypothesized that the site of cancer in the oral cavity affects referral delays, and we compared the risk of prolonged referral delays between gingival cancer and cancers at other sites. Most family dentists in Japan are general practitioners; therefore, the majority of their routine cases involve the treatment of dental caries and periodontitis. In particular, family dentists frequently treat patients with gingivitis or periodontitis. We hypothesized that the dentists' familiarity with gingival examinations also makes them accustomed to seeing severe gingival inflammation. Since gingival inflammation and malignancy are often similar in appearance,^{17,18,25} family dentists may have a high threshold for the diagnosis of gingival malignancy, and they may diagnose a malignant gingival lesion as gingival inflammation, leading to prolonged referral delays. However, in the present study, the gingival site of OC was not a significant risk factor for referral delays. If a specific OC site is confirmed as a risk factor for referral delays, it can be used as a cue for family dentists to focus their examinations. Further studies are required to clarify this point.

The possibility that several family dentists do not have sufficient knowledge of OC has been pointed out in a previous study.²⁹ One reason for this may be the nature of university education in dentistry. Ozdemir-Ozenen reported that dental university students in Istanbul, Turkey, had insufficient knowledge regarding some of the main concepts of OC risk factors, and they lacked confidence in

examining their patients.³⁰ They also highlighted the need to change the curriculum in dental universities.³⁰ Similar surveys have been performed worldwide and suggestions provided for improving the OC educational curriculum for dental students.^{31–35} These changes in undergraduate dental education are essential for improving OC diagnosis skills among family dentists and shortening referral delays.

Our study has a few limitations. The first limitation is related to the generalizability of the findings due to missing data. The number of patients with original OC was 189, among whom 95 were referred by family dentists. However, among these 95 patients, 32 were excluded, as their letters of referral did not include information regarding the day of the first visit to the family dentist and/or the diagnosis by the family dentist. In future studies, this information should be collected through direct interviews with the family dentist instead of relying on letters of reference. The second limitation was that the adjusted coefficient of determination (R^2) in this model was low. Only a limited number of confounding factors were adjusted for in our model; thus, other relevant confounding factors may not have been adjusted for in our model. For example, the specialty of the family dentist affects the duration of the consultation. Oral surgeons have high accuracy in discriminating OC from other lesions. Thus, if the family dentist has an extensive background in oral surgery training, the referral delay may be minimized. Thus, a thorough assessment of additional and appropriate confounding factors will be required to improve the study design in future investigations. The third limitation is that our study only surveyed the referral delay from family dentists, which is a part of professional delays in diagnosis. Diagnostic delay in OC is typically defined as the interval between symptom onset and histological diagnosis³⁶ and consists of two parts^{20,37}: patient delays and professional delays. Patient delay refers to the interval between the day patients experience some symptoms of OC to the day they visit any medical facility. Professional delay refers to the time from the first presentation to the health practitioner to the histological diagnosis. Our study primarily investigated professional delay. As patient delay has been reported to have a greater influence on OC than professional delays,^{20,36,37} future studies should aim to comprehensively evaluate both aspects while surveying the risk factors for diagnostic delays in Japan.

In summary, we showed that misdiagnosis of malignant lesions by family dentists was a significant risk factor for delayed referrals to core hospitals. Family dentists should unequivocally remain the first line of screening for OC. Our results will motivate family dentists to improve their ability to diagnose OC.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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