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Description	

Countermeasure and opportunistic screening systems for oral cancer

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ABSTRACT

Objectives: Tokyo Dental College started oral cancer screening in cooperation with a local dental association in 1992. Reveal the usefulness of Countermeasure and Opportunistic Screening Systems for Oral Cancer. The actual results of countermeasure and opportunistic oral cancer screening systems are reported.

Materials and Methods: Countermeasure screening for the public was performed in each region, and opportunistic screening was performed in a general dental clinic of a cooperating physician.

Results: In countermeasure screening, 19,721 persons were checked from 1992 to 2018; the gender ratio was 1:3. The close examination rate was 4.45%. The detection rates of oral cancer and oral potentially malignant disorders were 0.13% and 1.85%, respectively. In opportunistic screening, 29,912 persons were checked from 2006 to 2018; the gender ratio was 2:3. The close examination rate was 2.33%. The detection rates of oral cancer and oral potentially malignant disorders were 0.08% and 2.15%, respectively.

The close examination rate was significantly lower in opportunistic screening than in countermeasure screening. The oral cancer detection rates and the positive predictive value for cancer were equivalent. In addition, the detection rate of oral potentially malignant disorders was significantly higher in opportunistic screening than in countermeasure screening.

Conclusion: Oral cancer detection rates were equivalent between countermeasure and opportunistic screenings, and opportunistic screening were more effective on number of participants and the close examination rate, and the detection rate of oral potentially malignant disorders.

Introduction

Oral cancer is a serious and growing problem in many parts of the globe. Oral and pharyngeal cancers are grouped together as the sixth most common cancer in the world [1]. According to the World Health Organization (WHO), there are an estimated 657,000 new cases of oral and pharyngeal cancers each year and more than 330,000 deaths [2]. Especially in Japan, new and fatal cases are tending to increase [3]. More than 90% of oral cancers are squamous cell carcinomas (SCCs) [4]. Delayed diagnosis accounts for poor quality of life and a high mortality rate, since nearly half of oral cancer cases are at an advanced stage at the time of initial diagnosis [4]. Early detection and early treatment are crucial to help improve the survival rate of patients with oral cancer [5,6].

Patients typically present to a general dental practice when they experience oral discomfort. The dental general practitioners (GPs) are thus the frontline oral health screeners for oral abnormalities [7]. Oral cancer screening is important to detect early oral cancer and improve the survival rate [8]. Furthermore, GPs play a vital role in reaching correct decisions about lesions, and are thus crucial in avoiding unnecessary or delayed referrals and considerably reducing the mortality of SCC [9]. SCC may develop from oral potentially malignant disorders (OPMDs), such as leukoplakia, oral lichen planus, erythroplakia. It has been reported that early detection and management of oral epithelial dysplasia in OPMDs is an important step preventing malignant transformation [10].

The oral cavity can be accessed and examined easily. A thorough physical examination of the oral cavity, such as visual inspection and palpation, provides valuable insight into a person's overall health in general and their oral health in particular. An extraoral head and neck

physical examination, such as palpation of lymph nodes, is an integral component of the assessment of oral health [11]. Therefore, oral cancer screening with visual inspection and palpation requires no special equipment and is not invasive.

Tokyo Dental College (TDC) has been working on oral cancer screening since 1992 in cooperation with local Dental Associations, governments, and a base hospital [12,13]. This paper reports the results of oral cancer screening, as well as the future prospects.

Materials and methods

Countermeasure screening of oral cancer

Countermeasure screening of oral cancer started in Chiba-City in 1992, and the area for countermeasure screening of oral cancer has expanded over time. As of April 2019, it has been conducted in 15 areas. Examinees are recruited by public advertisements one to three times per year in each region. Oral surgeons in our college are the screeners for countermeasure screening at health centers and public meeting halls.

In all areas, the examinees were in principle over 40 years of age. The screening method was the same as that reported by the WHO [11-14], and after having received a standardized questionnaire, the medical interview was conducted. After that, visual inspection and palpation of the oral cavity was performed using lights, mirrors, and gauze at the individual booth. Subsequently, palpation of the neck lymph nodes was performed. The inspection and palpation were performed in a uniform order so that no areas in the oral cavity were overlooked. If a lesion requiring close examination or treatment was found, it was referred to a base hospital for close examination. Even in diseases that were not oral cancer and OPMDs, such as benign tumors and cysts, there were referred to a base hospital when close examination is required. At a base hospital, close examination was undergo including cytology and biopsy.

In this countermeasure screening of oral cancer, posters and leaflets about oral cancer and models of oral cancer were displayed. Even if there were no abnormalities in the oral mucosa, explanations and educational activities were conducted on the epidemiology and treatment of oral cancer.

In some areas, buddy systems were used [13]. In this buddy system, oral surgeons in our college and GPs of the local dental association in each region performed oral cancer screening together. This system aims to improve the medical examination and diagnostic skills related to the oral mucosa of general dentists through screening.

Opportunistic screening for oral cancer

Opportunistic screening for oral cancer started in Chiba-City in 2006, and the area for opportunistic screening of oral cancer has expanded over time. As of April 2019, it has been conducted in 4 areas. At present, opportunistic screening systems in Chiba-City and Sakura-City (Chiba Prefecture), Edogawa-Ward (Tokyo Metropolitan), and Koshigaya-City (Saitama Prefecture) have been delegated to the Dental Associations as administrative health promotion projects.

Opportunistic screening was performed at dental clinics where GPs had attended a lecture to become cooperating physicians (CPs) among members of the Dental Association in each region [12-14]. This opportunistic screening is performed at regular or annually determined periods each year in each dental clinic of an authorized CP. In addition, a renewal system has been established, and the CPs are constantly striving to acquire new knowledge and skills.

In all areas, the examinees were in principle over 40 years of age. Applicants for opportunistic screening contacted each Dental Association or administrative department by telephone or e-mail, and the date and CP clinic were determined. Opportunistic screening was conducted in the same way as countermeasure screening, with a

medical interview, visual inspection, and palpation. Liquid cytology was sometimes performed when there were suspicious or bothersome findings [14]. If there were obvious abnormal findings or lesions to be examined, the examinees were immediately referred to a base hospital.

The results of the 27-year countermeasure screening for oral cancer from 1992 to 2018 and the 13-year opportunistic screening for oral cancer from 2006 to 2018 were tabulated, including the number of patients, age, gender, and lifestyle at the visit. In addition, as an evaluation of the oral cancer screening, the close examination rate and oral cancer detection rate, the positive predictive value (PPV) for cancer, and the OPMDs detection rate were calculated.

To examine differences between countermeasure and opportunistic screening systems, the chi-squared test and Fisher's exact test were used, as appropriate. All statistical analyses were performed using SPSS version 25.0 (IBM, Tokyo, Japan). Values of $p < 0.05$ were considered significant. In addition, 95% confidence intervals (95% CIs) were also calculated. This study was approved by the Ethics Committee of TDC (authorization number 336) and performed in accordance with the requirements of the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013).

Results

Countermeasure screening

The number of participants in countermeasure screening tended to increase. The number of participants in countermeasure screening was 19,721 over the 27 years. By gender, there were 4,979 men (25.2%) and 14,742 women (74.8%), for a gender ratio (men: women) of 1:3. The age distribution is shown in Fig.1. There were many examinees in the 60 s to 70 s (57.9%).

As for reasons for consultation, "There are no symptoms" accounted for 56.5%. Next, "slow to heal stomatitis" accounted for 10.8%, "stains and pain" for 10.2%, "swelling" for 8.3%, "bleeding" for 3.1%, "dentures and crowns are hitting oral mucosa" for 2.5%, "delayed healing" for 1.1%, and other for 7.5%. As the symptoms, 80.2% were dental symptoms.

With respect to a life-time history of smoking, "no smoking" accounted for 79.6%, followed by "smoking in the past" at 16.0% and "current smoking" at 4.4%. With respect to drinking alcohol, "no drinking" accounted for 51.3%, with "drinking in the past" at 7.3%, "opportunity drinking" at 29.4%, and "everyday drinking" at 12.0%. Over time, habitual smoking and drinking tended to decrease.

As a result of the countermeasure screening for oral cancer, close examinations were performed for 878 cases, for a close examination
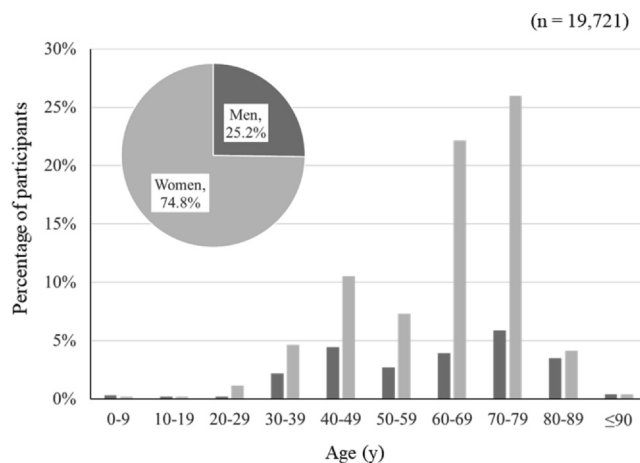

Fig. 1. Age and sex distributions of countermeasure screening. Men and women account for 25.2% and 74.8%. The gender ratio is 1:3. As for the age distribution, there are many examinees in the 60 s to 70 s (57.9%).

Table 1
Countermeasure screening for oral cancers.

	Countermeasure screening for Oral cancer
Participants (Number)	19,721
Gender, men *I* women	4,979/14,742
Close examination (Number)	878
Close examination rate(%)	4.45
Cancers detected (Number)	25
Cancer detection rate (%)	0.13
Positive predictive value for cancer (%)	2.85
OPMDs detected (Number)	365
OPMDs detection rate (%)	1.85

Table 2
Opportunistic screening for oral cancers.

	Opportunistic screening for Oral cancer
Participants (Number)	29,921
Gender, men *I* women	11,965/17,947
Close examination (Number)	698
Close examination rate (%)	2.33
Cancers detected (Number)	24
Cancer detection rate (%)	0.08
Positive predictive value for cancer (%)	3.44
OPMDs detected (Number)	642
OPMDs detection rate (%)	2.15

rate of 4.45%. A total of 25 cases of cancer were detected, for a cancer detection rate of 0.13%. The PPV for cancer was 2.85%. OPMDs were detected in 365 cases, for an OPMDs detection rate of 1.85% (Table 1).

Opportunistic screening

The number of participants in opportunistic screening tended to increase. The total number of participants was 29,912 over the 13 years. By gender, there were 11,965 men (40.0%) and 17,947 women (60.0%), for a gender ratio of 2:3. The age distribution is shown in Fig.2. Many participants were in their 60–70 s (65.2%).

With respect to a life-time history of smoking, "no smoking" accounted for 89.7%, followed by "smoking in the past" at 6.5% and "current smoking" at 3.8%. With respect to drinking alcohol, "no drinking" accounted for 62.4%, "drinking in the past" for 10.0%, "opportunity drinking" for 16.8%, and "everyday drinking" for 10.8%.

As a result of the opportunistic screening for oral cancer, close examinations were performed for 698 cases, for a close examination rate of 2.33%. A total of 24 cases of cancer were detected, for a cancer detection rate of 0.08%. The PPV for cancer was 3.44%. OPMDs were detected in 642 cases, for an OPMDs detection rate of 2.15% (Table 2).

Differences between countermeasure and opportunistic screening systems for oral cancer

Table 3 compares the countermeasure and opportunistic oral cancer screening systems. The number of participants in oral cancer screening was 19,721 over the 27 years for countermeasure screening and 29,912 over 13 years for opportunistic screening. The gender ratios were 1:3 for countermeasure screening and 2:3 for opportunistic screening; the

proportion of men was higher in opportunistic screening than in countermeasure screening ($p = 1.06E$-252, 95% CI = -0.156, −0.138).

As Life-time history, current smoking and everyday drinking alcohol rate for countermeasure screening were higher than for opportunistic screening (smoking: $p = 5.82E$-183, 95% CI = -0.097, −0.084, drinking: $p = 1.14E$-132, 95% CI = -0.120, −0.102).

The close examination rates were 4.45% for countermeasure screening and 2.33% for opportunistic screening; the close examination rate was significantly lower for opportunistic screening than for countermeasure screening ($p = 1.26E − 39$, 95% CI = 0.018, 1.265). The oral cancer detection rates were 0.13% for countermeasure screening and 0.08% for opportunistic screening ($p = 0.106$, 95% CI = -9.92, 0.0010). The PPVs for cancer were 2.85% for countermeasure screening and 3.44% for opportunistic screening; the PPV for cancer was higher for opportunistic screening than for countermeasure screening, but it was not significant ($p = 0.501$, 95% CI = −0.023, 0.011). In addition, the OPMDs detection rate was 1.85% for countermeasure screening and 2.15% for opportunistic screening; the OPMDs detection rate was significantly higher for opportunistic screening than for countermeasure screening ($p = 0.018$, 95% CI = −0.0055, −5.239).

Discussion

In Europe and the United States of America, oral cancer screening has been developed [15,16], and it has been reported that the prevalence rate of oral cancer has been decreasing [1,2,15,16]. However, in Japan, new and fatal cases of oral cancer are tending to increase [3]. Therefore, TDC started oral cancer screening in 1992 with the cooperation of the local Dental and Medical Association, the government, and the base hospital [12], and oral cancer screening continues. The objectives of oral cancer screening are early detection and treatment of oral cancer [2], discovery of other oral mucosal diseases, including OPMDs [17], awareness of local oral health, and maintenance and improvement of quality of life [18].

For cancer screening of other organs [19], "medical interview and stomach X-ray examination or gastroscopy" for stomach cancer, "medical interview and chest X-ray examination and sputum cytology" for lung cancer, "medical interview and fecal occult blood test" for colorectal cancer, "medical interview and visual inspection, cervical cytology, and pelvic examination" for cervical cancer, and "medical interview and mammography" for breast cancer are performed in Japan. All such cancer screenings are mildly invasive. We conducted oral cancer screening with reference to WHO in order to perform non-invasive screening "medical interview, visual inspection, and palpation". We consider it to be a form of cancer screening that makes use of the characteristics of the oral cavity, which is easy to inspect and palpate [2].

Table 4 shows the difference between countermeasure screening for oral cancer and that for other organs [19]. Of course, the number of participants in oral cancer screening is small compared with the results of countermeasure screening for cancers of other organs. The close

(n = 29,912)
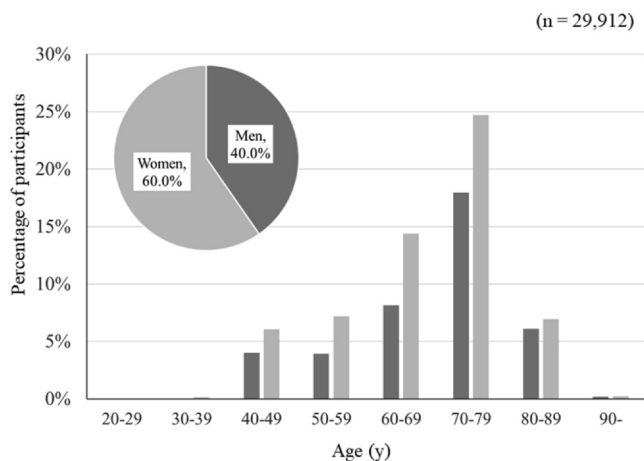
Fig. 2. Age and sex distributions in opportunistic screening. Men and women account for 40.3% and 59.7%, respectively, with a gender ratio of 2:3. As for the age distribution, there are many examinees in the 60 s to 70 s (65.2%).

Table 3

Compared between countermeasure and opportunistic screening for oral cancer.

	Countermeasure screening	Opportunistic screening	p value	95%CI
Gender ratio (Men: Women)	I:3	2:3	1.06E−252	−0.156, −0.138
Life-time history, %				
Smoking, %			5.82E−183	−0.097, −0.084
No smoking	79.6	89.7		
Smoking in the past	16.0	6.5		
Current smoking	4.4	3.8		
Drinking alcohol, %			1.14E−132	−0.120, −0.102
No drinking	51.3	62.4		
Drinking in the past	7.3	10.0		
Opportunity drinking	29.4	16.8		
Eve1yday drinking	12.0	10.8		
Close examination rate, %	4.52	2.33	1.26E−39	0.018, 1.265
Cancer detection rate, %	0.13	0.08	0.106	−9.92, 0.0010
Positive predictive value for cancer, %	2.85	3.44	0.501	−0.023, 0.011
OPMDs detection rate, %	1.85	2.15	0.018	−0.0055, −5.239

examination rate for oral cancer screening was 4.45%, whereas that for other cancer screenings were: 7.25% for stomach cancer; 1.51% for lung cancer; 6.52% for colorectal cancer; 2.18% for cervical cancer; and 7.99% for breast cancer; these rates were equivalent. The cancer detection rate was 0.13% for oral cancer, whereas that for other cancer screening was: 0.10% for stomach cancer; 0.03% for lung cancer; 0.17% for colorectal cancer; 0.04% for cervical cancer; and 0.28% for breast cancer: these rates were equivalent. In addition, the PPV was 2.85% for oral cancer, and that for other cancer screenings were: 1.50% for stomach cancer; 2.11% for lung cancer; 2.77% for colorectal cancer; 1.68% for cervical cancer; and 4.15% for breast cancer; these were also equivalent. Although oral cancer screening in the present study cannot be considered using the same indicators for the number of participants and implementation methods, the cancer detection rate was similar for cancer screening of other organs, and it was suggested that oral cancer screening contributes to early detection of oral lesions.

The number of participants in opportunistic screening for oral cancer is also increasing. We checked 19,721 persons over 27 years (730 persons per year) in countermeasure screening, while in opportunistic screening, 29,912 persons were checked over 13 years (1,762 persons per year). In opportunistic screening, more persons are checked in a shorter period of time. At the result, the oral cancer detection rates of countermeasure and opportunistic screening systems were equivalent. We previously reported that the oral cancer detection rate for opportunistic screening was higher than that for countermeasure screening in Chiba-City (opportunistic screening 0.14% vs countermeasure screening 0.09%) [13].

For the close examination rate, it was significantly lower for opportunistic screening than for countermeasure screening. As for the OPMDs detection rate, it was significantly higher for opportunistic screening than for countermeasure screening. The reason for the good result with opportunistic screening is that the participant can select a place and time of screening. In countermeasure screening has some limitations, such as number of persons checked, time and location. With respect to the place of screening, countermeasure screening is limited to designated health centers and public meeting halls, whereas in opportunistic screening, a nearby CP's dental clinic can be freely selected. With respect to the time, countermeasure screening is limited to a designated time one to three times a year, whereas in opportunistic screening, the date and time can be selected freely. Thus, the number of men participants increased, and the gender ratio improved significantly in opportunistic screening ($p = 1.06E−251$). In addition, close examination rate in opportunistic screening was lower than in countermeasure screening ($p = 1.26E−39$). The reasons were; first, since the countermeasure screening is often done as part of the dental examination business, many of the symptoms of participants are dental consultations. Second, since the opportunistic screening is performed by CPs, it can be a smooth transition to follow-up and treat OPMDs, and GPs play an important role as a primary medical institution, thus, only those who needed it were referred to the base hospital.

In terms of costs of opportunistic screening, the co-payment is about 500 to 1,000 yen, and the cost is kept low [13]. In cancer screening for other organs, the co-payment is about 500 to 3,000 yen [19]. Nagao et al. reported that opportunistic screening is more effective from the viewpoint of enhancing compliance and cost-effectiveness [20]. In particular, opportunistic screening in this study contributed to the discovery of OPMDs ($p = 0.018$). Ho et al. reported that the best chance for early-stage diagnosis occurs in OPMDs patients at their first oral screening in Taiwan [8]. They also showed that the major contribution to stage-shift and mortality reduction is from the screening diagnosis of OPMDs; thus, though any cancer diagnosis would require immediate medical attention, it is also important to ensure follow-up of any detected OPMDs.

Japan has 747 Dental Associations across all regions. A survey of the actual situation for oral cancer examination in Japan at the Dental Association reported that oral cancer screening was performed in 37.4% of the regions [21]. As for the type of screening, countermeasure screening accounted for 45.7%, and opportunistic screening accounted for 13.3%. In Japan, oral cancer screening has not yet spread, especially opportunistic screening. Further education on this issue will be needed.

Table 4

Countermeasure screening for oral and other cancers.

	Oral cancer[*]	Stomach cancer[**]	Lung cancer[**]	Colorectal cancer[**]	Cervical cancer[**]	Breast cancer[**]
Pruticipants (Number)	19,721	2,482,333	4,075,104	4,633,580	3,804,714	2,584,439
Close exrunination (Number)	878	168,218	65,041	286.815	80,882	176.439
Close exrunination rate (%)	4.45	7.25	1.51	6.52	2.18	7.99
Cru1cers detected (Number)	25	2,523	1,374	7.943	1,355	7,336
Cru1cer detection rate (%)	0.13	0.10	0.03	0.17	0.04	0.28
Positive predictive value(%)	2.85	1.50	2.11	2.77	1.68	4.15

* Data from the TDC.

** Data of the Ministry of Heath, Labour and Welfare, Japan. Comprehensive Survey of Living Conditions 2016.

We developed an oral cancer navigation system (Navi-System) to support and educate opportunistic screening for oral cancer in our college for the first time in Japan (JCPS KAKENHI Grant Number 24593008). This Navi-System is a system of medical cooperation between GPs and our college using the Internet (https://www.oralnavi.jp) [22]. With this Navi-System, in case of difficulties in judgment and diagnosis, GPs provide information on general and oral findings and intraoral photographs, including medical records and results of visual inspection and palpation, using the Internet. Then, an oral surgeon at our college will give suggestions on how to respond. Through these, we plan to further develop oral cancer screening.

On other hand, there were reports that only a visual inspection and palpation were not recommended for oral cancer screening [23,24]. In the present study, the cancer detection rate and PPV for oral cancer screening with "medical interview, visual inspection, and palpation" were equivalent for other organs; It shows sufficient results. We have been developing a non-invasive fluorescence visualization device with for more the early detection of lesions [25]. Fluorescence visualization is non-invasive, convenient, and real-time, and examinations can be repeated [26]. We are considering using it as an aid for discrimination between oral cancer [27] and OPMDs [28].

There were also report that targeted clinical examination of high-risk individuals may be more effective than countermeasure screening in facilitating early detection of oral cancers [29]. We also agree that measures against participants at high-risk are important. Targeting participants at high-risk may improve the detection rate of oral cancer and OPMDs. Then, oral cancer screening will be more effective. This is a future issue.

The present study had several limitations. First is the gender ratio of the participants: in general population of oral cancer, the gender ratio is 3:2 [3]. However, in the present study, the gender ratios of the countermeasure and opportunistic screening systems were 1:3 and 2:3, respectively. Although there is a trend to improvement, there were still few men participants [13]. Second, there are lifestyle factors: in general population of Japan, the smoking rate is 31.1% for men and 9.5% for women, and the drinking rate is 47.0% for men and 15.2% for women [30]. However, in the present study, the smoking rates in the countermeasure and opportunistic screening systems were 4.4% and 3.8%, respectively, and the drinking rates in the countermeasure and opportunistic screening systems were 12.0% and 10.8%, respectively. These were low rates. Smoking and drinking are considered risk factors for oral cancer, and it is important to involve a high-risk group that targets men who smoke and drink more in the future [31]. Third, this study reported the results for all regions, and no detailed study on regional differences has been made. In the future, it will be necessary to consider regional differences.

In this study, we reported on countermeasure and opportunistic screening systems for oral cancer. In particular, opportunistic screening were more effective in terms of the number of examinees, gender ratio, the close examination rate, and the OPMDs detection rate. In the future, we will strive to further disseminate and universalize screening activities, and we will continue to raise awareness for social recognition of the prevention and significance of oral cancer and the need for its early detection and treatment.

Declaration of Competing Interest

None.

Ethical approval

This study was approved by the Tokyo Dental College Ethics Committee (Authorization Number 336).

Patient consent

Consent was obtained from all participants in this study.

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