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Original Article

Visual screening of oral cavity cancer in a male population: Experience from a medical center

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Abstract

Background: We aimed to evaluate the effectiveness of an oral cavity cancer visual screening program conducted in a tertiary academic medical center. We also wanted to determine which group of participants was at greater risk of contracting oral cavity cancer.
Methods: Participants were first asked to relate their personal habits during the past 6 months. Visual screening of the oral cavity was then performed under adequate lighting and with proper instruments.
Results: From March 2005 to January 2010, 13,878 participants were enrolled in this study. The average age was 54.6 years. Positive lesions were identified in 726 participants (5.2%), and 282 of those participants (2.1%) had oral cavity cancers confirmed. The sensitivity and specificity of this study were 98.9% and 98.7%, respectively. Those participants who were habitual smokers, alcohol consumers, and betel quid chewers had the highest risk of developing oral cavity cancer when compared with those who did not have these habits (odds ratio = 46.90, 95% confidence interval = 33.15–66.35, $p < 0.001$).
Conclusion: The oral screening program conducted in a tertiary medical center was effective. We suggest that individuals aged ≥40 years or who are habitual cigarette smokers, alcohol consumers, and betel quid chewers should receive oral screening regularly so that potential oral cancer can be detected as early as possible.

Keywords: betel quid; medical center; oral cavity cancer; screening; smoking

1. Introduction

Oral cavity cancer is the 10th most common cancer in men globally. It is estimated that 190,000 new oral cavity cancer cases were diagnosed in 2008 worldwide, with 83,000 deaths.[1] In Taiwan, oral cancer has been one of the top 10 causes of death from cancer since 1991. According to the annual report from the Department of Health of the Executive Yuan, the death toll for oral cancer in males has been increasing at a surprising rate.[2] No significant advancement in the treatment of oral cancer has been made in recent years. Although a multidisciplinary approach to treatment has improved the quality of life for oral cancer patients, the relative 5-year survival rate has not changed much over the past decades.[3] Therefore, primary prevention such as cessation of tobacco smoking and alcohol consumption along with early detection are necessary control procedures to improve the prognosis for oral cancer.[4]

Anatomical accessibility makes visual inspection of the oral cavity a suitable method for oral cancer screening.[5] Sankaranarayanan et al, in their cluster-randomized controlled trial evaluating the outcome of visual screening on oral cancer

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mortality, showed that visual screening can reduce mortality in high-risk individuals and has the potential to prevent at least 37,000 deaths annually worldwide.[6] Another study reported a sensitivity ranging from 71% to 81% and a specificity of at least 99% when general dental practitioners performed oral mucosa screening.[7] Cuba has conducted an oral cancer case-finding program and it has increased the detection percentage of stage I oral cancer from 22.8% to 48.2%.[8]

Nevertheless, the majority of the screening programs reported in the literature were performed by dentists, stomatologists, or experienced health workers in a community-based setting. Few studies were conducted in medical centers. Therefore, the aim of this study was to evaluate the effectiveness of oral visual screening conducted in a tertiary academic medical center. In addition, we wanted to determine which group of enrolled participants was at greater risk of contracting oral cancer.

2. Methods

2.1. Participants

This hospital-based study was conducted at Taichung Veterans General Hospital, a tertiary referral center in central Taiwan. We implemented an optional oral screening program in March 2005. The study was conducted in accordance with the Declaration of Helsinki. All male patients who visited our clinic (Otolaryngology or Dental Department) aged 18 or older were eligible for enrollment in this study. Those who were reluctant to undergo oral screening were excluded. In January 2010, we opened a special clinic for oral screening which also accepted walk-ins. Participants were first asked to relate their personal habits during the past 6 months, including tobacco use, alcohol consumption, and betel quid chewing. Those who smoked cigarettes, drank alcohol, or chewed betel quid only on special occasions such as wedding banquets, family reunions, or birthday parties were not considered as habitual users. Next, visual screening of the oral cavity was performed by experienced otolaryngologists or dentists under adequate lighting and with proper instruments. A non-healing ulcer for more than 2 weeks, a persistent white or red lesion, a lesion that bled easily, or an irregular surface lesion inside the oral cavity were regarded as positive findings. Punch biopsy of abnormal lesions was performed after a detailed explanation. If the patient did not agree to further biopsy, follow-up was strongly recommended.

2.2. Statistical analysis

This study used descriptive statistics for general data presentation. Comparisons of nominal or ordinal variables between two groups were analyzed by the Chi-square test. Furthermore, relevant factors for contracting oral cavity cancer were analyzed by a multivariate logistic regression model. All statistics were calculated by SPSS for Windows, version 10.1 (SPSS Inc., Chicago, IL, USA). A p value <0.05 was considered to be statistically significant.

3. Results

3.1. Descriptive statistics

A total of 13,878 participants were enrolled in this study from March 2005 to January 2010. All were male and their ages ranged from 18 to 97 years with an average age of 54.6 years (±18.4 years). Habitual smokers accounted for 20.5% ($n = 2844$) of the studied population, whereas habitual drinkers and betel quid chewers accounted for 14.1% ($n = 1955$) and 6.8% ($n = 943$), respectively. A total of 1358 participants (47.7%) were smokers only, whereas 666 participants (23.4%) were smokers and alcohol consumers, 183 participants (6.4%) were smokers and betel quid chewers, and 637 participants (22.4%) were smokers, alcohol consumers and betel quid chewers. The majority of betel quid chewers (87.0%, $n = 820$) were also smokers, and only 6.7% ($n = 63$) were solely betel quid chewers.

A total of 726 participants (5.2%) were recorded to have positive lesions. Among those with positive lesions, 454 participants (62.5%) later received oral biopsy. Among those who received biopsy, 282 participants (61.7%) were proven to have oral cavity cancer. For those with negative pathological reports, 54 (31.4%) were ulcer or chronic inflammation, 47 (27.3%) were hyperkeratosis or parakeratosis, 19 (11.0%) were squamous cell papilloma, and 13 (7.6%) were verrucous hyperplasia. A total of 272 participants (37.5%) with abnormal oral cavity lesions were lost to follow-up and no further pathological report could be obtained. The reasons why participants with positive findings did not receive oral biopsy might be due to hesitation about invasive oral biopsy, extra payment for biopsy procedures, or looking for a second opinion. We further crosslinked the entire screened cohort with the Taiwan Cancer Registry database and found that three participants with initial negative screening results had oral cavity cancer within 6 months (Table 1). In order not to confound further analyses, we excluded those with positive lesions/yet no further biopsy during the follow-up period. Although 272 participants were excluded from the final analysis, there was little impact on the power of the statistic analysis due to the large population size. The sensitivity of our study was 98.9%, whereas the specificity was 98.7%. The positive predictive value and negative predictive value were 62.1% and >99.9%, respectively.

3.2. Bivariate analysis

After dividing all the participants into two groups according to the screening results, the positive group consisted of 726

Table 1
Crosstabulation of the results of screening and pathological results.

		Pathological results		Total
		Positive	Negative	
Screening results	Positive	282	172	454
	Negative	3	13,149	13,152
	Total	285	13,321	13,606

Table 2
Descriptive and bivariate analyses of the studied population according to screening results.

Variables	Patients, *n* (%) (*n* = 13,878)	Screening results		*p*
		Positive (*n* = 726) Patients, *n* (%)	Negative (*n* = 13,152) Patients, *n* (%)	
Age (y)				<0.001
18–39	3146 (22.7%)	109 (3.5%)	3037 (96.5%)	
40–49	2526 (18.2%)	196 (7.8%)	2330 (92.2%)	
50–59	2844 (20.5%)	250 (8.8%)	2594 (91.2%)	
≥60	5362 (38.6%)	171 (3.2%)	5191 (96.8%)	
Habitual smoker				<0.001
Yes	2844 (20.5%)	484 (17.0%)	2360 (83.0%)	
No	11,034 (79.5%)	242 (2.2%)	10,792 (97.8%)	
Habitual drinker				<0.001
Yes	1955 (14.1%)	359 (18.4%)	1596 (81.6%)	
No	11,923 (85.9%)	367 (3.1%)	11,556 (96.9%)	
Habitual betel quid chewer				<0.001
Yes	943 (6.8%)	328 (34.8%)	615 (65.2%)	
No	12,935 (93.2%)	398 (3.1%)	12,537 (96.9%)	

participants and the negative group consisted of 13,152 participants. Comparisons of variables between the two groups are presented in Table 2. There were significant differences between the two groups based on age (χ^2 value = 170.1, $p < 0.001$). Higher rates of positively identified lesions were found in middle-aged participants when compared with those of participants younger than 40 years or older than 60 years (Fig. 1). In addition, there was also a significant difference between the two groups in personal habits such as smoking, alcohol consumption, and betel quid chewing. Higher positive rates at oral screening were found in those who had habits of smoking, alcohol consumption, or betel quid chewing (Fig. 2).

After dividing all the participants according to the pathological results, the oral cancer group consisted of 285 participants and the control group consisted of 13,321 participants. Comparisons of variables between the two groups are presented in Table 3. There were significant differences between the two groups based on age (χ^2 value = 130.5, $p < 0.001$). Higher rates of malignant oral cavity cancers were found in middle-aged participants when compared with those of participants younger than 40 years or older than 60 years. In addition, there was also a significant difference between the two groups in personal habits such as smoking, alcohol consumption, and betel quid chewing. Higher rates of proven oral malignancy were found in those who had habits of smoking, alcohol consumption, or betel quid chewing.

Participants who screened positive for oral lesions were further divided into those who were willing to undergo oral biopsy and those who were not (Table 4). There were significant differences between the two groups based on age (χ^2 value = 16.49, $p = 0.001$). Middle-aged participants were more willing to undergo oral biopsy when compared with those younger than 40 years or older than 60 years. In addition, there was also a significant difference between the two groups in personal habits such as smoking, alcohol consumption, and betel quid chewing. Those who had habits of smoking, alcohol consumption, or betel quid chewing were more willing to undergo oral biopsy than those who did not

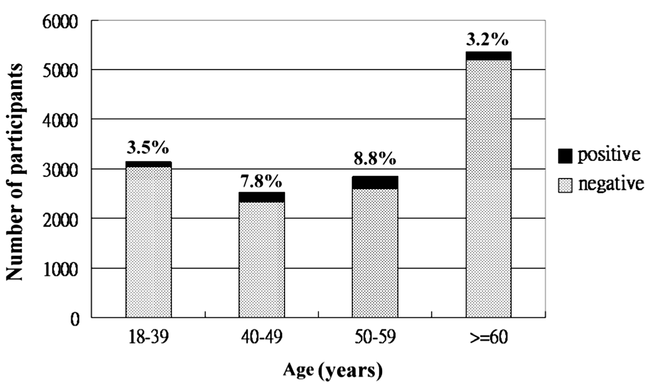

Fig. 1. The age distribution of the studied population and the positive rate of oral screening among different age groups.

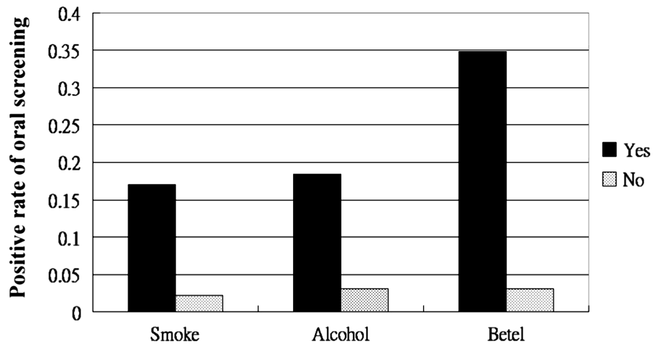

Fig. 2. Positive rates of oral screening in participants with or without habits of smoking, alcohol consumption, or betel quid chewing.

Table 3
Descriptive and bivariate analyses of the studied population according to biopsy results.

Variables	Patients, *n* (%) (*n* = 13,606)	Oral cavity cancer		*p*
		Yes (*n* = 285) Patients, *n* (%)	No (*n* = 13,321) Patients, *n* (%)	
Age (y)				<0.001
18–39	3088 (22.7%)	18 (0.6%)	3070 (99.4%)	
40–49	2459 (18.1%)	83 (3.4%)	2376 (96.6%)	
50–59	2765 (20.3%)	116 (4.2%)	2649 (95.8%)	
≥60	5294 (38.9%)	68 (1.3%)	5226 (98.7%)	
Habitual smoker				<0.001
Yes	2688 (19.8%)	214 (8.0%)	2474 (92.0%)	
No	10,918 (80.2%)	71 (0.7%)	10,847 (99.3%)	
Habitual drinker				<0.001
Yes	1844 (13.6%)	166 (9.0%)	1678 (91.0%)	
No	11,762 (86.4%)	119 (1.0%)	11,643 (99.0%)	
Habitual betel quid chewer				<0.001
Yes	835 (6.1%)	150 (18.0%)	685 (82.0%)	
No	12,771 (93.9%)	135 (1.1%)	12,636 (98.9%)	
Screen				<0.001
Positive	454 (3.3%)	282 (62.1%)	172 (37.9%)	
Negative	13,152 (96.7%)	3 (0%)	13,149 (100%)	

Table 4
Descriptive and bivariate analyses of participants with positive oral screening results.

Variables	Patients, *n* (%) (*n* = 726)	Oral cavity biopsy		*p*
		Yes (*n* = 454) Patients, *n* (%)	No (*n* = 272) Patients, *n* (%)	
Age (y)				0.001
18—39	109 (15.0%)	51 (46.8%)	58 (53.2%)	
40—49	196 (27.0%)	129 (65.8%)	67 (34.2%)	
50—59	250 (34.4%)	171 (68.4%)	79 (31.6%)	
≥60	171 (23.6%)	103 (60.2%)	68 (39.8%)	
Habitual smoker				<0.001
Yes	484 (66.7%)	328 (67.8%)	156 (32.2%)	
No	242 (33.3%)	126 (52.1%)	116 (47.9%)	
Habitual drinker				<0.001
Yes	359 (49.4%)	248 (69.1%)	111 (30.9%)	
No	367 (50.6%)	206 (56.1%)	161 (43.9%)	
Habitual betel quid chewer				0.022
Yes	328 (45.2%)	220 (67.1%)	108 (32.9%)	
No	398 (54.8%)	234 (58.8%)	164 (41.2%)	

have these habits. Comparisons of variables between the two groups are presented in Table 4.

Next, we divided participants who screened positive for oral lesions and underwent oral cavity biopsy into those with malignant and those with benign lesions. There were significant differences between the two groups based on age (χ^2 value = 17.99, $p < 0.001$). Participants aged ≥40 years had a higher rate of malignant lesions when compared with those younger than 40 years. In addition, higher rates of malignant lesions were also noted in participants with the habits of habitual smoking, alcohol consumption, and betel quid chewing. However, significant differences were only found in alcohol consumption and betel quid chewing groups. Comparisons of variables between the two groups are presented in Table 5.

Table 5
Descriptive and bivariate analyses of participants with positive oral screening results who received oral cavity biopsy.

Variables	Patients, *n* (%) (*n* = 454)	Oral cavity cancer		*p*
		Yes (*n* = 282) Patients, *n* (%)	No (*n* = 172) Patients, *n* (%)	
Age (y)				<0.001
18—39	51 (11.2%)	18 (35.3%)	33 (64.7%)	
40—49	129 (28.4%)	82 (63.6%)	47 (36.4%)	
50—59	171 (37.7%)	115 (67.3%)	56 (32.7%)	
≥60	103 (22.7%)	67 (65.0%)	36 (35.0%)	
Habitual smoker				0.093
Yes	328 (72.2%)	212 (64.6%)	116 (35.4%)	
No	126 (27.8%)	70 (55.6%)	56 (44.4%)	
Habitual drinker				0.042
Yes	248 (54.6%)	165 (66.5%)	83 (33.5%)	
No	206 (45.4%)	117 (56.8%)	89 (43.2%)	
Habitual betel quid chewer				0.036
Yes	220 (48.5%)	148 (67.3%)	72 (32.7%)	
No	234 (51.5%)	134 (57.3%)	100 (42.7%)	

3.3. Logistic regression model after adjustment of other variables

Using the presence or absence of pathologically proven oral cancer as the dependent variable, a multivariate logistic regression model for investigating the relevant risk factors for contracting oral cancer was devised. The results showed that those aged 50—59 years were more likely to develop oral cancer when compared with those under 40 years old (odds ratio, OR = 7.04, 95% confidence interval, 95% CI = 4.22—11.75, $p < 0.001$). Furthermore, those who were habitual smokers, alcohol consumers, and betel quid chewers had the highest risk of developing oral cancer when compared with those who did not have these habits (OR = 46.90, 95% CI = 33.15—66.35, $p < 0.001$). The results are shown in Table 6.

4. Discussion

In Taiwan, the annual production of betel nut has increased year by year since 1981.[9] This partially explains why the incidence of oral cancer has rapidly increased and why prevention of oral cancer has become a major public health issue. However, a large-scale oral cancer prevention program is difficult to implement owing to reasons such as budgetary insufficiency and health policies. Therefore, identifying those who are at potential risk of developing oral cancer and conducting oral screening in such a population might be a viable alternative measure. The World Health Organization has clearly recognized prevention and early detection as the main objectives in the control of oral cancer burden worldwide.[10]

In this hospital-based study, 13,868 participants underwent oral mucosa screening and 726 participants (5.2%) were found to have positive lesions. The reported percentage of suspicious lesions in the literature ranges from 1.3% to 16.3%,[6,7] which is

Table 6
Multivariate logistic regression model of risk factors for developing oral cancer.

Variables	Patients, *n* (*n* = 13,606)	Odds ratio	95% Confidence interval		*p*
			Lower limit	Upper limit	
Age (y)					<0.001
18—39[a]	3088	1.00			
40—49	2459	4.69	2.78	7.93	<0.001
50—59	2765	7.04	4.22	11.75	<0.001
≥60	5294	4.22	2.47	7.22	<0.001
Personal habits					<0.001
None[a]	10,231	1.00			
Smoking only	1314	5.67	3.74	8.66	<0.001
Alcohol consumption only	581	1.65	0.71	3.86	0.246
Betel quid chewing only	54	9.24	2.79	30.66	<0.001
Smoking + alcohol	645	9.98	6.45	15.46	<0.001
Smoking + betel quid	163	28.44	16.68	48.51	<0.001
Alcohol + betel quid	52	20.43	8.28	50.3	<0.001
Smoking + alcohol + betel quid chewing	566	46.90	33.15	66.35	<0.001

[a] Reference group.

comparable with that of our study. Among those who were found to have positive lesions, 454 participants later received biopsy and 282 participants were proven to have malignancy. Three participants who had negative oral screening results were found to have oral cancers within 6 months after cross-linking all the participants with the Taiwan Cancer Registry database. The sensitivity and specificity of this study were 98.9% and 98.7%, respectively, which were comparable to or even higher than those of other studies.[4,7] The reason might be that all the participants were examined by experienced otolaryngologists and dentists in our study, whereas previous studies used trained health workers or general dental practitioners as evaluators. Although some diagnostic aids were used in the screening of oral cancer, such as toluidine blue, brush biopsy, chemiluminescence, and tissue autofluorescence, convincing evidence to support the efficacy of the aforementioned approaches is lacking.[10] Therefore, visual inspection is still the main strategy for oral screening.

The prevalence of smoking in this study was 20.5%, which was similar to that of a previous investigation.[11] However, it was lower than that of a previous study conducted in Taiwan (rate of current smokers = 46.5%).[9] One possible explanation is the different definitions of smoking habit used in the aforementioned study and ours. The prevalence of alcohol consumption and betel quid chewing in this study was also similar to that of previous studies conducted in Taiwan.[11] In addition, almost all betel quid chewers were smokers (820 out of 943 participants), which was also another finding in previous studies conducted in Taiwan. [9,12] Therefore, the composition of the population in this hospital-based study is considered to be similar to that of the general male population in Taiwan.

Tobacco contains N-nitroso compounds, well-known carcinogens, which play a major role in the malignant transformation of oral cancer.[13] The mechanisms by which alcohol consumption induces oral cancer are unknown. The most likely explanation is that alcohol or its metabolites are human carcinogens.[14] Betel quid chewing not only causes genomic instability[15] but also has a close association with cell-mediated immunity,[16] which might play a role in the malignant transformation of the oral mucosa.

According to the Taiwan Cancer Registry, the median age at diagnosis of oral cancer is 51.0 years.[2] Therefore, it is easy to understand why those aged 40–59 years in this study were most likely to develop oral cavity cancer. By contrast, only 18 out of 3146 patients (0.6%) under the age of 40 in this study were proven to have contracted oral cancer. Thus, it might be reasonable to start oral mucosal screening of males when they reach the age of 40.

Ko et al, in their case-control study, showed that the incidence of oral cancer was 123-fold higher in those who smoked, drank alcohol, and chewed betel quid than in abstainers.[12] However, selection bias inevitably exists in case-control studies. In this study, it was interesting to note that those who drank alcohol only did not have increased risk of developing oral cancer. One possible explanation might be that we did not collect quantitative data on alcohol consumption. In addition, different types of alcoholic beverages have different effects on the development of oral cancers.[14] Previous studies found evidence of the synergic effect of smoking, drinking, and betel quid chewing on the risk of developing oral cancer.[9,12,14] This might be explained by the fact that betel quid chewers were proportionately heavier smokers, which was also true in the current study. Another study proposed that alcohol might facilitate the passage of carcinogens through cellular membranes. In addition, alcoholic consumption enhanced liver metabolizing activity in both humans and experimental animals and might, therefore, activate carcinogenic substances. Furthermore, alcohol might alter intracellular metabolism of the epithelial cells at the target site.[17] As a result, the oral mucosa would be more vulnerable to the effect of carcinogens transmitted by smoking and betel quid chewing.

Shuman et al, conducted a screening program in a tertiary care academic medical center and found that a minority of patients presenting to a head and neck cancer screening clinic had a suspicious lesion identified.[18] Only 0.9% of participants had malignant or premalignant lesions confirmed. The authors suggested that such screening programs should target patients with identifiable risk factors. Conversely, our study found 5.2% of participants had positive finding and 2.1% of them had malignant oral cavity cancer confirmed. The difference might be due to the dissimilar medical environments, as the accessibility of a medical center in the United States is generally poor when compared with that of Taiwan. There are approximately 20 medical centers in Taiwan and hence most of the population has access to a medical center.

A previous study on the demographic characteristics of participants who underwent oral screening found that lack of health insurance, tobacco use, male gender, separated marital status, and younger age were the significant predictors of a suspected malignant lesion.[18] However, another study found that those who evidenced abnormal findings were significantly older and smoked more packs of cigarettes per day than those participants who did not evidence abnormal findings.[19] As all our participants were covered by national health insurance, the difference between those with insurance and those without could not be investigated. However, we did find that older participants had higher rates of positive lesions identified when compared with that of younger participants. This might be because the peak age for oral cavity cancer in Taiwan is in the fifth decade.[2]

It was interesting to find that younger participants were less willing to undergo biopsy and the positive rate of malignant lesion in this age group was also lower when compared with that of elderly participants. In addition, those without the habit of habitual smoking, alcohol consumption, or betel quid chewing were more reluctant to receive oral biopsy, and the positive rate of malignant lesion in this group was also lower when compared with that of participants with the habit of habitual smoking, alcohol consumption, or betel quid chewing. One possible explanation might be that there are different levels of health awareness among various subgroups. In addition, if positive lesions were identified in those with the habit of habitual smoking, alcohol consumption, and betel quid chewing, physicians might strongly recommend that such participants undergo oral biopsy. The lower rate of malignant biopsy in the younger age group might be due to the fact that lesions were identified in the early stage of disease progression.[11] If we closely follow-up such participants, the identified lesions might turn out to be malignant after several years.

The statistical significance depends on both the effect size as well as the sample size. The unusually big sample size in this study may therefore result in some limitation in interpreting the statistical results. However, as the differences in cancer detection rates between the two groups (screening positive and negative groups) were huge, the effect size was therefore large enough and the power in the final statistic analysis was satisfactory. Although the positive predictive value was not high enough, it was acceptable. The reason is that the positive predictive value is not the only benchmark to evaluate the effectiveness of a test as it can be influenced by the prevalence of a disease. In addition, visual inspection is only a screening test. The definite diagnosis of oral cancer is based on the pathological result eventually.

There were certainly some limitations in this study. First, the external validity of the findings is limited because the study was conducted at a single institution. Selection bias inevitably exists when the study participants are recruited solely from a single medical center, and this might actually have had some effects on the possibly attenuated OR values associated with oral habits. In addition, we did not obtain information regarding quantities of consumption. Consequently, the dose–response relationship of these three risk factors for oral cancer cannot be demonstrated. Furthermore, the use of information from the National Cancer Registry within 6 months of screening as 'golden criteria' to evaluate the validity of the visual screening program might underestimate the actual situation. Lastly, we only recruited male participants. In future studies, it would be useful to compare these data with those obtained from female participants.

In conclusion, the oral screening program conducted in a tertiary medical center was effective. The sensitivity and specificity rates were both satisfactory. People aged ≥40 years or who were habitual cigarette smokers, alcohol consumers, and betel quid chewers had the highest risk of contracting oral cavity cancer. Therefore, we suggest that such individuals should receive oral screening regularly so that potential oral cancer can be detected as early as possible.

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