Original Research
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Active search screening for oral potentially malignant disorders and oral cancer in the city of Piracicaba

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Abstract: Oral cancer is a public health problem worldwide with approximately 300,000 new cases diagnosed every year and more than 170,000 deaths annually. Squamous cell carcinoma (SCC) accounts for approximately 90% of all oral malignancies and it is frequently preceded by lesions known as oral potentially malignant disorders (OPMDs). Screening programs for early detection of oral lesions have been conducted. Therefore, the objective of this research was to carry out an active search in a screening program in the city of Piracicaba, Brazil. High-risk patients were identified at the city's health center through their medical records and referred for dental consultation. Other patients who opportunistically sought dental care were also seen and if they did not present risk factors for SCC, they were considered low-risk. A total of 756 patients were examined, and 445 met the criteria for the high-risk group and 311 for the low-risk group. It was possible to diagnose 27 OPMDs and six SCCs – 21 OPMDs and six SCCs occurred in high-risk patients and six OPMDs in low-risk patients. A chi-square test was applied and a statistically significant value ($p = 0.006$) was obtained for the detection of OPMD and SCC in patients of the high-risk group. Screening of high-risk patients through active search proved to be an effective program for diagnosing OPMD and SCC. Therefore, we encourage its implementation on a large scale to reduce the current scenario of this disease.

Keywords: Mass Screening; Mouth Neoplasms; Precancerous Conditions; Squamous Cell Carcinoma of the Head and Neck; Leukoplakia, Oral.

Introduction

Lip and oral cavity cancers are considered a major public health problem, given their high incidence and mortality, and some authors consider these neoplasms the 18th most common type worldwide.[1,2] In 2018, these neoplasms were responsible for 354,864 new cases and 177,384 deaths worldwide.[2] It was estimated that, in 2020, 15,210 new cases would develop in the Brazilian territory, becoming the seventh most common neoplasms in the country.[3] It was also reported that these cancers caused 6,455 deaths in Brazil in 2018.[3]

Squamous cell carcinoma (SCC) represents approximately 90% of all lip and oral cavity malignancies and, in many cases, lesions known as oral potentially malignant disorders (OPMDs) precede SCC. This group of lesions is defined as "clinical presentations that carry a risk of cancer development in the oral cavity, whether in a clinically definable precursor lesion or in clinically normal mucosa."[4] It is well known that OPMD and SCC are most commonly associated with middle-aged patients with a history of chronic tobacco and/or alcohol consumption, as well as chronic sun exposure.[5-9] Frequently, SCC is diagnosed at late stages, which is associated with a poor prognosis for the patient when compared to cases diagnosed at early stages. A similar scenario is also seen in Brazil, where more than 50% of the cases are diagnosed at late stages.[10-13]

Wilson and Jungner[14] first described screening in 1968 as a public health program aimed at diagnosing malignant diseases at early stages. Since then, this method has been applied to several diseases, such as breast cancer and lip and oral cavity cancer.[14-21] Visual examination in screening programs has already been shown to have good sensitivity and specificity in detecting OPMD and SCC, regardless of the examiner's experience in diagnosing OPMD and SCC or of whether or not the examination is performed by a dental surgeon.[15-17] Speight et al.[18] have already reported that opportunistic screening for high-risk patients has shown to be cost-effective and that it could be even more effective if targeted at patients aged 40 to 60 years. Similarly, Lim et al.[17] and Monteiro et al.[20] suggested that screening for high-risk patients might be more efficient in detecting OPMD and SCC.

It has been previously reported by our group that, as in some developed countries such as the Netherlands, Spain, and the United Kingdom, malignant neoplasms are the most common cause of death in the city of Piracicaba.[23] Additionally, it was also reported that malignant lip and oral cavity neoplasms constituted the eighth most common cancer-related deaths in Piracicaba and that more than 50% of the patients were diagnosed at late stages.[23] Thus, Piracicaba seemed to be a good location for a screening program for the detection of OPMD and SCC.

Therefore, the aim of this study was to perform an active search in Piracicaba for the screening of patients at high risk for OPMD and SCC, in addition to assessing the efficiency of diagnosis of OPMD and SCC in these patients when compared to low-risk patients (patients of any age without risk factors).

Methodology

This was a cross-sectional, observational, comparative, non-randomized, open-label cohort study. The present research was carried out in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of Piracicaba Dental School.

This study was conducted at a secondary health care level using a mobile unit from a local hospital from May 2019 to February 2021. The mobile unit would drive through all neighborhoods of the city and a place of easy access for the local population was selected in each neighborhood so that people could take part in the screening program. Population recruitment was performed by two methods: active search and opportunistic screening.

Given that the main goal of screening was the early diagnosis of OPMD and SCC and the epidemiological profile of the patients,[5-9] the inclusion criteria for the high-risk group were age older than 40 years and a present or past history of chronic alcohol and/or tobacco consumption and/or chronic sun exposure. The exclusion criteria for the high-risk group were age less than 40 years and absence of tobacco and/or alcohol consumption and/or no chronic sun exposure (regardless of age).

In the active search, participants were invited by community health agents for a dental consultation on a previously designated location. The agents were instructed to invite only high-risk patients for consultation and to avoid the use of the word "cancer," which might scare the participants. Information on consumption of alcohol and tobacco, as well as age, was available through the medical records at the primary healthcare units, thus facilitating the

identification of high-risk patients by community health agents.

Opportunistic screening was performed on the same day and location as those of the screening by active search. Participants in this arm of the research had no scheduled appointment and spontaneously sought care at the mobile unit. The patients were also considered as high-risk if they met the inclusion criteria (tobacco and alcohol consumption). Otherwise, they were characterized as low-risk for further comparative analyses. All patients signed an informed consent form.

Screening was provided by two dental surgeons with a graduate degree in Oral Medicine and Pathology, experienced in the diagnosis of OPMD and SCC. Examination was performed at the mobile unit through oral visual examination using wooden spatulas for tissue retraction, and palpation. The mobile unit had a standard dental chair with an artificial white light source. Data on age, sex, skin color (self-reported), and history of consumption of tobacco and/or alcohol were collected by the examiners.

All patients with a suspicious lesion detected in the screening program were referred to a clinic specialized in Oral Medicine affiliated with the Piracicaba Dental School. All necessary clinical procedures were performed to confirm the diagnosis, including biopsy, if required. The time from biopsy to final diagnosis was one week. Variations of normal were not considered as disease.

All patient clinical data were coded and entered into a Microsoft Excel spreadsheet. Statistical analyses were carried out using IBM SPSS version 22.0 (IBM Corporation, New York, USA) with univariate analyses that included chi-square test and Fisher's exact test to assess the relationship between sociodemographic variables and the presence of OPMD and/or SCC. Variables with significant results in the univariate analyses were included in a multivariate analysis performed with a logistic regression model. A p value < 0.05 was considered statistically significant. Given that the aim of the screening programs was to detect OPMD and lip and oral cavity cancer, the two groups of diseases were clustered for statistical analyses. Sensitivity was calculated by dividing the number of true positives by the sum of true positives plus false negatives. Specificity was calculated by dividing the number of true negatives by the sum of false positives plus true negatives. Sensitivity and specificity were used to assess the efficacy of the current screening program in detecting OPMD/SCC.

Results

Figure summarizes the screening program according to its two arms and group of patients attended to (recall that active search included only high-risk patients); Table 1 shows the sociodemographic data per group of patients. The high-risk group had more male patients than females (1.2:1, male-female ratio), while low-risk group had more female patients than male ones (0.33:1, male to female ratio). Mean age was 57.03 years, ranging from 15 to 91 years. Most patients (n = 710) were older than 40 years.

Consumption of tobacco and/or alcohol was only reported by high-risk group patients. Most frequently, patients reported the history of consumption of both tobacco and alcohol (29.63%), followed by the consumption of tobacco only (23.02%) and alcohol only (6.22%).

From the 756 screened patients, 119 were referred for specialized consultation, among whom 91 were high-risk patients and 28 low-risk patients. Of those, slightly more than half (60.5%) showed up for consultation. Fifteen patients with suspicious lesions who missed their appointments were rescheduled for later dates. Despite the effort, none of them showed up for consultation. Most patients who missed their appointments were from the high-risk group (Table 2).

At the specialized clinic, 79 diseases were diagnosed. Actinic cheilitis (n = 13) was the most common disease, followed by leukoplakia (n = 12), frictional keratosis (n = 9), and SCC (n = 6). Table 3 shows the diagnosed diseases and their frequency and prevalence. In the present study, sensitivity and specificity were 96.67% and 97.67%, respectively.

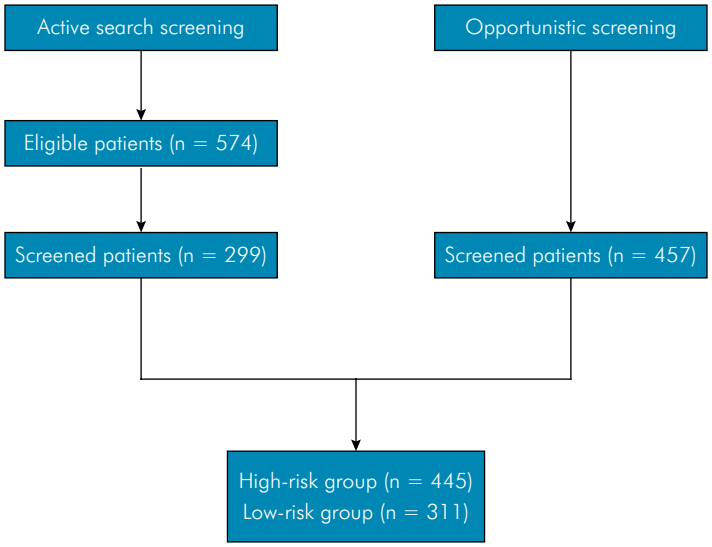

Figure. Profile of screening program arms, frequency of patients and group of patients.

Table 1. Sociodemographic data per group of patients screened in Piracicaba, Brazil, 2019–2021.

Variable	High-risk group		Low-risk group	
	(n)	(%)	(n)	(%)
Sex				
Male	243	32.14%	77	10.19%
Female	202	26.72%	234	30.95%
Age (years)				
> 40	445	58.86%	265	35.05%
< 40	0	00.00%	44	05.82%
Skin color				
White	242	32.01%	197	26.06%
Non-white	198	26.19%	107	14.15%
Smokers	174	23.02%	0	00.00%
Drinkers	47	06.22%	0	00.00%
Both	224	29.63%	0	00.00%
None	0	00.00%	311	41.14%

In this study, 21 OPMDs and six SCCs were diagnosed in high-risk patients, whilst only six OPMDs were diagnosed in low-risk patients. Thus, it was possible to observe a statistically significant association (p = 0.006) with a greater chance of diagnosing OPMD and/or SCC in high-risk patients (older than 40 years and with a history of alcohol and/or tobacco consumption) (Table 4).

Aiming to correlate sociodemographic data with the presence of OPMD and/or SCC, we observed that male patients (p = 0.001), white skin color (p = 0.002), and presence of both alcohol and tobacco consumption (p = 0.005) showed statistically significant differences. We also observed that patients older than 40 years (p = 0.251), who reported smoking only (p = 0.500) and alcohol consumption only (p = 0.142), did not show statistically significant differences (Table 4). The logistic regression model analyses, using OPMD and/or SCC as the dependent variable and sex, skin color, and consumption of both alcohol and tobacco as independent variables, showed that having white skin color (OR: 4.763, 95%CI: 1.800–12.604, p = 0.002) and being male (OR: 2.798, 95%CI: 1.230–6.361, p = 0.014) were significantly and independently related to the detection of OPMD and/or SCC (Table 5).

Discussion

To the best of our knowledge, the present study is one of the few in which the screening program

Table 2. Frequency of patient referral and provided care per groups, Piracicaba, Brazil, 2019–2021.

Variable	High-risk group		Low-risk group		Total	
	(n)	(%)	(n)	(%)	(n)	(%)
Referred	91	76.47	28	23.53	119	100
Attended	51	42.86	21	17.65	72	60.51

Table 3. Diseases diagnosed in the screening program, Piracicaba, Brazil, 2019–2021.

Disease	n	%	Prevalence (%)
Actinic cheilitis	13	16.45	01.71
Leukoplakia	12	15.18	01.58
Frictional keratosis	9	11.39	01.18
Squamous cell carcinoma	6	07.58	00.79
Fibrous hyperplasia	4	05.05	00.53
Traumatic ulcer	3	03.79	00.39
Oral erythematous candidiasis	3	03.79	00.39
Oral lichenoid reactions	3	03.79	00.39
Oral lichen planus	2	02.53	00.27
Inflammatory lymph node	2	02.53	00.27
Oral lymphoepithelial cyst	2	02.53	00.27
Amalgam tattoo	2	02.53	00.27
Palatal abscess	1	01.27	00.13
Epidermoid cyst	1	01.27	00.13
Atypical facial pain	1	01.27	00.13
Pyogenic granuloma	1	01.27	00.13
Hypercementosis	1	01.27	00.13
Inflammatory fibrous hyperplasia	1	01.27	00.13
Inflammatory papillary hyperplasia	1	01.27	00.13
Peripheral giant cell granuloma	1	01.27	00.13
Vascular lesion	1	01.27	00.13
Oral mucocele	1	01.27	00.13
Atypical odontalgia	1	01.27	00.13
Oral papilloma	1	01.27	00.13
Oral paracoccidioidomycosis	1	01.27	00.13
Necrotizing ulcerative periodontitis	1	01.27	00.13
Racial pigmentation	1	01.27	00.13
Sialolithiasis	1	01.27	00.13
Oral syphilis	1	01.27	00.13
Burning mouth syndrome	1	01.27	00.13
Total	79	100	10.38

Table 4. Comparison of the presence of OPMD and SCC with sociodemographic and group variables (univariate analysis).

Variables	Presence of OPMD and/or SCC – n (%)		p-value
	Yes	No	
Group			0.006
High-risk	27 (06.1)	418 (93.9)	
Low-risk	06 (1.9)	305 (98.1)	
Sex			0.001
Male	23 (07.2)	297 (92.8)	
Female	10 (02.3)	426 (97.7)	
Age years)			0.251
< 40	00 (00)	44 (100)	
> 40	33 (4.6)	677 (95.4)	
Skin color			0.002
White	28 (06.4)	411 (93.6)	
Non-white	05 (01.6)	300 (98.4)	
Smokers			0.500
Yes	06 (03.4)	168 (96.6)	
No	27 (04.6)	555 (95.4)	
Drinkers			0.142
Yes	04 (08.5)	43 (91.5)	
No	29 (04.1)	680 (95.9)	
Both			0.005
Yes	17 (07.6)	207 (92.4)	
No	16 (03.0)	516 (97.0)	

SCC: squamous cell carcinoma; OPMD: oral potentially malignant disorders.

Table 5. Comparison of the presence of OPMD and SCC with sociodemographic and group variables (multivariate analysis).

Variables	Exp (B)	95%CI		p-value
		Lower bound	Upper bound	
Sex	2.798	1.230	6.361	0.014
White	4.763	1.800	12.604	0.002
Both	2.027	0.941	4.367	0.071

OPMD: oral potentially malignant disorders; SCC: squamous cell carcinoma; CI: confidence interval.

focused on the detection of OPMD and lip and oral cavity cancer in high-risk patients, made by dental surgeons experienced in Oral Medicine and Pathology.

Screening for oral cancer and OPMD has already been shown to meet the criteria proposed by Wilson and Jungner.[14,16] Speight et al.[18] concluded that opportunistic screening could be cost-effective, which was later confirmed by Subramanian et al.[24] Moreover, Lim et al.[17] and Monteiro et al.[20] suggested that screening for high-risk patients could be more effective in detecting OPMD and SCC. Thus, this study aimed to conduct a screening program targeted at high-risk patients.

Two dental surgeons experienced in Oral Medicine and Pathology performed the examination through visual inspection and palpation, which has already been proven in several studies to be effective in detecting oral diseases, even if not performed by a professional with experience in oral diagnosis.[16,19,20,25] In this study, it was possible to observe a sensitivity of 96.67% and specificity of 97.67%. These data were similar to those of studies in which the examination was performed by dental surgeons without training or experience in the diagnosis of oral lesions,[15] by health professionals other than dental surgeons,[16] by experienced otolaryngologists and dental surgeons,[19] or by senior dental students.[20] Thus, we suggest that the screening should be performed by dental surgeons, regardless of experience in oral diagnosis, given the high sensitivity and specificity observed in the literature and in this current study.

Community health agents invited eligible patients for active search screening, which was performed in a mobile unity of a local hospital. From 574 patients with an appointment, only 299 (52.09%) showed up for consultation. Similarly, Downer et al.,[15] in a study in which the screening program was performed in the patient's workplace, reported that only 292 (52.8%) out of 553 eligible patients showed up for consultation. A lower compliance was observed in a study that was similar to ours. Andrade[1] reported that only 125 (15.62%) out of 800 eligible patients were seen. The highest attendance was reported by Sankaranarayanan et al.[25] in a study in which screening was performed in the patients' households, and out of 96,517 eligible participants, only 7.695 (7.97%) were not screened. These data suggest that a larger number of patients can be seen if screening programs are conducted in patients' households. Given that this might not be the easiest way to perform screening, we believe, just like Tomo et al.,[21] that a higher compliance could be observed if information on the benefits of the early diagnosis of lip and oral cavity cancer is provided. This fact can be observed in screening programs for breast cancer, a well-known disease by the lay population, which show a high compliance rate.[22]

In the present study, 119 patients were referred for specialized Oral Medicine and Pathology care. From these, 71 (60.17%) showed up for the consultation. In addition, 15 patients (12.60%) with suspicious lesions who missed the first appointment were recalled. However, they did not show up for consultation. Our data were similar to those reported by Sankaranarayanan et al.,[25] in which patient compliance was 58.88%, but compliance rates were lower than those reported by Monteiro et al.,[20] Andrade,[1] and Tomo et al.[21] in which the rates were as high as 96%, 81.25%, and 78.26%, respectively. Furthermore, Monteiro et al.[20] reported that patients attending to his screening program were "health literate," which explains the high compliance. It is known that patient awareness about oral cancer is low, showing poor knowledge of its signs, symptoms, and risk factors.[26] It is also known that current cancer awareness campaigns are limited and should focus on primary prevention.[27] Thus, this reinforces that improving awareness of the importance of early diagnosis of OPMD and SCC may increase patient compliance.

In the current study, the prevalence of oral lesions was 10.38% and that of OPMD and SCC was 04.34%, which is in accordance with other studies.[17,19-21] If we consider only high-risk patients, the prevalence of OPMD and SCC rises to 6.07%, which is slightly higher than what has been observed in previous studies.[17,19-21] Chang et al.[19] reported a prevalence of positive lesions of 5.20%, but the high prevalence might be because their study was performed at a tertiary health care academic medical center, thus

showing a higher chance of diagnosing positive lesions, given that patients at a hospital are more likely to have a disease. Meanwhile, other studies have shown prevalence rates of 1.18% to 4.15% for OPMD and SCC.[18,20,21] In another study, with methodology similar to ours, in which only high-risk patients were screened, Andrade[1] reported a prevalence of 3.20% for OPMD and SCC. Thus, we believe that screening programs focusing on high-risk patients will most likely show a prevalence of OPMD and SCC ranging from 03.20% to 06.07%. Additionally, in the current study, we had six diagnosed cases of SCC, showing a prevalence of 0.79%, but if only high-risk patients are included, this prevalence rises to 1.35%, which is considerably higher than what has been observed in the literature (0.10% to 0.29%).[17,20,21,25] In the study performed by Chang et al.,[19] the prevalence was 2.03%, but the high prevalence might be because of the place where the screening was performed. These data reinforce the need for screening programs similar to ours (focusing on high-risk patients) to be implemented on a large scale across the globe, given the high prevalence of diagnosed potentially malignant or malignant diseases.

It is well known that OPMD and SCC have a strong association with male sex, older patients, and presence of risk factors such as alcohol or tobacco consumption.[8,28-33] In the present study, we also found statistically significant more cases among male patients (p = 0.001), in patients who reported consumption of both alcohol and tobacco (p = 0.005), and in white patients (p = 0.002). In the logistic regression analysis, male sex (p=0.014) and white skin color (p=0.002) showed a significant and independent association with the presence of OPMD or SCC. However, it is important to emphasize that white skin color probably proved to be statistically significant because of the high prevalence of actinic cheilitis, a disease that is most frequently observed in these patients.[34-39] Lim et al.[17] found that male sex, heavy smoking, and heavy drinking in males showed a significant relation. Chang et al.[19] showed an independent value for patients older than 40 years or who were habitual cigarette smokers, alcohol consumers, and betel quid chewers. Monteiro et al.[20] reported that age older than 54 years was an independent and significant factor associated with the presence of a positive lesion. These findings suggest that performing screening programs focused on high-risk patients may be more effective in diagnosing OPMD and SCC when compared to low-risk patients.

In regard to what has been previously suggested in the literature, the main purpose of this study was to assess if screening of high-risk patients was more effective in diagnosing OPMD and SCC when compared to low-risk patients. Thus, from 445 high-risk patients, 21 OPMDs and six SCCs were diagnosed, whilst only six OPMDs were diagnosed in 311 low-risk patients. A statistically significant value (p= 0.006) for a greater chance of diagnosing OPMD and/or SCC was observed in patients older than 40 years with a history of alcohol and/or tobacco consumption. These data are of utmost importance, given that they confirm what has been previously speculated in the literature – that diagnosing this group of diseases in high-risk patients is more effective.[17,19,20] In addition to corroborating the reduction in mortality after the screening of high-risk patients, as pointed out by Sankaranarayanan et al.,[25] our findings are of paramount importance to improve the current scenario of OPMD and lip and oral cancer.

Conclusion

In conclusion, the present study has shown the importance of performing screening programs aimed at the early diagnosis of OPMD and SCC, focusing especially on the active search for patients older than 40 years with a history of tobacco and/or alcohol consumption (high-risk patients), because of a statistically significant higher chance of diagnosing these diseases in this group of patients. Thus, we encourage the implementation of such a screening program on a large scale to reduce the current scenario of this disease. However, one of the main problems of this study was the low attendance of patients, in particular of high-risk group, to the mobile unity, as well as for referral at a specialized clinic. Given so, we suggest that better awareness of the lay public may improve attendance at screening programs.

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