

Retrospective evaluation of risk factors for oral cavity and oropharynx cancers in patients under the program of head and neck cancers prevention

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Article history: Received: 26.04.2019 Accepted: 06.05.2019 Published: 22.05.2019

ABSTRACT:

Introduction: The aim of the study was to analyze the risk factors for oral cavity and pharyngeal cancer in people examined under the Head and Neck Cancer Prophylaxis Program.

Material and methods: The study was conducted in a total of 300 patients, including 186 women and 114 men, as part of the Head and Neck Cancer Prevention Program in 2014–2018. Before the laryngological examination, the patients completed a demographic and medical questionnaire regarding the risk factors of head and neck cancer, including education, reported disease symptoms, smoking addiction, number of cigarettes smoked daily, alcohol consumption, frequency of visits in a dental office, oral hygiene measures, number of sexual partners, oral sex, family medical history of head and neck cancer.

Results: The subjects reported the following symptoms: hoarseness 43.33%, difficulty swallowing 21.33%, pain or mouth burning 20.33% and other symptoms were observed in 46.33%. The main dental symptoms were: bleeding from the gums during teeth brushing in 48.89%, dry mouth 45.56%. Currently 20.33% of respondents smoke, whereas 54% of patients smoked in the past. In the analyzed material, the majority (80%) consumed alcoholic beverages. 27.67% of respondents admitted having oral sex, including 24.73% of women and 32.46% of men. After performing the extended diagnostics, the tumor was found in 10% of the subjects.

Conclusions: Statistical significance of differences was found: between hoarseness and alcohol consumption, both in women and in men, between hoarseness and smoking in women, between difficulty in swallowing and smoking in women, between burning/pain in the mouth and smoking in men, between hoarseness and the cultivation of oral sex in men, between the difficulty of swallowing and the practice of oral sex in the studied men and between burning/pain in the oral cavity and the occurrence of malignancy.

KEYWORDS:

Head and Neck Cancer Prophylaxis Program, oral cavity, oropharynx cancer, risk factors

INTRODUCTION

Head and neck cancers (H&NC) constitute a group of neoplasms located in the head and neck area (excluding the brain and the orbit). They are the sixth most frequent type of malignant tumor in Poland. There are twice as many patients with these types of tumor than patients with cervical cancer. According to the epidemiological data by GLOBOCAN 2012 (Cancer Incidence Mortality Prevalence Worldwide), only in 2012 head and neck cancers were diagnosed in almost 11000 people. In the same year nearly 6000 patients died due to the disease – about twice the mortality of motor vehicle accidents. Moreover, the incidence increased by 20% over the past 20 years [1]. According to the 2010 National Cancer Registry, oral cancers constitute 26 of all registered head and neck malignancies in Poland. They are more common in men

than women (M:K = 3.1:1.0), mainly due to more frequent occurrence of nicotine and alcohol addiction.

In the majority of cases malignancies of the lip, oral cavity and pharynx (89% in men and 87% in women) are diagnosed after the age of 50. The risk of diagnosis increases with age, reaching peak incidence in the seventh decade of life for males (about 50/105), while in women it stabilizes (12–16/105) beginning from the seventh decade of life.

In males, mortality due to malignant cancers of the lip, oral cavity and pharynx increased from mid-60's to mid-90's. Subsequently, mortality stabilized at about 6/105. In female population mortality indexes remained at a stable, low level (about 1/105) over the entire period.

Over 60% of patients have advanced disease at the time of diagnosis and 60% of that group dies within 5 years. Clinical studies indicate that if extended diagnostics of H&N cancer is performed at an early stage, survival rate increases to as much as 80–90% [1]. While posing significant threat to patient's life, head and neck cancers also lead to loss of speech, disorders of communication, sensory deficits, face deformation and, consequently, sense of estrangement, social alienation and significant life hardships.

Risk factors for oral and middle pharyngeal cancers include: nicotine/marihuana smoking, abuse of hard alcohols (men: 3 or more units of alcohol per day; women: 2 units), high-risk HPV infection, neglecting oral cavity and pharyngeal hygiene. At the same time it should be emphasized, that there is an increase in the number of newly diagnosed cases among men below the age of 40 years without a history of smoking or alcohol abuse [2–4]. The goal of this study is to retrospectively analyze the risk factors for oral cavity and pharyngeal cancers among patients examined in head and neck cancer prophylaxis program.

MATERIAL AND METHODS

A total of 300 patients, including 186 women (62%) and 114 men (38%) participated in the study. Before ENT examination patients filled out demographic and medical questionnaires regarding risk factors for head and neck cancers that contained information such as: education, symptoms, nicotine addiction, number of cigarettes, alcohol abuse, frequency of dental examinations, types of preparations used for oral cavity hygiene, number of lifetime sexual partners, involvement in oral sex, number of lifetime sexual partners with whom one was involved in oral sex, family history of head and neck cancers. Analysis of risk factors for oropharyngeal cancers among patients reporting to the Clinic for head and neck cancer prophylaxis program over the years 2014–2018 included:

- prevalence of individual risk factors for oropharyngeal tumors (smoking, alcohol abuse, risky sexual behaviors, vocational exposure to harmful substances) among patients depending on sex and age,
- clinical assessment of subjective symptoms reported by patients,
- correlation between symptoms reported by patients and results of ENT examination.

The obtained data were subject to statistical analysis using Chi2 test of independence. Results were considered statistically significant when the level of significance was less than 5 percentage points ($P < 0.05$). Study protocol was approved by the Biomedical Committee at the Medical University of Lodz (no. RNN/367/18/KE) on November 13, 2018.

RESULTS

Fig. 1. shows distribution of patient population depending on age range and sex. Study included patients in the following age ranges: up to 35 years – 36 subjects (12%), including 23 women (12.37%)

and 13 men (11.40%), 36–45 years – 52 subjects (17.33%) including 39 women (20.97%) and 13 men (11.40%), 46–55 years – 61 subjects (20.33%), including 55 women (29.57) and 33 men (28.95%), and over 65 years – 63 people (21%), 28 women and 35 men (30.70%). Statistically significant differences were noted between age range and sex of the studied subjects ($P = 0.003$) (Fig. 1.).

Forty-five of 300 subjects, including 24 women (12.9%) and 21 men (18.42%), had primary education (15%). One hundred and thirty-seven patients (45.67%), including 88 women (47.31%) and 49 men (42.98%) completed high school and 118 (39.33%) study participants, including 74 women (39.78%) and 44 men (38.6%) obtained higher education.

Ninety-six subjects (53.33%), including 63 women (59.43%) and 33 men (44.59%) performed intellectual work, while 33 respondents (18.33%) – 17 women (16.04%) and 16 men (21.62%) engaged in physical vocation. Fifty-one patients (28.33%), 26 women (24.65%) and 25 men (33.78%) declared mixed type of work.

Fig. 2. shows that participants reported the following symptoms: hoarseness in 130 cases (43.33%), including 81 women (43.55%) and 49 men (42.98%), difficulty swallowing in 64 cases (21.33%) – 43 women (23.12%) and 21 men (18.42%), respectively, pain/burning sensation in the oral cavity in 61 cases (20.33%) – 43 women (23.12%) and 18 men (15.79%). Other symptoms were observed in 139 subjects (46.33%) – 86 women (46.24%) and 53 men (46.49%), respectively. Three study participants (one woman and two men) reported no symptoms (Fig. 2.).

Seventy-seven subjects (42.78%), 49 women (46.23%) and 28 men (37.84%) reported at a dental clinic every six months. Seventy-four subjects (41.11%) – 46 women (43.4%) and 28 men (37.84%) visited dental office once a year. Twenty-nine participants (16.11%), including 11 women (10.38%) and 18 men (24.32%) visited a dentist with lesser frequency. Participating females reported to oral examination or treatment significantly more often (Fig. 3.).

According to the analyzed questionnaire 22 (12.22%) subjects, including 9 women (8.49%) and 13 men (17.57%), brushed their teeth once a day. As many as 118 study participants (65.56%) – 66 women (62.26%) and 52 men (70.27%), respectively, brushed their teeth twice a day. On the other hand, 40 subjects (22.22%) – 31 women (29.25%) and 9 men (12.16%), brushed their teeth three times a day or more. Described differences were statistically significant ($P = 0.011$). Females participating in the study brushed their teeth during the day significantly more often (Fig. 4.).

As shown in Fig. 5., 110 patients (61.11%), including 70 women (66.04%) and 40 men (54.05%), used oral rinses. Ninety-two subjects (51.11%), respectively – 61 women (57.55%) and 31 men (41.89%) used dental floss. Twenty-nine participants (16.11%), 13 women (12.26%) and 16 men (21.62%) used an interdental brush, 4 subjects (2.22%), including one woman (0.94%) and 3 men (4.05%) applied water irrigation. Eighteen participants (10%), 10 women (9.43%) and 8 men (10.81%), respectively, did not use any of the above-mentioned dental hygiene products (Fig. 5.). Bleeding from gums while brushing teeth occurred in 88 study participants (48.89%)

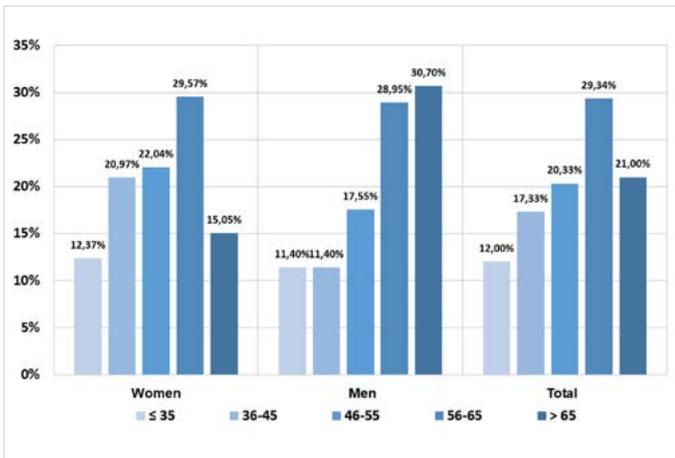


Fig. 1. Patient distribution depending on age and sex ($P = 0.003$).

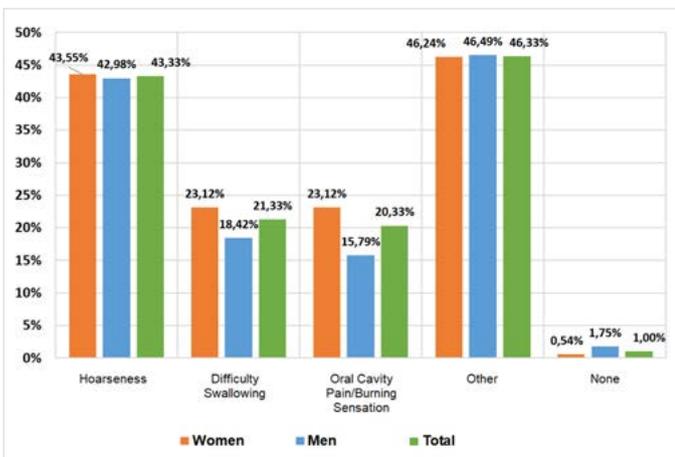


Fig. 2. Patient distribution depending on reported oropharyngeal symptoms and sex.



Fig. 3. Patient distribution depending on frequency of dental visits and sex ($P < 0.05$).

– 58 women (54.72%) and 30 men (40.54%). Eighty-two subjects (45.56%), 54 women (50.94%) and 28 men (37.84%), respectively, complained of oral cavity dryness. Unpleasant smell from the oral cavity was reported by 59 respondents (32.78%), including 36 women (33.96%) and 23 men (31.08%). Increased mobility of the teeth

concerned 14 subjects (7.78%) – 10 women (9.43%) and 4 men (5.41%). Significant gum edema was noted in 11 study participants (6.11%), 8 women (7.55%) and 3 men (4.05%). Spontaneous bleeding occurred in 8 patients (4.44%), including one woman (0.94%) and 7 men (9.46%). No such symptoms were noted in 35 subjects (19.44%), significantly less often women than men ($P = 0.011$), i.e. 14 (13.21%) and 21 (28.38%), respectively, as presented in Fig. 6.

Teeth prostheses were used by 56 studied subjects (31.11%), including 32 women (30.19%) and 24 men (32.43%). There were statistically significant differences between sexes in relation to the duration of prosthesis use (0.005).

Sixty-one study participants (20.33%), 39 women (20.97%) and 22 men (19.3%) admitted to smoking tobacco products.

One hundred and sixty-two subjects (54%) had a history of smoking, women significantly less often than men, i.e. 92 (49.46%) vs. 70 (61.4%), respectively ($P = 0.044$). Number of cigarettes smoked per day (Fig. 7.) ranged from 1 to 5 in 17 cases (10.49%), including 12 women (13.04%) and 5 men (7.14%); from 6 to 10 in 55 cases (33.95%), including 43 women (46.74%) and 12 men (17.14%); from 11 to 15 cases in 34 cases (20.99%), including 18 women (19.57%) and 16 men (22.86%); 16 or more in 56 cases (34.57%), 19 women (20.65%) and 37 men (52.86%). Described differences were highly statistically significant ($P < 0.001$). Examined men smoked significantly more cigarettes per day than women (Fig. 7.).

Forty-four respondents (24.44%), including 26 women (24.53%) and 18 men (24.32%), were exposed to passive smoking.

Two hundred and forty subjects (80%) consumed alcoholic beverages (Fig. 8.), women significantly less often than men, i.e. 140 (75.27%) vs. 100 (87.72%), respectively ($P = 0.009$).

Frequency of alcohol consumption among study participants was as follows: 3 subjects drank every day (1.25%) and only 3 of 100 men (3%); 13 subjects (5.42%) consumed alcohol 3–4 times per week and only 13 men (13%); 15 subjects (6.25%), including 4 women (2.86%) and 11 men (11%) drank 1–2 times per week; 209 respondents (87.08%), 136 women (97.14%) and 73 men (73%) declared occasional alcohol consumption. Described disproportions are highly statistically significant ($P < 0.001$). Weekly consumption of alcohol among examined women was significantly reduced compared to men.

The number of previous sexual partners was not significantly different between the sexes. Of all sexually active participants (three women have never had a sexual intercourse before), 240 (80.81%) – 154 women (84.15%) and 86 men (75.44%) had one to two partners. Forty subjects (13.47%), including 23 women (12.57%) and 17 men (14.91%), had between three and seven sexual partners. More than seven sexual partners were reported by 17 study subjects (5.72%), 6 women (3.28%) and 11 men (9.65%), respectively.

Eighty-three participants (27.67%), 46 women (24.73%) and 37 men (32.46%) admitted to engaging in oral sex. Fifty-nine subjects (71.95%) – 34 women (77.27%) and 25 men (65.79%), have

met one to three partners who engaged in oral sex. Eighteen subjects (21.95%), including 9 women (20.46%) and 9 men (23.68%) admitted to three to seven sexual partners. More than seven sexual partners were reported by 5 subjects (6.1%) – one woman (2.27%) and 4 men (10.53%).

In 171 study participants (57%), including 116 women (62.37%) and 55 men (48.25%) there was a family history of malignant tumors. Examined females reported malignancy in their family members more often than men ($P = 0.016$). Head and neck cancer was diagnosed in relatives of 58 study subjects (19.33%) – 42 women (22.58%) and 16 men (14.04%).

Thirty-three subjects (11%), including 20 women (10.75%) and 13 men (11.4%), had a history of cancer. Posterior pharyngeal wall lesions were observed in 152 subjects (50.67%), including atrophic changes in 70 patients (23.33%), erythematous mucosa in 48 patients (16%) and discharge in 34 patients (11.33%).

Nasal cavity abnormalities were noted in 109 examined subjects (36.33%), including: nasal septum deviation in 66 patients (22%), atrophy and bleeding in 30 persons (10%), and hypertrophy of nasal conchae in 13 patients (4.33%).

Pathologies of the pharynx were identified in 103 examined subjects (34.33%), such as: inflammation, GERD in 18 patients (6%), tumor in 9 patients (3%), Reincke's edema in 9 individuals (3%), and facial nerve palsy in 4 patients (1.33%).

Pathological lesions involving the tonsils were observed in 96 subjects (32%), including: atrophy in 39 patients (13%), inflammation in 25 patients (8.33%), hypertrophy in 15 subjects (5%), tumor in 3 patients (1%), and ulceration in one patient (0.33%).

Head and neck tumors were diagnosed in 17 study participants (5.67%). In 15 subjects (5%) lesions were present at the floor of the oral cavity, including: ulceration in 11 patients (3.66%) and inflammation in 4 subjects (1.33%).

In 9 examined subjects (3%) pathological changes were noted on the tongue, including inflammation in 4 patients (1.33%), tumor in 3 patients (1%), and ulceration in 2 patients (0.66%).

Eight subjects (2.67%), 4 women (2.15%) and 4 men (3.51%) had a history of head and neck tumors.

In the group of participants of the Head and Neck Cancer Prophylaxis Program, extensive diagnostics revealed a tumor of this area in 10% of cases.

DISCUSSION

Retrospective analysis demonstrated that people between 46 and 56 years and those above 60 years of age, i.e. the age groups where there risk of oral and midpharyngeal cancer is particularly high, reported to the prophylactic program most often (49.66% and 21%, respectively).

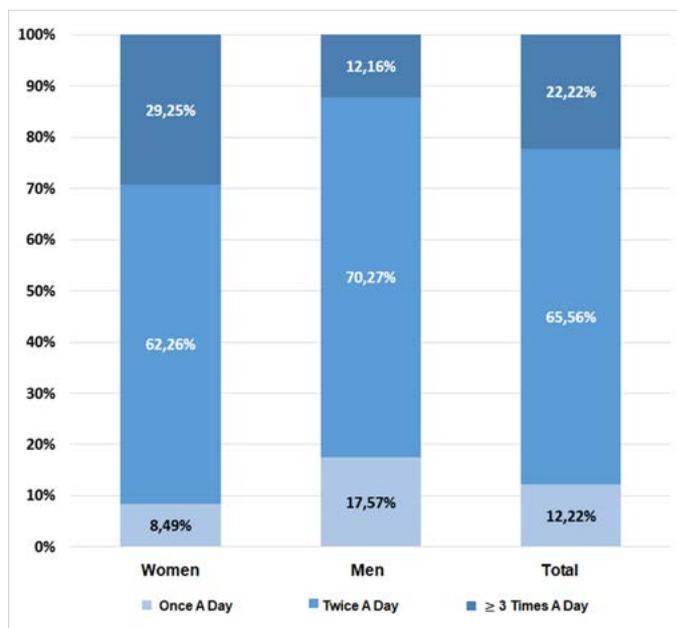


Fig. 4. Patient distribution depending on frequency of brushing teeth and sex ($P < 0.011$).

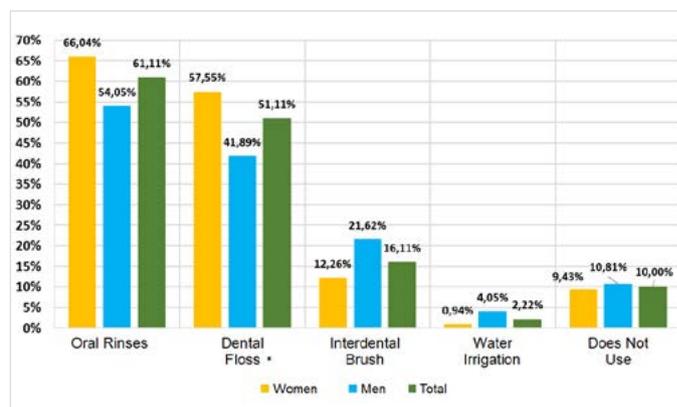


Fig. 5. Patient distribution depending on the type of used dental hygiene products and sex.

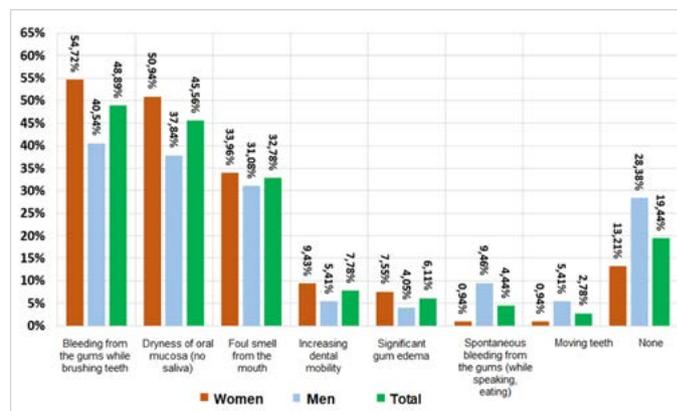


Fig. 6. Patient distribution depending on reported symptoms and sex ($P = 0.011$).

The group of so-called young people, which included individuals below 35 years and between 36 and 45 years of age, constituted 12% and 17.33%, respectively. In our study 20.97% of women and 19.3% of men admitted to nicotine addiction, while 54% of patients had a history of smoking and the number of cigarettes smoked

per day ranged from 16 or more in 34.57% of subjects and from 6 to 10 in 33.95% of individuals. Men smoked more cigarettes per day than women.

The majority of subjects, as much as 80%, in the analyzed material consumed alcoholic beverages. Women drank alcohol significantly less often than men and 87.08% of subjects consumed alcohol occasionally.

Alcohol and smoking increase the risk of head and neck tumors about 330-fold [2]. Smoking tobacco has greater impact on the development of laryngeal than oropharyngeal cancer, while alcohol consumption is more strongly correlated with oropharyngeal rather than laryngeal cancers. A statistically significant difference between hoarseness and alcohol consumption was noted for both women ($P = 0.007$) and men ($P = 0.032$).

Moreover, statistical significance was found with regard to the differences between: hoarseness and smoking in women ($P = 0.042$), between difficulty swallowing and smoking in women ($P = 0.049$), between oral cavity pain/burning sensation and smoking in men ($P = 0.049$). There was a statistical significance with regard to differences: between oral cavity pain/burning sensation and cancer in the examined women ($P = 0.018$) and men ($P = 0.025$). There was also statistical significance with regard to differences: between hoarseness and engaging in oral sex in men ($P = 0.020$), between difficulty swallowing and engaging in oral sex in men ($P = 0.036$).

In Poland, as in other European countries, a new phenomenon is observed, known as the “epidemiological phenomenon”, i.e. an increase in the number of new cases of head and neck cancer in people under 40 who have never smoked or abused alcohol. Studies indicate that human papillomavirus infection is the potential risk factor in this group. The second virus involved in the development of head and neck cancer is the Epstein-Barr virus, which is identified in 70–90% of patients with nasopharyngeal tumors [5–10].

A diet low in vegetables, fruit and vitamins is also a risk factor. Studies focus on the analysis of micro- and macroelements contained in food and their potential protective effect against the development of head and neck cancers. Such molecules as antioxidants are important for elimination of free radicals, which are responsible for DNA damage, changes in enzymatic activity or peroxidation of cell lipid membranes. The rule is that the less processed the food, the healthier and safer the food is for the body [11–12].

Improper oral hygiene, mechanical irritation of mucus membranes (prostheses), chronic fungal infections, immunodeficiencies or UV radiation (UVB in particular) contribute to development of gingival tumors. Also, one should not forget about occupational risk associated with exposure to nickel or chrome motherlode or exposure of woodworkers to inhalation of wood particles, who are at increased risk of development of maxillary sinus adenomas [13].

In the analyzed material, study participants usually reported dental visits once per six months (42.78%) or once a year (41.11%) – women significantly more often visited dentist’s office than men. Teeth were most often brushed twice a day – by 65.56% of sub-

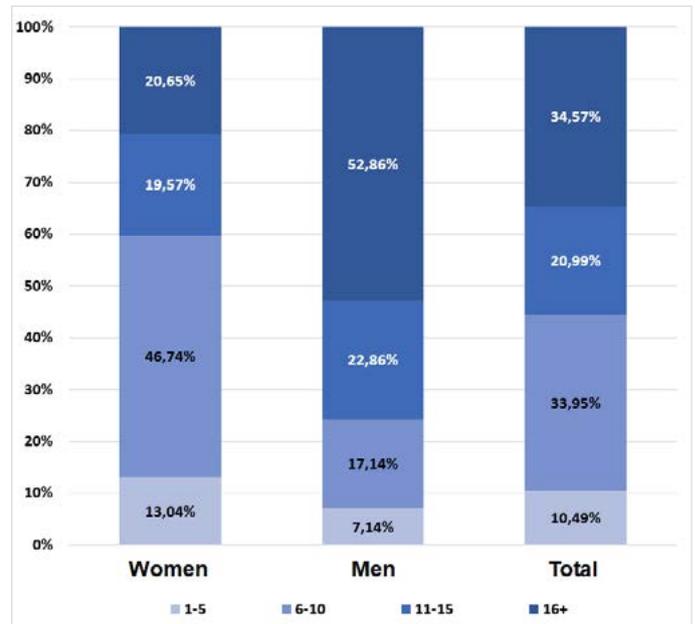


Fig. 7. Patient distribution depending on the number of smoked cigarettes and sex ($P = 0.001$).

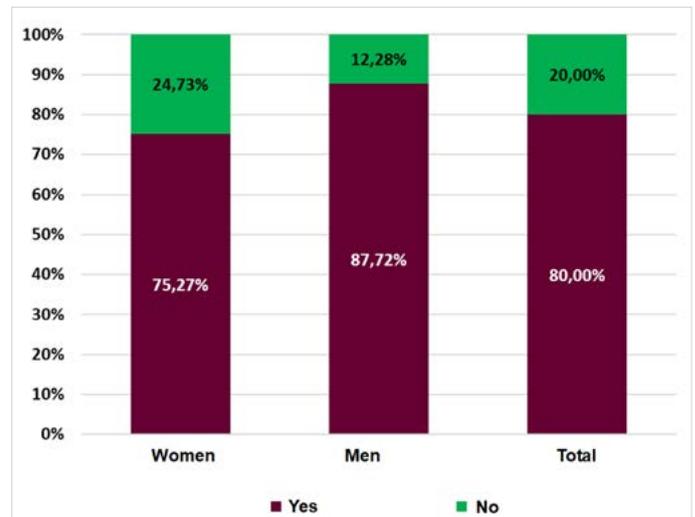


Fig. 8. Patient distribution depending on alcohol consumption and sex ($P = 0.009$).

jects, while oral rinses were used by 61.11% of subjects. The main dental symptoms included: gingival bleeding while brushing teeth in 48.89% of subjects and sensation of dryness in the oral cavity reported by 45.56% participants. It should be emphasized that no unified approach to prophylactic screening for HPV infection encompassing sexual organs or the oral cavity has been established to date [13].

Herrero et al. points to positive effects of vaccinating young women as a prophylaxis of HPV-dependent oropharyngeal tumors [14]. Genetic predisposition also plays a certain role as a risk factor for head and neck tumors. Genome damage is one of the most important risk factors for tumor development. It may lead to formation of abnormal proteins involved in cell cycle regulation and affect signal transduction, growth, mobility, or angiogenesis. Genetic mutations and chromosomal aberrations are the cause of cellular dysfunction

at many levels: they are responsible for abnormal growth, disrupted function of signaling molecules; regulation of cell cycle is disrupted. It may lead to gradual formation of neoplastic cellular phenotype. In our study we found that malignancy was present in the relatives of 57% of subjects, including 62.37% of women and 48.25% of men. Examined women significantly more often reported a family history of malignancy than men ($P = 0.016$). Head and neck cancer was diagnosed in relatives of 19.33% of study participants, including 22.58% of women and 14.04% of men. The 3rd, 4th and 5th Head and Neck Cancer Prevention Program Activity Weeks conducted in Lodz demonstrated growing social interest in prophylactic programs, especially cancer prophylaxis; thus, indicating the need for its continuation [1, 15]. Individuals at high risk of oral and mid-pharyngeal cancer should undergo a test for the presence of HPV.

CONCLUSIONS

1. Individuals screened in the Head and Neck Cancer Prophylaxis Program reported the following symptoms; hoarseness in 43.33%, difficulty swallowing in 21.33%, oral cavity pain or burning sensation in 20.33%; other symptoms were observed in 46.33% of subjects.
2. Most respondents reported to dental visits once per six months – 42.78%, once a year - 41.11% of subjects; women significantly more often underwent dental examination or treatment. The majority of subjects – 65.56%, brushed their teeth twice a day and as much as 61.11% of respondents used oral rinses.
3. The main dental symptoms were gingival bleeding while brushing teeth in 48.89% and sensation of dryness in the oral cavity in 45.56%.
4. Among respondents, 20.33% admitted to smoking nicotine products, while 54% had a history of smoking. The number of cigarettes smoked per day reached 16 or more in 34.57% of subjects and 6-10 in 33.95%, men smoking significantly more cigarettes per day than women.
5. In the analyzed material the majority of study participants – as much as 80%, admitted to alcohol consumption; women drank alcohol significantly less often than men and 87.08% of subjects reported occasional alcohol consumption.
6. In our study group, 27.67% of subjects admitted to engaging in oral sex, including 24.73% of women and 32.46% of men; 71.95% of subjects knew one to three partners who had oral sex.
7. Among study participants laryngological examination revealed inflammatory lesions within the larynx in 34.33%, palatal tonsils in 32%, the neck in 5.67%, at the floor of the mouth in 5%, on the tongue in 3% of subjects.
8. Among the subjects participating in the Head and Neck Cancer Prophylaxis Program 10% were diagnosed with a tumor in this area.
9. There was a statistical significance with regard to the following differences: between hoarseness and alcohol consumption in both men and women, between hoarseness and smoking in women, between difficulty swallowing and smoking in women, between pain/burning sensation in the oral cavity and smoking in men, between hoarseness and engaging in oral sex in examined men, and between pain/burning sensation in the oral cavity and occurrence of malignancy in both men and women.

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Word count: 4080 Tables: – Figures: 8 References: 15

Access the article online: DOI: 10.5604/01.3001.0013.1925 Table of content: <https://otolaryngologypl.com/resources/html/articlesList?issuelid=12453>

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Competing interests: The authors declare that they have no competing interests.

Cite this article as: Kowalski A., Olszewski J., Zielińska-Bliźniewska H.: Retrospective evaluation of risk factors for oral cavity and oropharynx cancers in patients under the program of head and neck cancers prevention; *Otolaryngol Pol* 2019; 73 (6): 24-31
