ORIGINAL ARTICLE

Different influences of risk factors on the development of head and neck tumors and other oncological diagnoses

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Summary

We focused on the research of risk factors for head and neck cancer (HNC) and the aim of our study was to confirm the influence of known external risk factors (alcohol and smoking) and further correlate the overall clinical and socio-economic status of the patient with HNC. In contrast to previous studies, we confirmed the results of the study with a control group of patients with other heterogeneous oncological diagnoses (HOD).

A non-standardized questionnaire focusing on socio-economic and behavioral risk factors was developed. We used a visual analogue scale (VAS from 0 to 10 cm) to measure the quality of life and clinical data were obtained retrospectively from medical records and from the UNIS database of the hospital system. According to the results of our study, we found significant differences in risk factors for HNC and HOD. In addition to lifestyle risks, we find statistically significant differences in socio-economic aspects and in family and social background.

The results and analysis of our study successfully met the proposed goals. The significant influence of smoking and alcohol on the development of HNC was confirmed and in connection with this a direct correlation between the influence of risky behavior, lower socioeconomic status, poor family and socioeconomic background and clinical factors on the development of head and neck cancer was demonstrated. The study showed a different etiology of HNC and HOD with respect to socioeconomic status.

Key words: head and neck cancer, oncology, quality of life, risk factors, socioeconomic status

Introduction

The global incidence of malignant diseases continues to increase [1], but mortality and prognosis have been improving due to better options in diagnosis and therapy.

However, mortality and prognosis have not improved significantly in the last three decades [1] for head and neck cancer (HNC). Nearly 650,000 new cases are diagnosed worldwide and nearly 300,000 patients die from the lethal disease every year [2]. The incidence of these tumors is highly variable and largely dependent on exposure to external risk factors. Patients with head and neck cancer largely consist of those who smoke and drink heavily and more than 60% of these patients come to a doctor with advanced disease stage [3]. Human papillomavirus (HPV) infection is another significant risk factor for tumors in this anatomical region. The treatment of advanced stages of head and neck cancer is very demanding and often so mutilating that it has serious consequences and patients are often unable to return to their original way of life [3].

Alcohol and smoking are still the main risk factors and the most common causes of death for/

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from this cancer in the developed world, although their side effects are well-known. This lethal disease is up to 85% caused by the risk factors and can be prevented by lifestyle changes (cessation of smoking dependence and alcohol consumption) and treatment of premalignant lesions (leukoplakia and erythroplasia), unlike other oncological diagnoses [4].

In the past, many studies have been proposed on the etiology of head and neck cancer and on their basis a large number of prevention campaigns and screening programs have been initiated [5]. However, current research calls into question the validity of these initiatives and the effectiveness of prevention and screening campaigns are still in question. A possible reason for these controversies may be that educational programs do not have sufficient evidence to justify them and individuals who are assessed during these studies may not represent a real risk group suitable for screening.

Most of these studies have repeatedly looked at the same research on already-known risk factors and the context of other potential risks or control groups has not been used. In the context of these facts, we focused on the research of risk factors for HNC and the aim of our study was to confirm the influence of known external risk factors (alcohol and smoking) and further correlate the overall clinical and socio-economic status of the patient with HNC [6]. In contrast to previous studies, we confirmed the results of the study with a control group of patients with other heterogeneous oncological diagnoses (HOD).

Methods

Participants and procedures

This was a retrospective analytical study of cases and controls, where risk factors of tumors in the head and neck were detected in comparison with other oncological diseases from the point of view of socio-demographic and socio-economic, behavioral and clinical aspects.

The research was carried out by the Radiotherapy and Oncology Clinic of the Third Faculty of Medicine of Charles University and the Faculty Hospital in Prague. From December 2015 to March 2019, hospitalized patients and outpatients were continuously approached to participate in the research.

Criteria for participation in the study were: cancer diagnosis, age > 18, willingness and physical ability to collaborate and interviewing ability. All patients signed a written informed consent to participate in the study, which was approved by the Ethics committee of the University Hospital Královské Vinohrady. (Approved on December 2, 2015, in Prague and number for the approval is *EK-VP-62-0-2015*).

Exclusion criteria for patients were: severe neurodegenerative diseases, patients with brain tumors, patients in the final stage of disease, and patients who were unable or unwilling to cooperate and complete the required information.

A non-standardized questionnaire focusing on socioeconomic and behavioral risk factors was developed. If patients did not understand any of the questions, they were explained or read by the researcher in a dedicated room. We used a visual analogue scale (VAS from 0 to 10 cm) to measure the quality of life where 10 is the best possible quality of life and 0 the worst possible quality of life. Clinical data were obtained retrospectively from medical records and from the UNIS database of the University Hospital Kralovské Vinohrady hospital system.

Of the 476 respondents that were approached, 52 did not complete the questionnaires, 24 declined to participate in the study and so they were excluded (n = 76) from the investigated sample. The final number of examined patients was 400.

HNC were defined according to categories C00-C14 and C30-C32 of the International Classification of Diseases (10th edition;ICD-10). Morphological information was described in accordance with the International Classification of Diseases (ICD-O) and morphological codes (3rd edition). Only malignancies with morphological codes for squamous cell type (morphological codes 8032, 8033, 8050–8052, 8070–8078, 8082–8084, 8094, 8123) were included in the group of patients with HNC.

Statistics

In two groups of patients (HNC vs. Others) the following demographic variables were assessed: age, sex (Male/Female), married (Yes/No), divorced (Yes/No), widow (widower) (Yes/No), the family in which the patients grew up (children 's home / 2-parent household / 1-parent household patients living alone (Yes/No), education (apprenticeship, primary school/ high school with graduation/ university), number of years of schooling; Clinical: Stage (I, II, III, IV), histopathological grade (G1, G2, G3, G4), GER (Yes/No), prosthesis/implant (Yes/No), Quality of life; risk factors: smoking (Yes/No), average number of years of active smoking, number of cigarettes smoked, alcohol (regular consumption / occasional consumption / abstainer) (the amount of beer drunk (0.5 l), wine (0.2 l) and hard alcohol (0.05 l).

All the quantitative variables were given as means and standard deviations. For qualitative variables the number and percentages were calculated. Statistical analysis of normally distributed quantitative variables (age, number of years of schooling, number of cigarettes smoked, average number of years of active smoking, the amount of beer drunk (0.5 l), wine (0.2 l) and hard alcohol (0,05 l) was carried out using the independent t-test sample to compare the HNC patients and control group of patients. Pearson's x2 test was used to examine whether there was a statistically significant difference in the observed categorical variables (sex, stage, histopathological grading, GER, presence of implant and prosthesis, family status, complete family, patients lived in the household alone, smoking, alcohol) between the two groups of patients. To evaluate the effect size, the

Cohen's d for t-test and Cramer's V or Phi (which are a measure of the strength of correlation between two categorical variables in contingency tables; Tables 1-4) for chi-square test were calculated. Statsoft's STATISTICA version 9 and IBM SPSS Statistics version 23 were used for statistical analysis. A p value <0.05 was considered statistically significant.

Results

The results of the study are summarized into logical units according to the investigated variables.

Demographic and clinical variables

A total of 400 patients were examined. The study group consisted of patients with head and neck cancer (HNC) (n=200), with 127 (64%) men and 73 (37%) women.

The control group consisted of patients with other different oncological diagnoses (HOD) (n=200) and there were 113 (58%) men and 87 (42%) women.

The sex representation ratio in both groups was almost balanced (p=0.219) and the strength of the correlation was weak. The average age at which cancer was diagnosed was very balanced in both groups (in HNC 62.58±9.908 and HOD group 62.68±17.17 years. According to Cohen's d, the difference was trivial.

We also examined the clinical stage in which the disease was diagnosed according to the TNM classification from clinical data and according to primary diagnosis. The most significant difference was in stage IV, where 120 (60.30%) patients were diagnosed with HNC and only 52 (26.00%) with HOD (p<0.001) and the strength of the correlation was very strong.

We also compared the histopathological examination of the grade of tumor differentiation. Grade 1 corresponded to the most differentiated tumor and grade 3 best corresponded best to the least differentiated tumor type. The largest difference in the proportion was found in the least differentiated tumors, which was diagnosed for HNC in 86 (43.00%) patients and for patients with HOD

Table 1. Age, Sex and clinical parameters of the two groups of patients HNC (N=200) and ODD (N=200): quantitative variables – means, standard deviations, Cohen's d and p-values of t-test; qualitative variables – numbers, percentages, Cramer's V (or Phi) and p-values of Pearson's x^2 test

Variables	HNC	HOD	Effect size	p value
	n (%)	n (%)		
Sex			0.0614* (weak)	0.220
Women	73 (36.5)	85 (42.5)		
Men	127 (63.5)	115 (57.5)		
Age	62.59 (9.908)	62.69 (13.173)	0.0009 [†] (small)	0.930
Clinical data				
Stage			0.3553* (very strong)	< 0.001
Ι	21 (10.55)	44 (22.00)		
II	17 (8.54)	45 (22.50)		
III	41 (20.60)	56 (28.00)		
IV	120 (60.30)	52 (26)		
Grade			0.2490* (strong)	< 0.001
1	21 (10.5)	42 (21.0)		
2	93 (46.5)	94 (47.0)		
3	84 (42.0)	39 (19.5)		
4	1 (0.5)	3 (1.5)		
Not given	1 (0.5)	22 (11.0)		
GER			0.4634* (very strong)	< 0.001
Yes	97 (48.5)	14 (7)		
No	103 (51.5)	186 (93)		
Prosthesis			0.0930* (weak)	0.063
Yes	57 (28.5)	41 (20.5)		
No	143 (71.5)	159 (79.5)		
Quality of Life	60.99 (16.71)	72.94 (15.63)	0.6932 ⁺ (medium)	< 0.001

*Cramer's V (Phi), †Cohen's d

Variables	HNC n (%)	HOD n (%)	Effect size	p value
Family and social background				
The family in which the patients grew up			0.2893 (very strong)	< 0.001
Children´s home	1 (0.5)	0 (0)		
Incomplete family	82 (41)	31 (15.5)		
Complete family	117 (58.5)	169 (84.5)		
Social and family background in which pa	tients grew up			
Patients lived in the household alone			0.1638 (strong)	0.001
Yes	68 (34)	39 (19.5)		
No	132 (66)	161 (80.5)		
Patients lived				
in marriages			0.1564 (strong)	0.002
Yes	98 (49)	129 (64.5)		
No	102 (51)	71 (35.5)		
Divorced			0.0901 (weak)	0.071
Yes	52 (26)	37 (18.5)		
No	148 (74)	163 (81.5)		
Widowed			0.0603 (weak)	0.228
Yes	38 (19)	29 (14.5)		
No	162 (81)	171 (85.5)		

Table 2. Variables related to family background and their comparison in both groups of patients - numbers and percentages, Cramer's V (or Phi) and p value of x^2 test

Table 3. Overview of variables related to education and professional classification and their comparison in both patient groups; means, standard deviations, Cohen's d and p-values of t-test; numbers, percentages, Cramer's V (or Phi) and p-values of Pearson's x^2 test

Variables	HNC	HOD	Effect size	p value
Education				
Number of years schooling	11.86 (2.254)	13.04 (1.9680)	0.5030 ⁺ (large)	< 0.001
Professional classification, n (%)				
Apprenticeship /primary school	109 (54.50)	64 (32)	0.2376 (strong)	< 0.001
High school with graduation	64 (32)	107 (53.5)		
College/University	27 (13.5)	29 (14.5)		

Table 4. Overview of variables related to risk behavior and comparison in both groups of patients, means, standard deviations, Cohen's d and p-values of t-test; numbers, percentages, Cramer's V (or Phi) and p values of Pearson's x² test

Variables	HNC	HOD	Effect size	p value
Smoking, n (%)				
Yes	156 (78)	94 (47)	0.3202* (very strong)	< 0.001
No	44 (22)	106 (53)		
Average number of years of active smoking	27.34 (17.66)	15.11 (19.22)	0.6299 [†] (medium)	< 0.001
Number of cigarettes smoked	18.59 (13.73)	6.78 (2.5471)	0.9166† (large)	< 0.001
Drinking alcohol, n (%)				
Regular consumption	97 (48.5)	32 (16)	0.3503* (very strong)	< 0.001
Occasional consumption	86 (43)	133 (66.50)		
Abstainer	17 (8.50)	35 (17.50)		
Type of alcohol drunk per week				
Amount of beer drunk (0.5 l)	8.35 (8.8442)	3.5775 (5.2332)	0.6568 [†] (medium)	< 0.001
Amount of wine drunk (0.2 l)	3.34 (3.78)	1.44 (1.59)	0.6552 [†] (medium)	< 0.001
Amount of hard alcohol drunk (0.05 l)	8.84 (9.24)	2.10 (4.23)	0.8507 ⁺ (large)	< 0.001

*Cramer's V (Phi), †Cohen's d

only in 39 (19.50%) (p<0.001), which was a strong correlation. We also found a significant statistical difference in the premorbid presence of gastroe-sophageal reflux, where in HNC this symptom was reported by 48.50% of the patients, while in the second group in only 14 (7%) (p<0.001), which was a very strong correlation.

The presence of an implant or prosthesis in the oral cavity was another issue studied. However, the differences for this variable were not significant and the strength of the correlation was weak.

We examined the quality of life as the last variable in this group. We found different values in both groups. In patients with HNC, the average value was 60.99 ± 16.71 , and in the second group 72.94 ± 15.63 (p <0.001), and according to Cohen's d the effect size was medium.

Subtypes of squamous cell carcinoma were represented in the HNC population from 100% (n = 200) and in the population of patients with other oncological diagnoses, gastrointestinal tract (GIT) tumors, urogenital tumors and breast tumors were most represented (Figure 1), according to the proposed requirements for the integrity of the studied group.

Family and social background

Several potential risk factors in terms of family background were examined. The first variable examined was whether the patient grew up in a

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1-parent household or 2-parent household. Here we found a statistically significant difference, as 82 (41%) patients with HNC grew up in a single-parent household and 1 (0.5%) patient in a children's home, while in the control group only 31 (15.5%) patients grew up in a single-parent household (p<0.001) and the strength of the correlation was very strong.

We also asked whether the patients lived alone for more than a year before the onset of the disease. 68 (34%) patients from the HNC group lived alone in the household while in the group with other oncological diagnoses (HOD) only 39 (19.5%) lived alone. According to the results (p<0.001) the strength of the correlation was strong.

We also investigated whether patients were married, widowed or divorced for at least a year before the onset of disease. 98 (49%) patients with HNC and 129 (64.5%) patients in the control group lived in marital union before the onset of disease again we found a statistically significant difference, (p<0.001) and the strength of the correlation was very strong. For other questions from this range of variables, the results were no longer significant and the strength of the correlation was weak for both variables.

Education and professional classification

We also focused on the length of education, which we determined as the total sum of years of

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Oncological Diagnosis in the Control Group

Figure 1. Proliferation ability of cells after interfering in SNHG1 detected via CCK-8 assay (**p<0.01 vs. NC-siRNA group).

schooling, (i.e. primary school, secondary school and college and university), and after that we determined the average. The average value of this sum was 11.86 (SD=2.524) in patients with tumors in the head and neck area and 13.03 (SD=1.9680) in the control group. According to the results of statistical research, we found a significant difference in both groups of patients (p <0.001), and according to Cohen's d, the difference was large.

Occupational classification of patients was another monitored variable. Patients were assigned to one of three groups (1 - apprenticeship, primary school, 2 – high school with graduation, 3 - University). The most significant difference was found between the two populations in subgroup 1, where 109 (54.50%) patients with HNC were included in this group and 64 (32%) in the control group. The opposite distribution is found in subgroup number 2, i.e. high school-educated patients, where we found 64 (32%) patients in HNC and 107 (53.50%) in the control group. We did not find a significant difference in subgroup No. 3 (university). The strengths of the correlations were strong.

Risky behavior

The most significant differences are found in cigarette smoking, as expected. In patients in the study group we recorded almost 30% more smokers: in HNC, 156 (78%) patients smoked in contrast to HOD, where only 99 (47%) patients smoked, p<0.001, which is a very strong correlation It was further confirmed that patients with HNC smoked on average almost 3 times more cigarettes per day than patients from the HOD group. According to Cohen's d, the size effect was medium. In patients in both groups, we also asked about the number of years they had been actively smoking and again calculated the average exposure time. Patients with HNC reported a mean number of years (mean = 27.34, SD = 17.66) that was almost twice as long as patients with HOD (Mean = 15.1050, SD = 19.21), p <0.0001, a large effect size.

We also found significant differences in alcohol consumption. We divided the patients in both populations into three groups. The first group consisted of abstainers (A1), the second group consisted of patients who consume occasionally (A2), meaning they do not drink one alcoholic beverage every day (meaning 0.02l of wine, 0.5l of beer or 0.05l of hard alcohol and the last third group consisted of patients who consume alcohol regularly (A3). In patients diagnosed with HNC, almost 33% higher regular alcohol consumption was reported than in HOD and abstinence in the HNC group was only 17 (8.50%) (p<0.001) and the strength of the correlation was very strong.

We also looked at the type of alcohol that patients consume. We divided the type of alcohol that patients consumed into 3 groups: wine (0.2) l), hard alcohol (0.05 l), and beer (0.5 l). We calculated the average total values and chose the week of consumption in our research as the time interval, especially because for patients who did not drink alcohol daily, it would be very difficult to determine the daily dose and the data could be skewed. The results show that patients with HNC drink almost 4 times more hard alcohol per week than HOD (p<0.0001), and the effect size was large. Patients with HNC also drink more than twice as much beer and wine than patients from the control group (p<0.0001). In both cases the size effect was medium. We found a statistically significant difference according to all examined parameters related to alcohol use.

Discussion

The aim of our study was to provide a clear and comprehensive analysis of risk factors in patients with HNC and their different representation in comparison with the control group of patients with HOD.

According to the analysis of demographic data, the ratio of women and men in both groups was without statistically significant difference and also the average age of individuals in the primary diagnosis of the disease in both groups was almost the same.

It was found that more than 26% of patients with HNC were diagnosed in a locally advanced or metastatic stage of the disease, in contrast to the group of patients with HOD, according to the primary staging and subsequent description according to the TNM classification. This result is in agreement with sources from the literature, which state that more than 70% of patients with HNC come to the initial diagnosis in a late stage [7].

The causal relationships of these data have not yet been fully clarified, but this condition is most often correlated with lower socioeconomic status in patients with HNC and associated with higher rates of smoking and alcohol abuse, as well as with insufficient prevention of risky behavior [8].

We also compared histopathological examination of the grade of differentiation within the clinical data. A significantly higher grade and thus more aggressive tumor type was found in patients with HNC compared to the control group. There are few foreign sources that would provide valid data in this context. Fang et al studied the association of histological differentiation with the clinical manifestations of oral cancer, but found no significant association between the grade of tumor differentiation and age, sex, tumor size, bone invasion, depth of invasion, or a history of exposure to known carcinogens. Instead, nodal metastases, extracapsular spread, and perineural invasions were very closely associated with the tumor grade [9]. We can assume that the grade of tumor grade is directly proportional to the stage of the primary disease and thus confirms the validity of the previous statement that patients with HNC come to primary diagnosis with more advanced disease stages than patients with HOD.

In the group of patients with HNC, a higher proportion of the presence of premorbid gastroesophageal reflux disease was confirmed. The effect of smoking and alcohol plays a significant potentiating role, as tobacco smoking is the most important etiological factor in GER and alcohol acts as a trigger for reflux episodes [10], both of which reduce esophageal sphincter pressure, which in turn induces reflux [11].

Family and social background of patients was another area of the examined variables. With regard to meeting the objectives of the study and providing a complete overview of the effects of risk factors in the timeline, we tried to monitor the socio-economic and family background from childhood to the present.

The first variable examined was the family background in the patient's childhood.

Children from divorced families have been shown to be more prone to risky behaviors, especially with regard to smoking, alcohol and early drug use, and more often these individuals are more likely to become lifelong addicts [12,13]. Our results confirm the aforementioned findings, as we detected almost 30% more patients from singleparent families in HNC. The connection can be deduced from the fact that alcohol and smoking are the main risks for head and neck cancer, and individuals from single-parent families have a higher tendency for this risky behavior at a much younger age and also more often fall into these lifelong addictions.

We also asked whether the patients lived in a separate household for more than a year before the onset of the disease. The difference in both groups was again significant and it was shown that patients with HNC lived alone more often than patients with HOD according to our results. We can assume the most likely cause to be a greater tendency to socially isolate/distance oneself, consequently leading to an increased risk of addiction to smoking or alcohol in patients who do not have strong family support [14]. The re-

sult can be a deterioration in the quality of life, financial background, and also the prognosis of patients [15].

Marital status before the onset of the disease was also the subject of the research.

Significantly more patients with HOD were married, and this result may be related to the findings of the Schaefer study, which demonstrates a positive effect of marriage on the stage of primary diagnosis of tumor [16]. Furthermore, it was shown that the support of cancer patients' partners improved their prognosis in early primary staging [17,18] and a positive effect on the reduction or complete elimination of nicotine addiction and alcohol consumption [19] was demonstrated.

Another item examined was the average length of education. The average value of patients with head and neck tumors was up to two years lower than in the control group according to the results.

Previous findings have shown that the total number of years of education is positively correlated with intelligence [20] and it was be confirmed that fewer years of education and lower financial income are associated with an increased risk of head and neck cancer [21]. The correlation between the development of HNC and lower levels of education can be caused by limited access to information on prevention, lifestyle and disease in general, including diagnosis and treatment [22].

We also monitored the professional classification of patients in this context. The HNC group was dominated by patients who were trained or had only a basic education, and HOD had the most patients in the group with a high school diploma. The sources of literature that have dealt with this issue are very limited. However, it was found that individuals living in the poorest conditions with impossibility of education have a significantly higher risk of developing HNC than people who have a higher level of education [21,22]. Johnson came to similar conclusions, confirming the increased incidence of HNC in men who were trained or had only completed primary school [23].

We also investigated the current quality of life. We encountered a significantly higher and therefore better quality of life in patients with HOD according to our results. The sources of the literature dealing with the quality of life of patients with HNC are relatively extensive, but the results of these studies are inconsistent. One of the most extensive studies on this topic was conducted by Mehanna et al, who found that the correlation between quality of life and survival in patients with HNC is not currently proven by sufficient clinical data, but the relationship between quality of life, psychosocial factors and long-term survival exists [24]. The worse quality of life in the population of patients with HNC can be explained by a more advanced stage of disease in which the tumor is diagnosed and also by very demanding and often very mutilating therapy affecting facial deformity, speech, communication and food intake. Patients with HNC often do not end tobacco and alcohol dependence even during therapy, and these circumstances again lead to further deterioration in quality of life and a reduction in overall survival rates.

We also included repeatedly confirmed risk factors, especially smoking and alcohol abuse, in the study. Cigarette smoking is a major risk factor for HNC, but it is also heavily involved in the development of other types of cancer, including lung, esophageal, bladder and pancreatic tumors (tobacco smoke). We demonstrated a significant difference between the two groups of patients with a significantly higher percentage of nicotine/ tobacco use in patients with HNC in all monitored items related to tobacco abuse, as expected. This result is in agreement with all previous studies dealing with the research on risk factors in HNC [3,25]. We can state that the effect of smoking is the major risk factor for HNC. We found similarly significant differences in both groups in alcohol use according to our findings and in connection with previous research. Although some studies have found a higher incidence of chronic alcohol abuse in higher socioeconomic classes, it has been shown that a greater proportion of the negative consequences of increased alcohol exposure are found in lower-income groups [8].

Current evidence suggests that the socioeconomic differences and the negative impact of alcohol consumption on the human body consist mainly in the quality of the alcohol consumed and the experience of the negative consequences associated with this risk factor. However, the exact nature of these complex relationships requires further extensive study [8].

We must also consider factors in general, such as the geopolitical, cultural and socio-economic situation, as well as individual factors such as community context, family, peer influences, biological predispositions, prenatal alcohol exposure, psychological factors and socio-demographic features (e.g. sex, age, race, ethnicity, culture, religion and socio-economic status), in the context of the data presented above [26]. These factors interact linearly with each other at different levels over time to indicate opportunities for alcohol and a direct correlation between the influence of risky

smoking exposure and the associated negative consequences for an individual's health [26,27]. These data positively correspond to our previous findings regarding the sociodemographic-clinical status of patients with HNC. A study in Canada even showed that cancers caused by smoking and alcohol abuse are much more common in the lower socioeconomic class, and we found more breast and testicular cancers in the upper socioeconomic class [28]. Weaknesses in the healthcare of individual countries also play a role in these conclusions [28,29].

Smoking, excessive alcohol consumption and health care shortages are fundamental determinants of health, but we must also consider the fact that inequalities in general living conditions in the political, economic, social and cultural spheres also play a large role. However, the different living conditions between individual countries and the resulting influence on the outbreak of HNC do not lie only in political and social security.

Lifestyle risk factors have a much more significant impact on the incidence and mortality of HNC even in countries with high socio-economic levels [28]. In the future, studies dealing with the overall context of the influence of risk factors in HNC and their relationship to the socio-economic position of the individual in society should be conducted.

Limitation of the study

We can consider as a limitation of our research that only patients from one oncology center participated. The study involved mainly residents of Prague and therefore the different influence of risk factors of life in the village compared to the city was not documented.

We deliberately excluded HP-positivity from the study because HPV is of considerable importance as a risk factor in HNC, but in our research we compared HNC with a group of patients with other oncological diagnoses and in most of them HPV did not play a significant role as a risk factor. Respondents may also have considered some questions about their socio-economic situation to be too personal, which may have influenced the validity of their answers.

Conclusion

The results and analysis of our study successfully met the proposed goals. The significant influence of smoking and alcohol on the development of HNC was confirmed and in connection with this

behavior, lower socioeconomic status, poor family and socioeconomic background and clinical factors on the development of head and neck cancer was demonstrated.

The variables proposed in our study were compared to a control group of patients with HOD, and the validity of the above data and findings was supported by different results in both groups, in contrast to previous research. This project could then serve as a basis for further follow-up research into the risk factors of these serious diseases and further participate in the renewal of prevention campaigns in the context of risky behavior and the emergence of oncological diseases.

Conflict of interests

The authors declare no conflict of interests.

References

- IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol 100, A Review of Human Carcinogens. Lyon, France: International Agency for Research on Cancer; 2011. http :// monographs.iarc. fr /ENG/Monographs/PDFs/index.php.Accessed November 2,2011.
- IARC Preamble to the IARC Monographs. Lyon, France: International Agency for Research on Cancer; 2006.http://monographs.iarc.fr/ENG/ Preamble/index. php.Accessed November 2, 2011.
- 3. List MA, Siston Amy, Haraf D et al. Quality of life and performance in patients with advanced head and neck cancer with concomitant chemoradiotherapy: prospective examination. J Clin Oncol 1999; 17:1020-8.
- Downer MC, Moles DR, Palmer S, Speight PM. A systematic review of test performance in screening for oral cancer and precancer. Oral Oncol 2004;40:264-73.
- Sankaranarayanan R, Ramadas K, Thomas G et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. Lancet 2005;365:1927-33.
- 6. Leemans CR, Braakhuis BJ, Brakenhoff RH, 2011. The molecular biology of head and neck cancer. Nat Rev Cancer 2011;11:9-22.
- Guntinas-Lichius O, Wendt T, Buentzel J et al. Head and neck cancer in Germany: a site specific analysis of survival of Thurigian cancer registration database. J Cancer Res Clin Oncol 2010;136:55-63.
- Hobdell MH, Oliveira ER, Bautista R, Myburgh NG, Lalloo R, Narendran S, Johnson NW. Oral diseases and socio-economic status (SES). Br Dent J 2003;194:91-6; discussion 88.
- 9. Fang KH, Kao HK, Cheng MH et al. Histological differentiation of primary oral squamous cell carcinomas in an area of betel quid chewing prevalence. Otolaryngol Head Neck Surg 2009;141:743-9.
- Yamamichi N, Mochizuki S, Asada-Hirayama I, Mikami-Matsuda R, Shimamoto T. Lifestyle factors affecting gastroesophageal reflux disease symptoms: a cross-sectional study of healthy 19864 adults using FSSG scores. BMC Med 2012;10:45. doi: 10.1186/1741-7015-10-45.
- 11. Ness-Jensen E, Lagergren J. Tobacco smoking, alcohol

consumption and gastro-oesophageal reflux disease. Best Pract Res Clin Gastroenterol 2017;31:501-8.

- Fagan PF, Churchill A. (2012). The Effects of Divorce on Children. www.marri.us. Retrieved 17 October 2013 from http://downloads.frc.org /EF/EF12A22.pdf.
- Brown SL, Rinelli LN. Family Structure, Family Processes, and Adolescent Smoking and Drinking. J Res Adolescence 2010;20:259-73.
- 14. DiMatteo RM, Lepper HD, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Medicine 2000;160:2101-7.
- Wong YK, Tsai WC, Lin JC et al. Socio-demographic factors in the prognosis of oral cancer patients.Oral Oncol 2006;42:893-906.
- Schaefer EW, Wilson MZ, Goldenberg D, Mackley H, Koch W, Hollenbeak CS.Effect of marriage on outcomes for elderly patients with head and neck cancer. Head Neck 2015;37:735-42.
- 17. Aizer AA, Chen MH, McCarthy EP et al. Marital status and survival in patients with cancer. J Clin Oncol 2013;31:3869-76.
- Zhang J, Gan L, Wu Z, Yan S, Liu X, Guo W. The influence of marital status on the stage at diagnosis, treatment, and survival of adult patients with gastric cancer: a population-based study. Oncotarget 2016. Feb 15.
- 19. Lindstrom M. Social capital, economic conditions, marital status and daily smoking: a population-based study. Public Health 2010;124:71-7.
- 20. Al-Dakkak I. Socioeconomic status and head and neck cancer. Evid Based Dent 2010;11:57-8.
- 21. Pokhrel A, Martikainen P, Pukkala E, Rautalahti M, Seppa K, Hakulinen T. Education, survival and avoidable deaths in cancer patients in Finland. Br J Cancer 2010;103:1109-14.
- 22. Hussain SK, Lenner P, Sundquist J, Hemminki K. Influence of education level on cancer survival in Sweden. Ann Oncol 2008;19:156-62.
- 23. Benard VB, Johnson CJ, Thompson TD et al. Examining the association between socioeconomic status and

potential human papillomavirus associated cancers. Cancer 2008;113:2910-8.

- 24. Mehanna HM, De Boer MF, Morton RP. The association of psycho-social and survival in head and neck cancer. Clin Otolaryngol 2008;33:83-9.
- 25. Blot WJ, McLaugilin JK, Winn DM et al. Smoking and drinking in relation to oral and pharyngeal cancer. Cancer Res 1988;48:3282-7.
- 26. Al-Dakkak I, Khadra M. Socio-economic status and upper aerodigestive tract cancer. Evid Based Dent 2011;12:87-8.
- 27. Johnson S, McDonald JT, Corsten MJ. Socioeconomic factors in head and neck cancer. J Otolaryngol Head Neck Surg 2008;37:597-601.
- 28. Mackillop WJ, Zhang-Salomons J, Groome PA, Paszat L, Holowaty E. Socioeconomic status and cancer survival in Ontario. J Clin Oncol 1997;15:1680-9.
- 29. Booth CM, Li G, Zhang-Salomons J, Mackillop WJ. The impact of socioeconomic status on stage of cancer at diagnosis and survival: a population-based study in Ontario, Canada. Cancer 2020;116:4160-7.