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Evaluating the reasons for delays in treatment of oral cavity cancer patients

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ABSTRACT

The growing increase in oral cavity cancer (OSCC) incidence constitutes a severe diagnostic-therapeutic problem – and early diagnosis, as well as medical treatment remain important priorities of maxillofacial oncology. The aim of this paper was to determine the reasons for delays in the diagnostics and treatment of oral cavity cancer patients. The study focused on 248 patients (=56.1 years) post-surgery, in which delays in diagnostics and treatment were reported. As for the causes, most frequently, in 171 cases (69.0%), patient delays were reported, in 56 cases, physician delays were observed, and in 21 cases (8.5%), organizational reasons were to blame. The median time period between the onset of the symptoms and seeking medical attention was 143 days. Time interval between the first contact with a doctor and commencement of oncological treatment was 33.2 days approximately. The majority of the patients were not aware of the oral cavity cancer risk. Misdiagnosis of symptoms as inflammation, as well as prolonged antibiotic therapy and diagnostics constitute main reasons for physician and organization-al/health care system delays. Raising patients' awareness of cancer risk, as well as educational and promotional programs for physicians are the principal goals of a strategy aiming to enhance oral cancer diagnosis.

INTRODUCTION

The incidence of malignant tumors is steadily increasing in the world, including Poland. As for mouth, throat and larynx cancers, Oral Squamous Cell Carcinoma (OSCC) accounts for more than 90% of all cases [1]. In 2018, 350 thousand of new head and neck cancer cases were diagnosed throughout the world [2].

According to the epidemiological data and the Polish National Cancer Register, the number of new malignant tumor cases has doubled since the 90s, reaching more than 140.5 thousand annually. Each year, three thousand new oral cavity cancer cases are reported in the country. Oral cavity cancer is diagnosed three times more often in men than in women, and the risk increases in patients over 50 years of age, especially in the sixth and seventh life decades. Smoking and alcohol abuse are among the risk factors. In patients under 50 years of age, HPV infection is an important risk factor [3].

Despite significant diagnostic progress and use of new oral cavity cancer treatment therapies, five-year survival rate is still low and has remained unchanged for a few decades, in comparison to Western European countries and the United States of America. Unfavorable treatment results and prognoses are related to late diagnosis and implementation of oncological treatment, among others [4]. Cancer diagnosis at an early stage of its development significantly limits the extent of surgical procedures, enhances long-term treatment results and positively affects the quality of the patients' life after the conclusion of the treatment. Early diagnosis and commencement of the oral cavity cancer treatment are among the principal problems of maxillofacial oncology [5]. The aim of this paper was to evaluate and determine reasons for delays in diagnosis and radical causative treatment in oral cavity cancer patients.

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MATERIAL AND METHODS

Study design and study sample

The study focused on a group of 248 patients, who accounted for 28.7% of 864 patients treated during 15 years period of time at the Department of Maxillofacial Surgery of the F. Chopin Clinical Hospital No. 1 in Rzeszow (Poland), and in case of which delays in oral cavity cancer diagnostics and treatment were reported. The main inclusion criterion for the patients involved: time interval between the onset of first symptoms in the oral cavity and seeking medical attention, time at which clinical diagnosis was established, and time till commencement of the treatment. The following were evaluated: demographics, including patients' education and age; cancer location and extent-– in relation to the time interval between the onset of the first cancer symptoms and seeking medical attention. Also, time between seeking medical attention from a GP and seeking medical attention from a specialist physician, as well as time between seeking medical attention from a specialist physician and commencement of treatment, were evaluated. The group of patients that met the inclusion criteria was divided according to the reasons for treatment delays using a tool developed by Pack and Gallo for the World Health Organization (WHO) [6], including: patient delays, when time interval between the onset of the first disease symptoms and seeking medical attention was longer than three months. If the time interval between first medical examination and referral for a specialist (oncological) treatment was longer than one month, it was assumed that physician delay related to the diagnostic process took place. Organizational delays occurred when the interval between first medical examination and diagnosis, and implementation of causative treatment (surgery, radiotherapy) was longer than one month. The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of University of Rzeszow, Poland, Medical College, (protocol code 22/10/2020).

Statistical analysis

Statistical analysis was carried out using Statistica 13.1 developed by StatSoft.

Qualitative data were analyzed. Relationships between variables were analyzed using the chi-square test by Pearson. More frequent incidence of an answer (in comparison to others) was verified by means of a two-tailed test. The results were displayed as frequency, numbers and percentage, for which contingency and simple tables were used. Significance level was set to be $p<0.05$.

RESULTS

The studied group was composed of 248 patients who attended our clinic between 2000 and 2015 due to oral cavity cancer, and included 157 men (63.3%) and 91 women (36.7%), which means that the men-to-women ratio was 1.7:1. The age of the patients who underwent surgery ranged between 38 and 84 years (average 56.1 years). The largest groups were those composed of 67 patients aged 61 to 70 (27.1%). Most frequently, i.e. in 89 patients (35.9%), floor of the mouth OSCC was diagnosed, and in 72 patients (29.0%), tongue cancer was detected. Lower gingiva cancer affected 33 patients (13.3%), while ethmoidomaxillary massif and palate were identified as primary cancer sites in 30 patients (12.1%). Moreover, 19 patients (7.7%) were treated for cheek mucous membrane cancer, while 5 patients (2.0%) suffered from lower lip cancer.

Patients sought treatment at different TNM stages. Accordingly, 89 patients (35.9%) were diagnosed with stage III (T2N1M0; T3N1M0) OSCC, stage I (T1N0M0) was detected in 86 patients (34.7%), while stage II (T2N0M0) affected 52 patients (20.9%). Furthermore, 21 patients (8.5%) were in stage IV (T4N0M0; T4N1M0) of advancement.

Based on the data gathered when analyzing the medical history of 248 patients, three groups of causes were distinguished: patient delays, GP delays related to diagnostics (physician delay) and organizational/health care system delays. Data is presented in Table 1.

Table 1. Reasons for delays in commencement of treatment

Reasons for delays in commencement of treatment	n	%
Patient delay	171	69.0%
Physician delay	56	22.6%
Organizational/health care system delay	21	8.5%
Total	248	100.0%

The observations carried out by the authors of this paper show that the first type of delays was related to patients who postponed seeking medical attention after observing the first symptoms. No pain during first stages of cancer development, ignoring other local symptoms and attributing them to irrelevant, temporary oral cavity inflammation were quoted as the most common reasons for delays in seeking medical attention from a GP, and were observed in 109 patients (55.6%). Other reasons were: ignoring symptoms such as food intake and swallowing difficulties, as well as trying to self-treat using herbal mouth rinses, over-the-counter ointments and heating compresses – as reported in the case of 26 patients (12,2%), while 22 patients (11.2%) postponed seeking medical attention hoping for self-healing and remission of symptoms. In addition, fear of cancer diagnosis was a reason for delay in seeking medical attention in case of 34 patients (18,3%).

In order to determine the reasons for patient delays, time interval between noticing the first symptoms and seeking medical attention from a physician needs to be taken into account. On average, it took the patients 79 days to seek medical treatment. Only 62 patients (24.9%) consulted a doctor within the first month from the onset of symptoms, and 64 patients (25.8%) consulted a family medicine doctor or a dentist within one to three months from the onset of the symptoms, the remaining 122 patients (49.3%) delayed the decision to seek medical attention for more than three months; among them, 59 patients consulted a doctor after six months, while 5 patients (2.1%) waited more than a year to do so. The above data are indicative of the treated patients' low health awareness.

The time interval between the patients' seeking medical attention for the first time and commencement of diagnostic procedures or deciding to refer a patient for a specialist treatment in a reference oncological center determines the reasons for delays in treatment due to the fault of the doctor. In 56 cases (23.4%), GPs were to blame for the delay, which was caused by prolonged diagnostics. In case of this group, average waiting time for receiving causative treatment was 33.2 days. Potential reasons behind the GPs' postponing the decision to refer the patients for specialist treatment are presented as prolonged antibiotic therapy and the use of anti-inflammatory treatment in the form of rinses and anti-inflammatory drugs, postponing the decision to take a specimen for histopathological verification, surgical and dental procedures: incision, puncture, tooth extraction. As for other reasons behind delays in commencement of specialist treatment, organizational/health care system related delays need to be mentioned, and greater details regarding this issue can be found in Table 2.

Table 2. Detailed analysis of organizational delays

Reasons for organizational delays in treatment	n	%
Waiting for medical ultrasound	7	33.3%
Waiting for CT scan or MRI	4	19.0%
Difficulties in histopathological diagnosis (waiting for the reference center to verify it)	10	47.6%
Total	21	100.0%

In the studied group, organizational delays were reported in 21 cases (8.4%); most frequently, *i.e.* in 10 patients, prolonged waiting for the histopathological examination caused by the need to verify the results in a reference center was to blame; 7 patients had to wait for medical ultrasound for a long time, while 4 patients had to wait for performance and description of CT scan or MRI.

In the next part of the study, reasons for delays in commencement of specialist treatment of the OSCC patients, demographic-social factors depending on the patients' age, place of residence and education, were analyzed. The research shows that in the group of 248 patients with OSCC, reasons for delays did not depend on the patients' sex ($p = 0.087$). The variables concerning the relationship between the causes of delays in commencement of OSCC treatment and the age of the patients are presented in Table 3.

Table 3. Reasons for delays *vs* patients' age

Age	Patient delays		Physician delays		Organizational delays		Total
	n	%	n	%	n	%	n
< 40	1	50.0%	0	0.0%	1	50.0%	2
41-50	20	40.8%	24	49.0%	5	10.2%	49
51-60	43	68.3%	12	19.1%	8	12.7%	63
61-70	51	76.1%	9	13.4%	7	10.5%	67
71-80	43	86.0%	7	14.0%	0	0.0%	50
> 80	13	76.5%	4	23.5%	0	0.0%	17
Total	171	69.0%	56	22.6%	21	8.5%	248
p	$\chi^2(10)=40.09$; $p<0.001$						

Observations of the authors, also confirmed by the statistical analysis, have shown (chi-square test) that in case of the younger patients, delays in diagnostics and treatment were statistically ($p<0.001$) more frequently related to organizational/health care system reasons. Reasons for patient-delayed treatment were the same for each age group. Table 4 provides information regarding reasons for delays in relation to the patients' place of residence.

Table 4. Reasons for delays *vs* patients' place of residence

Place of residence	Patient delays		Physician delays		Organizational delays		Total
	N	%	n	%	n	%	n
Rural areas	117	75.0%	27	17.3%	12	7.7%	159
Cities and towns	54	58.7%	29	31.5%	9	9.8%	89
Total	171	69.0%	56	22.6%	21	8.5%	248
$\chi^2(2)=7.71$; $p=0.021$							

Data gathered in Table 5 show a statistically significant relationship between the patients' place of residence and reasons for delay in commencement of causative-oncological treatment ($p = 0.021$). In case of inhabitants of towns and cities, the delays were most frequently related to prolonged diagnostics and treatment performed by GPs, as well to the organization of the health care system. As for the inhabitants of the rural areas, the delays were more often patient-related, which has been confirmed by the statistical analysis. Table 5 shows data regarding the influence of the education of the patients treated for oral cavity cancer on delays in treatment.

Table 5. Reasons for delays *vs* patients' education

Education	Patient delays		Physician delays		Organizational delays		Total
	n	%	n	%	n	%	
Primary	114	77.6%	23	15.7%	10	6.8%	147
Secondary	49	59.0%	29	34.9%	5	6.0%	83
Higher	8	44.4%	4	22.2%	6	33.3%	18
Total	171	69.0%	56	22.6%	21	8.5%	248
$\chi^2(4) = 27.28$ $p < 0.001$							

In the studied group, a statistically significant relationship between patients' education and delays in treatment and seeking medical attention ($p <0.001$) was demonstrated. In case of patients with higher education, organizational/health care related delays were most common, while patient delays were statistically more frequent among less educated patients.

DISCUSSION

According to a great number of publications, prognoses following malignant tumors treatment are related to the stage of the disease: the earlier the diagnosis, the more favorable the prognoses [7-9]. Patients with malignant tumors still seek medical attention too late, at the late stages of the disease, which drastically decreases their chances of recovery and puts them through burdensome and aggressive treatment. Improvement of oral cavity cancer (OSCC) treatment results does not depend upon introducing new treatment methods, but is significantly related to early diagnosis and determining the causes that delay the treatment. Therefore, it is important to identify the reasons for delays

in cancer diagnosis and treatment, and eliminating them could improve the treatment efficiency [10,11]. The results of the studies performed and epidemiological data suggest three main reasons for delays in oral cavity cancer treatment, which perhaps influence the long-term treatment results [12].

Of 248 patients treated for OSCC at the Department of Maxillofacial Surgery of the F. Chopin Clinical Hospital No. 1 in Rzeszow (Poland), 63.3% of the men underwent surgery, which was statistically significant ($p<0.001$). In the studied group, of statistically significance, there were more patients inhabiting rural areas (64.1%) ($p<0.001$). Similar data have also been encountered in other publications [13,14]. In addition, average age of patients that underwent surgery was 56.1, and the largest group was constituted by patients aged 61-70, who accounted for 27.1% of all patients. Moreover, patients aged over 50 prevailed in the studied group, which is consistent with the observations noted by other authors [15,16].

Despite a statistically significant predominance of male patients among which delays in treatment were observed, no statistical relationship between reasons for delays in treatment and patients' sex was observed. However, patient delays were close to statistically significant.

A statistically significant relationship between inhabiting rural areas and patient delays was reported ($p=0.021$). As for patients inhabiting towns and cities, delays in commencement of treatment were usually on the part of GPs and due to organization-al/health care system-related reasons. Based on the results obtained, which also correspond with data encountered in specialist literature, e.g. authors such as Carvalho and Tromp [17,18], there is a relationship between patients' education and delays in treatment. Statistically, in case of patients with primary education, patient delays were most common, while in case of patients with higher education, organizational negligence of the health care system, e.g. waiting for the results of specialist examinations, which delayed the treatment, was identified [19,20].

Various authors point to the statistically significant correlation between stage of the cancer disease and patient delays [21,22]. In the material presented in this paper, a statistically significant relationship ($p=0.002$) between more advanced OSCC and GP delays was also observed. Time interval between noticing first alarming symptoms in the oral cavity and seeking medical attention from a GP in the studied group was 143 days approximately, which coincides with the data presented by other authors [23,24]. Time interval between seeking medical attention from a GP and commencement of specialist treatment was 33.2 days, and the largest group, i.e. 42.3% patients was referred for oncological treatment between 15th and 30th day from their first GP appointment. Our study reveals that GPs significantly more frequently ($p=0.043$) attempted to treat primary sites of oral cavity tissue neoplastic infiltrations, which were thought to be inflammations, by means of antibiotic therapy, which significantly delayed the commencement of specialist treatment. In the literature, several authors draw attention to delays that result from the misdiagnosis of oral cavity neoplastic infiltrations and tumors as inflammations [25,26]. Improper diagnostic procedures performed by many doctors indicate their limited oral cavity cancer diagnostic and differentiating abilities. High incidence of misdiagnoses at early stages of treatment demonstrates the need to include issues related to oral cavity cancer prevention and early diagnosis in under- and postgraduate medical trainings [27].

On the side of patients, low awareness of oral cavity symptoms and lesions that can be related to cancer, has been observed. This is why the role of medical educators and promotional campaigns, which could affect the level of knowledge on malignant tumors in a positive way, should be noted. Moreover, it is essential to focus on health education of the society and encourage people to obtain regular medical check-ups at family medicine and dental clinics, as well as to draw their attention to health related benefits resulting from oral cavity self-examination and immediate seeking of medical attention from a GP trained in diagnosing neoplastic processes [28].

Organizational health care system delays are most frequently related to prolonged waiting time for imaging examinations and histopathological examination results essential in cancer diagnostic process. Eliminating these limitations is difficult mainly due to shortage of radiological and histopathological staff, which, alongside increasing number of cancer patients, is related to limited capacity of radiology and pathology facilities.

CONCLUSIONS

1. Delays in oral cavity cancer are most frequently patient-related. Despite access to self-evaluation of oral cavity lesions, the majority of the patients are not aware of the cancer risk.
2. Diagnostic errors, namely, misdiagnosing early symptoms of neoplastic lesions as inflammations, and treating them by means of prolonged antibiotic therapy, are still observed, which demonstrates a further need for both pre- and postgraduate medical trainings.
3. Possibility of improvement lies in raising the patients' oncological awareness by organizing promotional and educational programs, providing direct contact with health care system employees in the media, as well as developing preventive programs as part of campaigns for oral cavity health.

AUTHORS' STATEMENT

We do not declare any conflict of interests that could affect the objectivity and credibility of the work

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REFERNCES

1. Murphy CT, Galloway TJ, Handorf EA, Egleston BL, Wang LS, Mehra R, et al. Survival impact of increasing time to treatment initiation for patients with head and neck cancer in the United States. *J Clin Oncol.* 2016;34:169-78.

2. Noor A, Stepan L, Kao SS, Dharmawardana N, Ooi EH, Hodge JC, et al. Reviewing indica-tions for panendoscopy in the investigation of head and neck squamous cell carcinoma. *J Laryngol Otol*. 2018;132:901-5.
3. Sobin L, Gospodarowicz M, Wittekind C. *TNM classification of malignant tumours*. 7th ed. Hoboken (NJ): John Wiley & Sons, Inc.; 2011.
4. Franco J, Elghouche AN, Harris MS, Kokoska MS. Diagnostic delays and errors in head and neck cancer patients: opportunities for improvement. *Am J Med Qual*. 2017;32:330-5.
5. Awan KH. Oral Cancer: Early Detection is Crucial. *J Int Oral Health*. 2014;6(5):i–ii. PMID: 2539581.
6. Pack GT, Gallo JS. The culpability for delay in treatment of cancer. *Am J Cancer*. 1938;9:443-62.
7. Balasooriya-Smeekens C, Walter FM, Scott S. The role of emotions in time to presentation for symptoms suggestive of cancer: a systematic literature review of quantitative studies. *Psychooncology*. 2015;24:1594-604.
8. Tromp DM, Brouha XD, De Leeuw JR, Hordijk GJ, Winnubst JA. Psychological factors and patient delay in pa-tients with head and neck cancer. *Eur J Cancer*. 2004;40:1509-16.
9. Brouha XD, Tromp DM, Hordijk GJ, Winnubst JA, de Leeuw JR. Oral and pharyngeal cancer: analysis of patient delay at different tumor stages. *Head Neck*. 2005;27:939-45.
10. Grafton-Clarke C, Wen Chen K, Wilcock J. Diagnosis and referral delays in primary care for oral squamous cell cancer: a systematic review. *Br J Gen Pract*. 2019;69(679):e112-e126.
11. Chen Z, King W, Pearcey R, Mackillop WJ. The relationship between waiting time for radiotherapy and clinical out-comes: a systematic review of the literature. *Radiother Oncol*. 2008;87:3-16.
12. Teppo H, Koivunen P, Hyrynkangas K, Alho OP. Diagnostic delays in laryngeal carcinoma: professional diagnostic delay is a strong independent predictor of survival. Head Neck. 2003;25:389-94.
13. Teppo H, Alho OP. Relative importance of diagnostic delays in different head and neck cancers. *Clin Otolaryngol*. 2008;33:325-30.
14. Goy J, Hall SF, Feldman-Stewart D, Groome PA. Diagnostic delay and disease stage in head and neck cancer: a sys-tematic review. *Laryngoscope*. 2009;119:889-98.
15. Vaisanen JA, Syrjala AM, Pesonen PR, Pukkila MJ, Koivunen PT, Alho OP. Characteristics and medical-care-seeking of head and neck cancer patients: a population-based cross-sectional survey. *Oral Oncol*. 2014;50:740-5.
16. Noonan B. Understanding the reasons why patients delay seeking treatment for oral cancer symptoms from a primary health care professional: an integrative literature review. *Eur J Oncol Nurs*. 2014;18:118-24.
17. Tromp DM, Brouha XD, Hordijk GJ, Winnubst JA, de Leeuw JR. Patient factors associated with delay in primary care among patients with head and neck carcinoma: a case-series analysis. *Fam Pract*. 2005;22:554-9.
18. Carvalho AL, Pintos J, Schlecht NF, Oliveira BV, Fava AS, Curado MP, et al. Predictive factors for diagnosis of advanced-stage squamous cell carcinoma of the head and neck. *Arch Otolaryngol Head Neck Surg*. 2002;128:313-8.
19. Tromp DM, Brouha XD, Hordijk GJ, Winnubst JA, Gebhardt WA, van der Doef MP, et al. Medical care-seeking and health-risk behavior in patients with head and neck cancer: the role of health value, control beliefs and psychological distress. *Health Educ Res*. 2005;20:665-75.
20. Stefanuto P, Doucet JC, Robertson C. Delays in treatment of oral cancer: a review of the current literature. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2014;117:424-9.
21. Tromp DM, Brouha XD, Hordijk GJ, Winnubst JA, de Leeuw RJ. Patient and tumour factors associated with ad-vanced carcinomas of the head and neck. *Oral Oncol*. 2005;41:313-9.
22. van Harten MC, Hoebers FJ, Kross KW, van Werkhoven ED, van den Brekel MW, van Dijk BA. Determinants of treatment waiting times for head and neck cancer in the Netherlands and their relation to survival. *Oral Oncol*. 2015;51:272-8.
23. Primdahl H, Linnet Nielsen A, Larsen S, Andersen E, Ipsen M, Lajer C, et al. Changes from 1992 to 2002 in the pretreatment delay for patients with squamous cell carcinoma of larynx or pharynx: A Danish nationwide survey from DAHANCA. *Acta Oncologica*. 2006;45:156.
24. Lyhne NM, Christensen A, Alanin MC, Bruun MT, Jung TH, Bruhn MA, et al. Waiting times for diagnosis and treatment of head and neck cancer in Denmark in 2010 compared to 1992 and 2002. *Eur J Cancer*. 2013;49:1627-33.
25. Amir Z, Kwan SY, Landes D, Feber T, Williams SA. Diagnostic delays in head and neck cancers. *Eur J Cancer Care* (Engl). 1999;8:198-203.
26. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. *Br J Cancer*. 2009;101(2):S5-S8.
27. Vedsted P, Olesen F. Early diagnosis of cancer-the role of general practice. *Scand J Prim Health Care*. 2009;27:193-4.
28. Osazuwa-Peters N, Adjei Boakye E, Hussaini AS, Sujijantarat N, Ganesh RN, Snider M, et al. Characteristics and predictors of oral cancer knowledge in a predominantly African American community. *PLoS One*. 2017;12(5):e0177787.