Causes for delay before specialist consultation in head and neck cancer

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Abstract

Background: Head and neck cancers are often diagnosed at a late stage, thus resulting in a generally poor prognosis. This is partly attributable to patients' hesitancy in seeking treatment. However, the length and causes of these patient delays remain relatively unknown.

Material and methods: We included all new head and neck cancer patients treated at our tertiary care center between 2016 and 2017. Using a patient questionnaire, we collected data on patients´ symptoms and other factors related to seeking medical care, and recorded both patient- and primary health care--related delays. We then compared the data collected from these patients to patient and tumor characteristics collected from hospital records, and analyzed various causes for delay before a specialist consultation to the Department of Otorhinolaryngology – Head and Neck Surgery.

Results: Among the patients (n = 142) in our study, the median patient delay was 35 d with 73% of patients seeking medical care within 3 months. In comparison, the median primary health-care delay was 20 d. Certain symptoms influenced patient delay. Hoarseness and breathing difficulties correlated with longer patient delay while patients with a lump on the neck had a shorter delay. Patient delay was associated with certain tumor-related factors such as the tumor site and the presence of regional metastases, which resulted in shorter patient delay. None of the patient-related factors appeared to impact delay. Important factors influencing primary health-care delay included the initial location visited and whether any follow-up visit was scheduled or not.

Conclusions: Although most patients sought medical advice without a major delay and were adequately referred, we found that long delays existed. Raising awareness of the symptoms of head and neck cancer among general population and health-care providers is probably the best way to get patients to curative treatment without delay.

Introduction

Head and neck cancer (HNC) is the seventh most common non-skin cancer worldwide with an estimated 700,000 new cases diagnosed annually [1]. Survival of head and neck cancer (HNC) remains low despite advanced treatment modalities [1], whereby the stage of disease markedly affects survival [3]. Many studies support the notion that delays affect survival [2-6]. The underlying causes are multifactorial and require evaluation. General practitioners (GP) play a crucial role in symptom recognition and cancer diagnostics [7]. Further, patients' response to bodily sensations and symptoms vary, thus affecting their search for medical care [8]. Patients with early stage disease can often be managed with single modality treatment, with fewer recurrences in follow-up and better overall survival compared with advanced stage disease.

Olesen et al. [9] defines different time intervals from the first symptom until treatment initiation. Delay before treatment may be divided into patient- and health care--related delay. A health care--related delay may be further divided into primary health care (PHC) delay and a specialist health care delay. PHC includes visits to a GP, a dentist, a private otorhinolaryngologist or other specialist, or to a hospital emergency department. In our study, specialist health care delay includes the time interval from the first referral to specialist-care Department of Otorhinolaryngology – Head and Neck Surgery (ENT department) until the start of treatment. Olesen et al. [9] called this period "Delay in secondary health care".

Much effort is placed on minimizing hospital delays [5,10-12]. A recent study on hospital delays in a sample of more than 50,000 HNC patients showed that delays from diagnosis to the initiation of curative treatment independently affected survival [13]. In addition, a meta-analysis concluded that with each month without treatment, the relative risk of death was increased by 1.16 [14].

Delays may occur before patients seek medical care. Patient-related delays in the management of HNC as well as the underlying causes for these remain relatively unknown. A review of oral cancer showed that patient-related delay represents the most important factor influencing delay before treatment [15]. Socioeconomic factors and behavioral tendencies, such as the heavy use of alcohol, appear to associate with delay [16-18]. In addition, tumor site, the presence of symptoms and the heterogeneity and duration of symptoms before seeking medical care all influence delays

[19-21]. Thus, patients with mild symptoms or no perception of malignancy may seek medical attention later and may present with advanced disease [22,23]. Investigating the underlying causes for delay provides a possibility to discover means to shorten these delays. It seems reasonable to assume that any effort to decrease patient and treatment delays will improve cancer diagnosis at an earlier stage, thereby resulting in a better prognosis.

In this study, we examined the lengths and causes for delays before referral to ENT department, that is, patient and PHC delays – in a one-year cohort of all new, consecutive HNC patients treated at our institution.

Patients and methods

We included all new adult HNC patients, but not those with thyroid cancer, treated at the Department of Otorhinolaryngology – Head and Neck Surgery at the Helsinki University Hospital over a one-year period (January 14, 2015 through January 14, 2016). Our tertiary care center is the main specialist-care HNC center in Southern Finland with a referral area of 1.9 million inhabitants. To collect our data, we used a patient questionnaire and hospital records. In addition, we did not include patients with a previous HNC and patients incapable of understanding or completing the questionnaire (due to, for example, dementia). The self-administered questionnaire was distributed after the cancer diagnosis before definitive treatment or in case patient did not return the questionnaire during outpatient clinic appointment, sent by mail. It consisted of questions with pre-established set of choices on symptoms, the time of appearance of the initial symptom or sign, the time of first contact with a health care provider, the time of the first visit with a GP (or a dentist, a private otorhinolaryngologist, a hospital emergency department), the number of health care visits before referral to the ENT department and the patient's perception whether his or her disease was considered as benign or possibly malignant. The Research Ethics Board at the Hospital District of Helsinki and Uusimaa approved the study design (record number: 398/13/03/02/15) and an institutional permission was granted to complete this study. All patients who participated in the study signed a written consent form.

Data from hospital records included patient and tumor characteristics. Patient-related factors consisted of patient age, sex, history of smoking, the use of alcohol, education, employment and the place of residence (Table 1). We used commonly applied dose limits to measure the excessive use of alcohol (15 or more drinks per week for men and 8 or

more drinks per week for women) [24]. Tumor sites were documented according to ICD-10 classification codes, while TNM classification adhered to the seventh edition of the UICC cancer staging manual [25]. For our analysis, we grouped tumor sites as follows: oral cavity, oropharynx, hypopharynx, nasopharynx, larynx (differentiating glottic, supraglottic, subglottic and transglottic subsites), nose and paranasal sinuses, major salivary glands and unknown primary. In addition, tumors were divided into three groups based on histological types: squamous cell carcinomas (SCC) and its variants, salivary gland carcinomas and others. Table 2 summarizes the tumor-related characteristics.

We also used the following time intervals in our analysis: 1. Patient delay represents the time period from the appearance of the first symptom to the initial contact with a health care provider; 2. PHC delay represents the time period from the patient´s first contact with a health care provider to receiving the referral to specialist-care treatment (Figure 1). For this study, we used the term 'total delay before referral to specialist-care Department of Otorhinolaryngology – Head and Neck Surgery (ENT Department)' (TD), which included both patient and PHC delays. We double-checked the delay data from hospital records which are based on the interview at the initial visit to our ENT Department, where the doctor typically asks about the duration of symptoms. If there was a major difference in delay times between these two sources of information, we used the information found in hospital records as it is documented before the cancer diagnosis. This source of information was preferred to better avoid recall bias and patients' potential fear of being judged by doctors for postponing their search for medical care, when the nature of the disease is revealed. In most of the cases the delay information received from questionnaires were in line with the data found in hospital records. In our analysis, we compared these three delay parameters to patient symptoms as well as to patient and tumor characteristics. PHC delay was analyzed separately according to the initial place of visit: GP, private otorhinolaryngologist, dentist or hospital emergency department.

We used SPSS version 24 (SPSS, Inc., Chicago, IL, USA) for all statistical analyses. The distributions of delays skewed to the right, since most patients reported shorter delays than the average. Therefore, we employed nonparametric tests in our statistical analysis. When analyzing the delay in two independent groups, we employed the Mann-Whitney U-test; when analyzing more than two independent groups, we employed the Kruskall-Wallis test. The post-hoc p values for the Kruskall-Wallis test included a Bonferroni correction. Patient delays, PHC delays and TD are reported using the median values. Multivariable linear model was employed to adjust for other factors and to examine which factors independently associated with delay. As the distribution of delay data was positively skewed, natural log-transformation

was performed for delay variables. Factors with a p-value less than 0.2 in univariate analysis were included in the multivariable analysis. The extent of the disease was adjusted using stage instead of T class and/or N class to avoid collinearity problems. Tumor site was not used in multivariable models because of high correlation with stage. Specific symptoms were not included in the multivariable analysis as they are considered to result from the disease. Results of multivariable analysis are expressed using adjusted geometric means and their 95% confidence intervals. We considered $p < .05$ statistically significant.

Results

During the study period, 202 new HNC patients were referred to our department. From these, 6 patients refused to participate in the study, 22 patients did not return the questionnaire and 32 patients did not fulfil the inclusion criteria for several reasons. Patients were not included because they were incapable of understanding the questions due to dementia (n = 12), they were unable to speak Finnish or Swedish (n = 8), they had a previously diagnosed HNC (n = 6), they presented in a poor overall condition (n = 3) or they were incapable of completing the questionnaire due to other factors (n = 3). The remaining 142 patients completed the questionnaire and formed our study cohort.

Among the 142 patients in our study, 104 (73%) were men and 38 (27%) were women with a mean age of 62 years (range, 21--86). Table 1 summarizes other patient-related factors. SCC and its variants comprised most of the tumors (n = 117; 82%), and the most common site was the oropharynx (n = 47; 33%). Table 2 shows all of the tumor-related factors. The majority of patients (n = 138; 97%) were treated with a curative intent, while four (3%) received palliative care.

Pain represented the most common symptom reported affecting 51% of all patients. The most important main initial symptom reported by patients leading them to seek medical care was a lump on the neck (n = 45; 31%). Table 3 summarizes patient-reported symptoms and their relation to delays.

The median patient delay was 35 days (mean, 128 days; range, 0 days--8.9 years; Figure 2). The patient delay was less than three months for 72.5% of patients. We found no significant correlation between patient characteristics and patient delay (Table 1). Age did not have a statistically significant correlation with patient delay (r_s=0.031, p=0.715), primary health care delay (r_s=-0.029, p=0.733), or TD (r_s=0.031, p=0.713). However, patient delay was significantly associated with tumor site and nodal disease (Table 2), and with specific symptoms: hoarseness and difficulties breathing resulted in longer delays, whereas patients reporting a lump on the neck associated with significantly shorter delays (Table 3).

The median PHC delay was 20 days (mean, 98 days; range, 0 days--14 years) and 27% of patients sought medical advice within a week after noticing symptoms. Overall, the PHC delay was less than 3 months in 78.9% of patients. The initial place of visit significantly impacted the PHC delay (p = .016). More specifically, patients who contacted a private otorhinolaryngologist (n = 21) had a significantly shorter PHC delay before referral to ENT department than those who contacted a GP (n = 97; p = .027). Among all patients, 97 (73%) initially contacted a GP, 21 (16%) a private otorhinolaryngologist, 8 (6%) a hospital emergency department and 7 (5%) a dentist. Among patients grouped by initial contact point, the median PHC delays were 21, 4, 17 and 24 days, respectively. The remaining 9 patients did not report these data. Overall, TD, which included both patient and PHC delays, was less than 3 months in 53.5% of patients.

At the initial visit, 74 (55%) patients were referred directly to our ENT department, 29 (21%) received treatment or further examinations through a scheduled new appointment, 11 (8%) received treatment without any further appointments and 21 (16%) received no treatment or follow-up visits. The remaining 7 patients did not report these data. Patients referred for specialist treatment or who received a new appointment at the initial visit had a significantly shorter median PHC delay than patients who received no follow-up visits (14 days vs. 102 days; p < .001). On average, patients had 2 (mean 2.4) visits to a physician before a referral for specialist treatment. The number of visits significantly correlated with the PHC delay (p < .001). In addition, 55 (39%) patients had 1 visit, 33 (23%) 2 visits, 17 (12%) 3 visits, 14 (10%) 4 visits and 10 (7%) 5 or more visits. The remaining 13 patients did not report these data. The median PHC delays in these groups of patients were 11, 20, 35, 50 and 175 days, respectively. Regarding patients' perception of the GPs expression of the disease, 55 (39%) patients reported that the disease was considered benign by the physician at the initial visit, 29 (21%) were told they had a possible malignancy and 56 (40%) expressed no opinion. Two patients did not report these data.

Multivariable analysis (Table 4) revealed that patient delay and total delay in stage 0-II disease were significantly longer than in stage III-IV disease. Patients, who contacted a private otorhinolaryngologist had significantly shorter PHC delay than patients who contacted a GP. PHC delay and TD were shorter among patients, who had 1-3 visits before referral to ENT Department than those who had 4 visits or more.

Discussion

We assessed the length of and causes for patient and primary health care (PHC) delays in the management of head and neck cancer (HNC). To date, we know of no similar studies on more common malignancies, such as lung, prostate and breast cancer. Some previous studies on HNC have focused on a single or a few cancer sites [21,26]. Furthermore, some studies have divided patients into delay and non-delay groups with no clear criteria, but did not analyze delay as a continuous variable [16,21,27]. This study, however, addresses delays among all HNC sites, and includes a large variety of relevant patient- and tumor-related factors.

In our patient population consisting of all consecutive new HNC cases, patients´ delay in seeking medical care associated with specific symptoms, signs and tumor characteristics, whereas none of the patient characteristics appeared to associate with delays. About one-fourth of patients sought medical care within a week. The majority of patients (73%) sought medical care within 3 months after initially noticing symptoms. The mean patient delay in our study (4.3 months) was in agreement with a review on oral cancer that reported a mean patient delay of 3.5 to 5.4 months [15]. However, using the mean rather than the median delay can be misleading, since delays are not normally distributed. In our cohort, the majority (79%) of patients had a shorter delay than the mean, while a few patients reported very long delays of more than a year (Table 5).

The most important symptoms or signs affecting patient delay included a lump on the neck, hoarseness and difficulties breathing. A lump on the neck, typically caused by lymphatic metastasis, encouraged patients to seek medical care sooner than other symptoms. Thus, it appears that a lump on the neck presenting as a palpable tumor mass in a visible location is a symptom that raises patient awareness of potentially malignant disease, a conclusion supported by other studies [6,26]. Similarly, the presence of lymphatic metastases (N+ class) correlated significantly with shorter median

patient delay (28 vs. 57 days) and total delay before referral to ENT department (TD) (48 vs. 116 days) [23]. Avoiding disease progression due to delays is of utmost importance to improving the possibility for prompt curative treatment for locally advanced disease [20]. By contrast, hoarseness correlated with longer patient delay. Hoarseness represents a common symptom in numerous benign conditions and is a well-known adverse effect of smoking that often appears gradually. In glottic cancer, hoarseness might be the only symptom. Hence, patients may easily misjudge the nature of their symptom and postpone seeking medical care. In fact, physicians usually assessed hoarseness correctly as a sign of malignancy and, therefore, PHC delay was short. Difficulties in breathing also resulted in a longer patient delay and longer TD. This finding might seem counterintuitive since one might assume that difficulty breathing would lead a patient to seek medical care immediately. After reviewing the data, it seemed that some patients reporting breathing problems in fact suffered from nasal obstruction. The presence of pain or its intensity had no effect on delays among our study population, an observation similarly reported by Amir et al. [19]. Even if patients required painkillers daily, their delay in seeking medical care was not shorter. It seems that currently available pain medications adequately relieve pain, thus patients do not suspect cancer. Contrary to our findings, Väisänen et al. [23] found that patients experiencing pain reported shorter patient delay.

In addition, we found that none of the sociodemographic factors (age, sex, education, employment, place of residence) affected delay times, a finding consistent with other studies [6,19,20,26,28]. In our cohort, excessive alcohol consumption did not correlate with patient delay since both current and previous heavy drinkers exhibited similar delays compared to moderate drinkers and those who reported complete abstinence. Based on our study, we may only speculate the possible reasons why alcohol use may alter medical care seeking behavior. Other studies found an association between excessive alcohol consumption and longer patient delay [16,17]. Our study also revealed no correlation between tobacco smoking and patient delay. In two other studies, heavy smokers had generally shorter patient delay than light smokers [16,20]. Brouha et al. [16] suggest that this finding might be explained by the fact that heavy smokers acknowledge their increased risk for HNC and are more aware of any possible signs and symptoms of cancer. Yet, Väisänen et al. [23] reported that almost 50% of patients who smoke remained oblivious to this risk. Furthermore, we found no impact from patient employment on patient delay. In the literature, findings regarding the effect of socioeconomic status on patient delay vary. Some researchers reported that a lower socioeconomic status leads to longer patient delays [28,29], although a study from Great Britain did not support this hypothesis [20]. Similar to findings from Great Britain, however, the Finnish national public health care system allows patients to seek medical

care regardless of income, which may explain these differences across studies [20,28,29]. In our cohort, educational level and delays were not correlated, a finding consistent with Noonan et al. [28]. Patients' psychological and psychosocial factors influence health behavior but for practical reasons they were not examined in this study [30,31].

Tumor characteristics are crucial. Often, the tumor site, size, invasion to surrounding tissues and possible metastases cause diverse symptoms and eventually lead a patient to seek medical care. In this study, tumor site significantly correlated with patient delay and TD. The most notable difference was found for laryngeal cancers. Specifically, patients with supraglottic cancer had a median patient delay of 14 days compared to glottic cancer with a median delay of 133 days. Supraglottic tumors are often larger before they cause notable symptoms [21]. Blocked nose is a common symptom in the general population and thus cause indifference about this symptom. This might explain long delays for patients with tumors of the nose and paranasal sinuses. In the literature, the relationship between cancer site and patient delay vary greatly. Some studies reported a correlation between cancer site and patient delay [20,21], while others did not [6,19,23,26]. Patients with a salivary gland carcinoma, which tends to grow slowly, reported considerably longer PHC delay in our cohort than those with SCC. We found no correlation between T class and patient delay, a finding consistent with other studies [19,23,26]. At some sites, tumors can become fairly large before causing any notable symptoms, while the severity and emergence of symptoms vary. A positive N class tumor correlated with shorter patient delay and TD, which represented the primary cause of the correlation between more advanced disease stage and a shorter delay. The association between the stage of the disease and patient delay has been extensively studied with varying findings [6,10,21,23,26,27]. Patients may also experience various symptoms and the intensity of symptoms in a different way, which might affect the latency to seek for medical care [8].

The type of first contact with medical care patients reported played a crucial role in their referral to specialist care. A visit to a private otorhinolaryngologist more often resulted in a referral to a specialist for treatment during the initial visit with a significantly shortened PHC delay than after visiting a GP. In addition, patients with a scheduled follow-up appointment had a significantly shorter median PHC delay (14 vs. 102 days), a finding consistent with a similar study [32]. Too often, a patient's symptoms are interpreted as benign or treated as an infection (Table 6) [33]. Without information on the reference population that would represent patients with similar symptoms but who do not have cancer, it is hard to evaluate the reasons behind longer PHC delays among GPs. A GP might encounter only few new HNC patients during his/her career but thousands of patients with similar symptoms without any malignancy. This

aspect would be of interest to study in the future. Given our findings, it seems appropriate to schedule at least a follow-up visit if the patient presents with symptoms potentially caused by HNC. If symptoms persist, the patient should be referred to a specialist without delay.

Our study allowed for a structured and comprehensive data collection method. Yet, this also carries some limitations. As such, some patients were unable to complete the questionnaire for various reasons and were, therefore, not included in the study. Among these patients, palliative treatment was significantly more common (27% vs. 3%). At least some of these patients who did not fulfil the inclusion criteria would most likely have a longer delay due to their general health condition. Nevertheless, the cohort still included 70% of the annual HNC patients treated at our tertiary care center. The patient questionnaire was administrated after cancer diagnosis, which might have had an influence on the patient's ability to accurately recall the onset of symptoms and lead to falsely reconstructed sequence of events as the outcome is known. In order to minimize recall bias, the delay data were double-checked from hospital records. Furthermore, the recall bias might vary between different symptoms, as some symptoms are more noticeable than others. In addition, patient reported data are always subjective, and, thus, open to interpretation. Furthermore, if a patient reported multiple symptoms, the sequence of the emergence of symptoms remained unclear. Our study also includes patients who experienced a delay of more than a year (Tables 5 and 6). This highlights the need for continuous education and awareness raising of disease and possible cancer-related symptoms among both the general population and health care personnel. We did not investigate the effect of p16/HPV status in this study, because it has role only in certain tumor sites, almost exclusively in the oropharynx. Furthermore, the number of patients with some tumor sites remained limited. Therefore, our analysis of delays in patients presenting with tumors at different subsites calls for further study.

In conclusion, we show that symptoms, tumor-related factors and decisions made during the first contact with health care providers influence delay before specialist consultation. The majority of patients seek medical care fairly early and exceptionally long delays were fairly rare. Raising awareness of HNC symptoms among general population and GPs is the way to get patients to curative treatment without long delay.

Legends to the figures

Figure 1. Definitions of delays as used in this study.

Figure 2. Patient delay chart (n = 142 patients). Eleven patients had a delay of over one year due to the wide time range (12--107 months) not presented in this chart.

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