Diagnoses of suspected cancer in otolaryngology practices in Germany

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Abstract. The aim of this study was to estimate the prevalence of suspected head and neck cancer (HNC) diagnoses made by otolaryngologists in a population with subsequently confirmed cancer diagnoses in Germany. This study included patients with an initial documentation of confirmed cancer diagnosis made in 137 otolaryngology practices between January 2012 and December 2016 (index date). The main outcome of the study was the prevalence of diagnoses of suspected cancer in otolaryngology practices within one year prior to the first documentation of a confirmed cancer diagnosis. The association between the defined demographic and clinical variables with diagnoses of suspected cancer was analyzed using a logistic regression model. A total of 6,446 patients received a confirmed cancer diagnosis. A total of 23.1% of the population received a diagnosis of suspected cancer within 12 months prior to the first documentation of a confirmed cancer diagnosis. Patients over the age of 50 (ORs ranging from 1.44 to 1.55) and men (OR=1.52) were more likely to receive a diagnosis of suspected cancer compared with patients aged 50 or under and women. Cancer of the pyriform sinus (OR=3.00) and cancer of the thyroid gland (OR=0.27) were associated with increased and decreased odds of a diagnosis of suspected cancer compared to laryngeal cancer respectively. Overall, approximately 23% of individuals received a diagnosis of suspected cancer within a year prior to the first documentation of confirmed HNC.

Introduction

Head and neck cancers (HNCs) are the ninth most prevalent cancers in the world and are associated with high mortality rates (1). Recent research has shown that the incidence of several of these cancers has significantly increased in both men and women over the past few years in Germany (2). The study also found that the five-year overall survival rate was lower than 50%, underlining the major impact of HNCs on the global health in this country.

HNCs involve a variety of symptoms which can also be found in non-malignant disorders (e.g., dysphagia, dysphonia, and oral ulceration) (3). For example, a 2000 study including more than 350 HNC patients discovered that almost 60% of the population reported difficulties swallowing prior to treatment (4). Another work estimated that mild to severe dysphagia affected between 5 and 52% of patients diagnosed with oral, laryngeal, oropharyngeal, or hypopharyngeal tumors (5). In the case of dysphonia, Cohen and colleagues recently found that this symptom was reported by nearly 1% of individuals in a study involving 55 million people, and that in most cases it was related to acute laryngitis, nonspecific dysphonia, benign vocal fold pathology, chronic laryngitis, or laryngeal cancer (6). These findings suggest that the clinical presentation of HNCs is very unspecific, thus rendering these cancers difficult to diagnose (7,8).

Regrettably, little is known about how HNCs are diagnosed in specialized practices and about initial suspicions among otolaryngologists concerning a potential tumor based on the symptoms affecting their patients. Therefore, the goal of the present study was to estimate the prevalence of suspected HNC diagnoses made by otolaryngologists in a population with subsequently confirmed cancer diagnoses in Germany.

Materials and methods

Database. The present retrospective study used data from the Disease Analyzer database (IQVIA). This database compiles demographic, clinical, and pharmaceutical data obtained in an anonymous format from computer systems of clinical practices (9). IQVIA regularly assesses the quality and exactness of the data (e.g., diagnoses and drug prescriptions), and the Disease Analyzer database has been found to be representative of clinical practices in Germany (9). Finally, this database has already been used for previous studies focusing on cancer (10-12).

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Study population. This study included patients with an initial documentation of confirmed cancer diagnosis from 137 otolaryngology practices made between January 2012 and December 2016 (index date).

Study outcome and variables. The main outcome of the study was the prevalence of diagnoses of suspected cancer in otolaryngology practices within one year prior to the first documentation of a confirmed cancer diagnosis. The suspicion of cancer was defined using several ICD-10 codes for cancer (malignant neoplasms of lip (C00), base of tongue (C01), other and unspecified parts of tongue (C02), gum (C03), floor of mouth (C04), palate (C05), other and unspecified parts of mouth (C06), parotid gland (C07), other and unspecified major salivary glands (C08), tonsil (C09), oropharynx (C10), nasopharynx (C11), pyriform sinus (C12), hypopharynx (C13), other and ill-defined sites in the lip, oral cavity and pharynx (C14), nasal cavity and middle ear (C30), accessory sinuses (C31), larynx (C32), thyroid gland (C73), and non-Hodgkin lymphoma (C85)) in combination with the phrase 'suspicion of' or 'exclusion of'. Additionally, the following diagnoses were included and classified as 'suspected cancer': Granuloma, leukokeratosis and leukoplakia of vocal cords (J38.3), leukoplakia and other disturbances of oral epithelium, including tongue (K13.2), neoplasm of uncertain behavior of oral cavity and digestive organs (D37), neoplasm of uncertain behavior of middle ear and respiratory and intrathoracic organs (D38), neoplasm of uncertain behavior of thyroid gland (D44.0), neoplasm of uncertain behavior of parathyroid gland (D44.2), neoplasm of uncertain behavior of craniopharyngeal duct (D44.4), neoplasm of uncertain behavior of carotid body (D44.6), neoplasm of uncertain or unknown behavior of other and unspecified sites (D48).

Statistical analyses. The demographic variables included age and gender. The association between defined demographic and clinical variables and diagnoses of suspected cancer was analyzed using a logistic regression model. A P-value <0.05 was considered statistically significant. All analyses were carried out using SAS 9.3 (SAS Institute, Cary, USA).

Results

This retrospective study included 6,446 patients with documentation of a confirmed cancer diagnosis (Table I). The mean age was 62.1 years (SD=14.3 years), and 63.2% of patients were men. The three most frequent cancer diagnoses were neoplasms of larynx (23.3%), non-Hodgkin lymphoma (13.8%), and neoplasms of oropharynx (12.0%). Approximately 23.1% of the population received a diagnosis of suspected cancer within 12 months prior to the first documentation of a confirmed cancer diagnosis. The results of the logistic regression model are displayed in Table II. Patients over the age of 50 were more likely to receive a diagnosis of suspected cancer compared to patients aged 50 or under (ORs ranging from 1.44 to 1.55). In addition, these odds were also significantly higher in men than in women (OR=1.52). Compared to laryngeal cancers, cancers of pyriform sinus (OR=3.00) and of hypopharynx (OR=1.64) were associated with an increase in the probability of having received a diagnosis of suspected cancer, whereas cancers of floor of mouth (OR=0.74), of unspecified major salivary glands (OR=0.39), of ill-defined sites in the lip, oral cavity and pharynx (OR=0.39), of accessory sinuses (OR=0.35), of thyroid gland (OR=0.27) and non-Hodgkin lymphoma (OR=0.62) were associated with a decrease in this probability.

Discussion

To the best of our knowledge, this is the only study to investigate initial suspicions among specialists regarding potential malignant diagnoses. The major finding yielded by this study is that cancer was suspected by otolaryngologists only in a relatively small proportion of patients subsequently diagnosed with HNCs. Before proceeding, one must consider that the rate of suspected cancer diagnoses made by general practitioners in Germany is even lower (5%) (12). The most likely hypothesis to explain the primary result of the present analysis is that symptoms associated with HNCs can also be found in other benign disorders. In 2012, researchers demonstrated that 536,943 patients out of nearly 55 million individuals from the U.S. received diagnoses of dysphonia (0.98% of the population) (6). Additionally, the authors estimated that laryngeal cancer was only the fifth most frequent cause of dysphonia (2.2%) following acute laryngitis (42.1%), nonspecific dysphonia (31.2%), benign vocal fold pathology (10.7%), and chronic laryngitis (9.7%). In a later study, Bhattacharyya found that 9.5 million adults reported symptoms of dysphagia in the U.S. in 2012 (13). Interestingly, only one out of four patients sought medical help and only one out of three of these individuals were given a final diagnosis. Stroke (11.2%), neurological disorders (7.2%), and HNCs (4.9%) were the three most common causes of dysphagia. These two studies clearly underline the lack of specificity of the symptoms associated with tumors of the head and neck.

Another important finding of our work is that the probability of having received a diagnosis of suspected cancer was associated with several demographic and clinical variables. First, diagnoses of suspected cancer were more frequent in men and in older individuals than in women and younger individuals. This result might be explained by the fact that HNCs are more often diagnosed in older men (1,14,15). Therefore, it is possible that otolaryngologists are more likely to suspect cancer when dysphagia, dysphonia and other HNC-related symptoms are present in men and older patients compared to women and younger patients. Second, we showed that the probability of having received a diagnosis of suspected cancer varied with the type of cancer. Of particular importance was cancer of the pyriform sinus, the most common malignant tumor of the hypopharynx (16), and other cancers of the hypopharynx which were associated with a higher chance of having received this diagnosis compared to laryngeal cancers. In 2008, Hall and colleagues studied a population of nearly 600 individuals and estimated that the typical patient with squamous cell carcinoma of the hypopharynx was an unemployed man around 65 years of age with a low socioeconomic status, high comorbidity level, and frequent drinking habit (17). The presence of this specific sociodemographic profile in patients affected by common symptoms might have triggered suspicions among otolaryngologists regarding the potential malignant etiology of these symptoms. Another explanation is that cancers of the hypopharynx are difficult to detect in non-specialized practices

Table I. Baseline characteristics of the population (IQVIA, Disease Analyzer Database).

Variable	Patients with confirmed cancer diagnosis (N, %)
Total	6,446
Demographic variables	
Age (Mean, SD)	62.1 (14.3)
≤50 years	1,192 (18.5)
51-60 years	1,543 (23.9)
61-70 years	1,709 (26.5)
71-80 years	1,502 (23.3)
>80 years	500 (7.8)
Men	4,074 (63.2)
Women	2,372 (26.8)
Cancer diagnoses (ICD codes)	
Malignant neoplasm of lip (C00)	83 (1.3)
Malignant neoplasm of base of tongue (C01)	242 (3.8)
Malignant neoplasm of other and unspecified parts of tongue (C02)	400 (6.2)
Malignant neoplasm of gum (C03)	28 (0.4)
Malignant neoplasm of floor of mouth (C04)	310 (4.8)
Malignant neoplasm of palate (C05)	76 (1.2)
Malignant neoplasm of other and unspecified parts of mouth (C06)	89 (1.4)
Malignant neoplasm of parotid gland (C07)	190 (3.0)
Malignant neoplasm of other and unspecified major salivary glands (C08)	54 (0.8)
Malignant neoplasm of tonsil (C09)	422 (6.6)
Malignant neoplasm of oropharynx (C10)	773 (12.0)
Malignant neoplasm of nasopharynx (C11)	106 (1.6)
Malignant neoplasm of pyriform sinus (C12)	14 (0.2)
Malignant neoplasm of hypopharynx (C13)	420 (6.5)
Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx (C14)	51 (0.8)
Malignant neoplasm of nasal cavity and middle ear (C30)	89 (1.4)
Malignant neoplasm of accessory sinuses (C31)	137 (2.1)
Malignant neoplasm of larynx (C32)	1,491 (23.3)
Malignant neoplasm of thyroid gland (C73)	582 (9.0)
Non-Hodgkin lymphoma (C85)	889 (13.8)

due to the localization of this anatomical region. Thus, general practitioners might directly refer patients displaying hypopharyngeal symptoms to otolaryngologists for further examination. On the other hand, it is possible that a significant proportion of cancers of the mouth and of major salivary glands are diagnosed in general practices. In line with this hypothesis, we found that the probability of having received a diagnosis of suspected cancer in otolaryngology practices was significantly lower for malignant neoplasms of the floor of the mouth and of major salivary glands. Finally, cancers of the thyroid gland were associated with the lowest probability of having received a diagnosis of suspected cancer. This last finding might be explained by the fact that thyroid cancers are often diagnosed by endocrinologists in Germany (18,19).

There are several limitations which should be mentioned at this point. The major limitation of the present retrospective study is that suspected and confirmed HNC diagnoses relied only on ICD 10 codes and texts entered by otolaryngologists. It is possible that in some cases, no diagnoses of suspected cancer were documented even if the physician did indeed suspect cancer, but that patients were instead referred to hospitals with unspecified diagnoses. Of particular importance is the lack of TNM information as well as data concerning molecular markers which could have potentially increased the internal validity of the study. Second, there was no information concerning the diagnosis of HNCs in other practices (e.g., general or endocrinological practices) and in hospitals. Therefore, we were unable to investigate the prevalence of diagnoses of suspected cancer in HNC patients followed in other settings in Germany. Finally, data on socioeconomic status and lifestyle-related risk factors were also unavailable. The two main strengths of this works are the number of patients and the various types of cancer available for analyses.

Overall, approximately 23% of individuals received a diagnosis of suspected cancer within a year prior to the first

Table II. Association between demographic/clinical variables and diagnoses of suspected cancer in patients followed in otolaryngology practices (logistic regression model).

Variables	Proportion of patients with diagnoses of suspected cancer within one year prior to the date of confirmed cancer diagnosis (N,%)	Odds ratio (95% CI)[a]	P-value[a]
Total	1,490 (23.1)		
Demographic variables			
≤50 years	183 (15.4)	Reference	
51-60 years	390 (25.3)	1.54 (1.26-1.89)	<0.001
61-70 years	436 (25.5)	1.52 (1.25-1.85)	<0.001
71-80 years	362 (24.1)	1.44 (1.18-1.77)	<0.001
>80 years	119 (23.8)	1.55 (1.18-2.02)	0.001
Male	1,097 (26.9)	1.52 (1.33-1.75)	<0.001
Female	393 (16.6)	Reference	
Cancer diagnoses			
Malignant neoplasm of lip (C00)	24 (28.9)	1.11 (0.68-1.81)	0.679
Malignant neoplasm of base of tongue (C01)	54 (22.3)	0.74 (0.54-1.03)	0.073
Malignant neoplasm of other and unspecified parts of tongue (C02)	111 (27.8)	1.07 (0.85-1.38)	0.588
Malignant neoplasm of gum (C03)	6 (21.4)	0.77 (0.31-1.93)	0.580
Malignant neoplasm of floor of mouth (C04)	68 (21.9)	0.74 (0.55-0.99)	0.040
Malignant neoplasm of palate (C05)	17 (22.4)	0.81 (0.47-1.42)	0.468
Malignant neoplasm of other and unspecified parts of mouth (C06)	18 (20.2)	0.71 (0.42-1.21)	0.208
Malignant neoplasm of parotid gland (C07)	46 (24.2)	0.97 (0.68-1.38)	0.850
Malignant neoplasm of other and unspecified major salivary glands (C08)	6 (11.1)	0.39 (0.16-0.92)	0.031
Malignant neoplasm of tonsil (C09)	111 (26.3)	0.95 (0.74-1.21)	0.672
Malignant neoplasm of oropharynx (C10)	174 (22.5)	0.84 (0.69-1.04)	0.109
Malignant neoplasm of nasopharynx (C11)	20 (18.9)	0.68 (0.41-1.13)	0.135
Malignant neoplasm of pyriform sinus (C12)	7 (50.0)	3.00 (1.03-8.76)	0.044
Malignant neoplasm of hypopharynx (C13)	161 (38.3)	1.64 (1.31-2.07)	<0.001
Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx (C14)	7 (13.7)	0.39 (0.18-0.88)	0.024
Malignant neoplasm of nasal cavity and middle ear (C30)	20 (22.5)	0.86 (0.51-1.44)	0.568
Malignant neoplasm of accessory sinuses (C31)	15 (11.0)	0.35 (0.20-0.61)	0.002
Malignant neoplasm of thyroid gland (C73)	43 (7.4)	0.27 (0.20-0.39)	<0.001
Non-Hodgkin lymphoma (C85)	157 (17.7)	0.62 (0.51-0.77)	<0.001
Malignant neoplasm of larynx (C32)	425 (28.5)	Reference	

documentation of confirmed HNC. Age, gender, and the type of cancer were associated with the probability of receiving this suspected diagnosis.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

KK, ML, LS, ID, AS and LJ contributed substantially to the conception, design, and interpretation of the data, revised the manuscript critically for important content and gave the final approval of the version to be published.

Ethics approval and consent to participate

German law allows the use of anonymous electronic medical records for research purposes under certain conditions. According to this legislation, it is not necessary to obtain informed consent from patients or approval from a medical ethics committee for this type of observational study that contains no directly identifiable data. Therefore, no waiver of ethical approval was obtained from an Institutional Review Board or ethics committee. The authors had no access to any identifying information at any moment during the analysis of the data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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