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Differential survival trends for patients with tonsillar, base of tongue and tongue cancer in Sweden

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SUMMARY

Tonsillar, base of tongue and tongue cancer have similar anatomical and histopathological appearances but present differences in prognosis. Human papillomavirus (HPV) is a known risk factor for tonsillar and base of tongue cancer, and a survival benefit has been shown for these tumors; however, HPV prevalence in tongue cancer is low. Tonsillar, base of tongue and tongue cancer patients registered in the Swedish Cancer Registry between 1960 and 2004 were followed from the date of cancer diagnosis until death, emigration out of Sweden, or the end of a follow-up (5 years since cancer diagnosis), whichever occurred first. The relative survival rate was computed as the ratio of the observed to the expected survival rate, in which the latter was inferred from the survival of the entire Swedish population in the same age, sex and calendar year stratum. The relative survival rate has improved significantly over time for patients with tonsillar and base of tongue cancer although delineated by different patterns. However, the relative survival rate in tongue cancer patients exhibited only a very modest improvement during the same time period. Contrary to the overall improved survival for patients with tonsillar and base of tongue cancer, the patients with tongue cancer show a very modest improvement in Sweden since 1960. Further studies are warranted to elucidate more effective treatment options for tongue cancer patients.

Introduction

In Sweden, the incidence of tonsillar and base of tongue cancer has increased significantly over the last 30–40 years, while both the prevalence of known risk factors, such as smoking and heavy alcohol consumption, and the incidence of other smoking-related cancers have decreased.[1,2]

Human papillomavirus (HPV) has been hypothesized to be involved in the carcinogenesis of oropharyngeal cancer, and accumulating molecular and epidemiological data now show that high-risk types of HPV are responsible for a subset of oropharyngeal cancer.[3–5] Based on these findings, the International Agency for Research on Cancer (IARC) now recognizes HPV as a risk factor for oropharyngeal cancer. HPV occurs in 45–93%[6,7] of studied tonsillar cancer cases, and the prevalence of HPV in tonsillar cancer has increased significantly over the last decades. In fact, HPV is hypothesized to be responsible for a threefold increase observed both in the incidence and proportion of HPV-positive tonsillar cancer in Sweden over the last few decades.[7,8] Base of tongue cancer is the second most common oropharyngeal cancer in Sweden,[9] and although base of tongue cancer resembles tonsillar cancer histopathologically, previous studies have shown that its prognosis is worse.[10–12] Our group and others have shown that the prognosis for patients with HPV-positive tonsillar and base of tongue cancer is better than for patients with HPV-negative tumors, which is independent of nodal status, age, stage, tumor differentiation or gender.[5,13–16] Cancer in the oral tongue is usually associated with poor prognosis. Using the SEER database, Rusthoven and colleagues[17] found that the survival for this tumor group has not improved between 1988 and 2004, although some conflicting results have been reported.[18,19] In contrast to tonsillar cancer, HPV prevalence in oral tongue tumors is still low, and no distinct correlation between HPV prevalence and the prognosis of tongue cancer patients has been observed.[20,21]

Hakulinen and colleagues assessed the changes of survival and incidence in oral and oropharyngeal cancers in the Nordic countries. However, they analyzed the trends for tongue and base of tongue cancer together and included nasopharynx and hypopharynx in the oropharyngeal group.[22]

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Chaturvedi and colleagues showed an improved survival in potentially HPV-positive oral squamous cell carcinomas in comparison to potentially negative carcinomas in a large cohort.[23] To what extent the results of this study by Chaturvedi can be extrapolated to the Swedish population is yet unknown. In order to explore the survival trends of these cancer types, we used data from the Swedish Cancer Registry to assess the changes in the relative survival over time.

Material and methods

The Swedish Cancer Registry was established in 1958, and physicians throughout Sweden have been reporting all cancer cases to the registry. Because both clinicians and pathologists/cytologists report cancer cases based on biopsies, fine needle aspiration or surgically resected tissue, many cases have been verified twice. The Swedish Cancer Registry has been estimated to be 98% complete from 1960 onwards but not during its first two years (1958 and 1959).[24,25]

The registry has used the 7th version of the International Classification of Diseases (ICD-7) as its coding scheme during the entire study period. Data available in the registry include the following: a 10-digit personal registration number assigned to all Swedish residents, gender, date of diagnosis, age at diagnosis, basis of diagnosis, index for cancer found incidentally in autopsy, index for first or secondary cancers and pathology code.

To avoid the effect due to the occurrence of other cancers on survival rates, we only included primary tonsillar cancer or tongue cancer, i.e., data on patients without any previously diagnosed cancer in the Cancer Registry. The inclusion criteria were the following: ICD-7 code 145.0 for tonsillar cancer, ICD-7 code 141 for tongue cancer and the pathology codes 146 and 196 for squamous cell carcinoma and undifferentiated carcinoma, respectively. The code 141.0 represents base of tongue cancer.

The vital status of the cases was determined by linkage to the nationwide Swedish Causes of Death Registry, and any emigration out of Sweden was assessed by linkage to the nationwide Swedish Emigration Registry.

Statistical analyses

For the nationwide cohort, to explore any secular trend of survival rates, patients were grouped by calendar period of diagnosis into five groups: 1960–1969, 1970–1979, 1980–1989, 1990–1999 and 2000–2004. Patients were followed up from the date of cancer diagnosis until death, emigration out of Sweden, or at the end of a follow-up (5 years since cancer diagnosis), whichever occurred first.

The observed survival rate for each group was estimated using the life-table method.[26] The relative survival rate was computed as the ratio of the observed to the expected survival rate, in which the latter was inferred from the survival of the entire Swedish population in the same age, sex and calendar year stratum. The age-standardized relative survival rate[27] was also estimated using age distribution (<50, 50–59, 60–69, and $\geqslant$70) at cancer diagnosis among all patients. To investigate independent effects of patient characteristics along with the calendar period, we also fit gender-specific Poisson regression models for excess mortality adjusting for follow-up time, period of diagnosis and age at diagnosis.[28] This model was estimated in the framework of generalized linear models assuming a Poisson distribution for the observed number of deaths.

Results

A total of 2303 cases were diagnosed with tonsillar cancer between 1960 and 2004. After excluding 36 invalid cases, 2267 remained in the final cohort of tonsillar cancer patients. For base of tongue cancer, a cohort of 857 cases was initially identified. After excluding 82 cases with histopathology other than squamous cell carcinoma or undifferentiated carcinoma and 3 invalid cases, 772 remained in the final cohort of base of tongue cancer patients. Similarly, we excluded 119 cases with histopathology other than squamous cell carcinoma or undifferentiated cancer from the initially identified 3286 tongue cancer patients. We further excluded 26 invalid cases, leaving 3141 patients in the final tongue cancer cohort.

Table 1
Observed and relative 5-year survival for patients with tonsillar, base of tongue and tongue cancer, stratified by period and sex.

	Men				Women			
Period of diagnosis	No. of patients	Mean age	Crude observed survival (%)	Age-standardized relative survival (%)	No. of mean	Patients age	Crude observed survival (%)	Age-standardized relative survival (%)
Tonsillar cancer								
1960–1969	180	62.9	26.8 (20.6–33.5)	32.9 (19.2–49.6)	59	63.8	36.8 (24.7–48.9)	42.9 (17.1–65.4)
1970–1979	225	63.1	23.7 (18.3–29.4)	29.1 (16.8–43.0)	100	65.5	43.0 (33.2–52.4)	54.8 (30.7–72.1)
1980–1989	319	62.6	29.9 (24.9–35.0)	36.7 (25.1–48.3)	151	61.9	45.7 (37.6–53.4)	49.5 (32.9–64.2)
1990–1999	495	59.9	49.3 (44.8–53.6)	51.1 (41.8–60.1)	212	61.7	55.7 (48.7–62.1)	60.7 (45.9–72.9)
2000–2004	390	58.8	61.5 (56.5–66.2)	62.0 (51.1–71.7)	136	58.5	61.8 (53.1–69.3)	60.8 (40.5–73.5)
P value for trend			$p = 0.02$	$p = 0.03$			$p < 0.01$	$p = 0.06$
Base of tongue cancer								
1960–1969	45	67.4	20.0 (9.9–32.7)	22.2 (10.3–50.5)	14	66.4	28.6 (8.8–52.4)	26.2 (14.1–70.0)
1970–1979	113	64.6	15.2 (9.3–22.4)	18.8 (6.1–36.7)	28	71.8	39.3 (21.7–56.5)	45.0 (32.5–71.4)
1980–1989	136	63.5	28.7 (21.3–36.4)	32.0 (16.5–49.5)	49	66.1	28.6 (16.8–41.5)	33.2 (9.0–60.2)
1990–1999	147	61.6	39.3 (31.4–47.1)	41.1 (24.7–57.5)	58	63.4	55.2 (41.6–66.9)	58.3 (29.8–77.7)
2000–2004	135	61.6	50.4 (41.7–58.4)	51.3 (32.7–67.8)	47	63.3	50.5 (35.5–63.8)	52.5 (22.1–76.2)
P value for trend			$p = 0.02$	$p = 0.01$			$p = 0.13$	$p = 0.12$
Tongue cancer								
1960–1969	250	63.9	32.8 (27.1–38.7)	39.3 (25.7–53.2)	249	69.3	37.7 (31.6–43.7)	48.3 (33.0–62.1)
1970–1979	338	64.0	37.1 (32.0–42.2)	45.5 (32.7–58.1)	284	70.8	41.3 (35.6–47.0)	56.3 (41.3–68.3)
1980–1989	421	61.9	38.0 (33.4–42.7)	42.1 (31.7–52.7)	323	69.5	38.1 (32.8–43.4)	49.0 (35.8–61.1)
1990–1999	479	62.3	41.0 (36.6–45.4)	44.5 (34.8–54.1)	342	66.9	45.8 (40.5–51.0)	54.6 (42.5–65.2)
2000–2004	247	60.9	42.2 (35.9–48.2)	43.9 (30.8–56.7)	208	66.3	52.4 (45.4–58.9)	60.4 (44.4–73.6)
P value for trend			$p < 0.01$	$p = 0.36$			$p = 0.05$	$p = 0.19$