

Chapter 8

Cancer of the Larynx

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INTRODUCTION

The larynx, positioned in the neck slightly below the point where the pharynx divides into separate respiratory and digestive tracts, is critical to breathing, swallowing, and speaking. The glottis is the portion of the larynx where the vocal cords are located. The area above the vocal cords is referred to as the supraglottis and that below the vocal cords as the subglottis.

This chapter provides survival analyses for 14,950 histologically confirmed adult cases of cancer of the larynx. Cases were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). Cancer of the larynx is second only to oral cavity cancer as the most common cancer of the upper aerodigestive tract (1). Tobacco and alcohol use are widely recognized as the key causative factors for many of these tumors (2). The cell type of origin for the vast majority of these tumors is squamous cell (3).

MATERIAL AND METHODS

The NCI contracts with medically oriented nonprofit institutions, such as universities and state health departments, to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous

cell carcinomas of the skin and in situ carcinoma of the uterine cervix.

SEER selects participating institutions on the basis of two criteria: their ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. At times, registries will withdraw; at times, registries will be added. This analysis is based on data from 12 geographic areas, that collectively contain about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, Seattle, San Jose, and Los Angeles; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, the others for 1988 to 2001.

To ensure maximal ascertainment of cancer cases, each registry abstracts the records of all cancer patients in hospitals, laboratories, and all other health service units that provide diagnostic services. Data collected by SEER registries on each patient include patient demographics, primary tumor site, tumor morphology, diagnostic methods, extent of disease, and first course of cancer-directed therapy. A separate record is coded for each primary cancer. All patients are followed from diagnosis to death, allowing detailed survival analysis.

Table 8.1: Cancer of the Larynx: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

| Number Selected/Remaining | Number Excluded | Reason for Exclusion/Selection |
|---------------------------|-----------------|--|
| 19,807 | 0 | Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only) |
| 16,660 | 3,147 | Select first primary only |
| 16,516 | 144 | Exclude death certificate only or at autopsy |
| 16,445 | 71 | Exclude unknown race |
| 16,433 | 12 | Exclude alive with no survival time |
| 16,428 | 5 | Exclude children (Ages 0-19) |
| 15,145 | 1,283 | Exclude in situ cancers for all except breast & bladder cancer |
| 15,007 | 138 | Exclude no or unknown microscopic confirmation |
| 14,950 | 57 | Exclude sarcomas |

Table 8.2: Cancer of the Larynx: Number and Distribution of Cases by Age (20+), Sex, Race, Primary Site, Historic Stage and Grade, 12 SEER Areas, 1988-2001

| Characteristics | Cases | Percent |
|--|---------------|---------|
| Total | 14,950 | |
| Age 20+ (Years) | 14,950 | |
| 20-29 | 29 | 0.2 |
| 30-39 | 228 | 1.5 |
| 40-49 | 1,360 | 9.1 |
| 50-59 | 3,485 | 23.3 |
| 60-69 | 5,128 | 34.3 |
| 70-79 | 3,623 | 24.2 |
| 80+ | 1,097 | 7.3 |
| Sex | | |
| Male | 11,975 | 80.1 |
| Female | 2,975 | 19.9 |
| Race | | |
| White | 12,190 | 81.5 |
| Black | 2,148 | 14.4 |
| Other | 612 | 4.1 |
| Primary Site | | |
| Glottis (ICD-O C32.0) | 8,160 | 54.6 |
| Supraglottis (ICD-O C32.1) | 4,920 | 32.9 |
| Subglottis (ICD-O C32.2) | 211 | 1.4 |
| Laryngeal Cartilage (ICD-O C32.3) | 80 | 0.5 |
| Overlapping Lesion (ICD-O C32.8) | 650 | 4.3 |
| Larynx, NOS (ICD-O C32.9) | 929 | 6.2 |
| SEER Historic Stage | | |
| Localized | 7,472 | 50.0 |
| Regional | 6,373 | 42.6 |
| Distant | 538 | 3.6 |
| Unstaged | 567 | 3.8 |
| Grade (Differentiation) | | |
| Well differentiated; Grade I | 2,501 | 16.7 |
| Moderately differentiated; Grade II | 6,775 | 45.3 |
| Poorly differentiated; Grade III | 2,916 | 19.5 |
| Undifferentiated; anaplastic; Grade IV | 140 | 0.9 |
| Unknown | 2,618 | 17.5 |

SEER has collected extent of disease (EOD) information on all cancers since the inception of the program. The detail and amount of information collected, however, have varied over time.

Relative Survival

The survival analysis is based largely on relative survival rates calculated by the life-table method. The relative rate is used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as observed survival divided by expected survival, adjusts for the expected mortality that the cohort would experience from other causes of death. When relative survival is 100%, a patient has the same chance to live 5 more years as a cancer-free person of the same age and sex.

Stage Classification

SEER historic stage is used in this chapter to classify the extent of cancer within and beyond the larynx. Categories include in situ, localized, regional, distant, and unstaged. The cases with a SEER stage of in situ are excluded from this study, as seen in Table 8.1. An invasive neoplasm confined entirely to the organ is classified as localized. A neoplasm that has extended either beyond the organ or into regional lymph nodes is defined as regional. Distant stage is defined as a neoplasm that has spread to parts of the body remote from the primary tumor. Cancers that lack sufficient information to assign stage are defined as unstaged.

Exclusions

As shown in Table 8.1, patients were excluded from this study for any of the following reasons: larynx cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up, patients less than 20 years old, in situ cases, cases without microscopic confirmation, and sarcomas.

RESULTS

The demographic characteristics of the patient and morphologic characteristics of the tumors are displayed in Table 8.2. About 66% of the people in this sample are aged 60 years or older. The majority of patients are white and male. The majority of tumors were based in the glottis while approximately one-third of the tumors were supraglottic. At the time of diagnosis, one-half of the tumors were localized.

Table 8.3: Cancer of the Larynx: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

| Race/Sex | Cases | Percent | Relative Survival Rate (%) | | | | | |
|--------------|--------|---------|----------------------------|--------|--------|--------|--------|---------|
| | | | 1-Year | 2-Year | 3-Year | 5-Year | 8-Year | 10-Year |
| Total* | 14,338 | 100.0 | 87.8 | 78.3 | 72.5 | 65.0 | 57.3 | 52.8 |
| White Male | 9,761 | 68.1 | 89.3 | 80.6 | 75.1 | 68.2 | 61.0 | 56.6 |
| White Female | 2,429 | 16.9 | 85.8 | 76.0 | 70.4 | 62.1 | 54.2 | 48.6 |
| Black Male | 1,686 | 11.8 | 83.3 | 70.5 | 62.9 | 54.5 | 45.2 | 41.2 |
| Black Female | 462 | 3.2 | 81.4 | 69.8 | 63.2 | 51.2 | 41.5 | 38.9 |

* Relative survival not computed for Other Race

Race and Sex

The 1-, 3-, 5-, 8- and 10-year relative survival rates by race and gender are shown in Table 8.3 and Figure 8.1. The 5-year relative survival rate for whites was 65% and for blacks was 53%. The 5-year relative survival rate was 61% for males and 57% for females. White males had the best 5-year relative survival at 68%, followed by white females, black males, and black females. The median observed survival for both white males and white females was 79 months, while for black males it was 48 months and for black females 50 months.

Stage at Diagnosis.

In Table 8.4 and Figure 8.2 survival is stratified by SEER historic stage at diagnosis. Localized tumors account for 50% of larynx tumors followed by regional (42.6%), unstaged (3.8%) and distant (3.6%). Five-year relative survival rate varies by stage from 83% for localized to 19% for distant. The median observed survival for patients with localized disease was 115 months, regional disease was 43 months, and distant disease was 11 months.

Grade at Diagnosis

Table 8.5 presents the 1-, 3-, 5-, 8- and 10-year relative survival rates by grade at diagnosis for all cancers of the larynx. At each time interval shown there is a clear survival gradient as tumor grade goes from well differentiated to undifferentiated.

Table 8.6 presents 5-year relative survival rates by race, sex, and stage. For patients with localized disease, white males had the best survival at 85%, followed by white females 78%, black males 75%, and black females 68%. For patients with regional disease white males and females had a 5-year relative survival of about 50%, while that of black males and females was approximately 42%.

Site at Diagnosis

Relative survival for patients with tumors of the glottis, supraglottis, and subglottis is shown in Figure 8.3. The median observed survival for patients with glottic cancer at presentation was 111 months, for supraglottic tumors was 43 months, and for subglottic tumors was 30 months.

Figure 8.1: Cancer of the Larynx: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

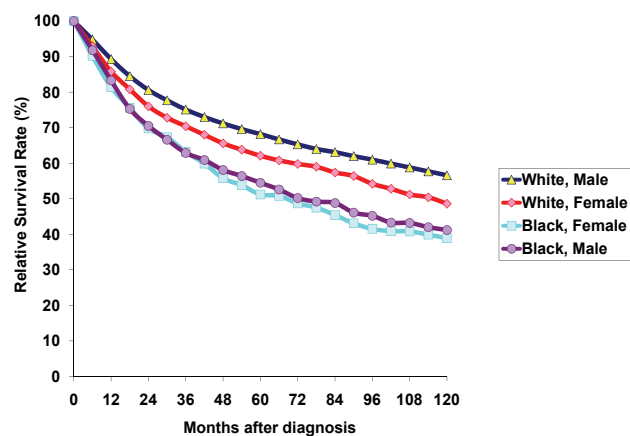


Figure 8.2: Cancer of the Larynx: Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

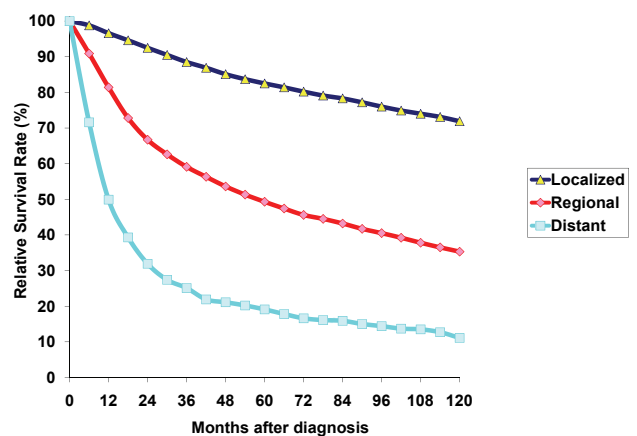


Table 8.4: Cancer of the Larynx: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

| Historic Stage | Cases | Percent | Relative Survival Rate (%) | | | | | |
|----------------|--------|---------|----------------------------|--------|--------|--------|--------|---------|
| | | | 1-Year | 2-Year | 3-Year | 5-Year | 8-Year | 10-Year |
| Total | 14,950 | 100.0 | 87.9 | 78.4 | 72.7 | 65.2 | 57.6 | 53.1 |
| Localized | 7,472 | 50.0 | 96.6 | 92.5 | 88.5 | 82.5 | 76.0 | 71.9 |
| Regional | 6,373 | 42.6 | 81.4 | 66.7 | 59.1 | 49.3 | 40.5 | 35.3 |
| Distant | 538 | 3.6 | 49.9 | 31.9 | 25.1 | 19.1 | 14.4 | 11.1 |
| Unstaged | 567 | 3.8 | 81.7 | 69.5 | 63.5 | 58.2 | 47.6 | 46.2 |

Table 8.5: Cancer of the Larynx: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Grade, Ages 20+, 12 SEER Areas, 1988-2001

| Grade | Cases | Percent | Relative Survival Rate (%) | | | | | |
|--|--------|---------|----------------------------|--------|--------|--------|--------|---------|
| | | | 1-Year | 2-Year | 3-Year | 5-Year | 8-Year | 10-Year |
| Total | 14,950 | 100.0 | 87.9 | 78.4 | 72.7 | 65.2 | 57.6 | 53.1 |
| Well differentiated; Grade I | 2,501 | 16.7 | 94.0 | 89.2 | 85.4 | 79.3 | 71.0 | 66.0 |
| Moderately differentiated; Grade II | 6,775 | 45.3 | 89.3 | 79.4 | 73.2 | 66.3 | 58.9 | 54.1 |
| Poorly differentiated; Grade III | 2,916 | 19.5 | 80.2 | 65.7 | 57.4 | 47.6 | 39.3 | 34.6 |
| Undifferentiated; anaplastic; Grade IV | 140 | 0.9 | 75.1 | 56.5 | 53.0 | 37.6 | 31.4 | 22.7 |
| Unknown | 2,618 | 17.5 | 87.4 | 80.9 | 77.3 | 70.1 | 62.9 | 60.1 |

Table 8.6: Cancer of the Larynx: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Historic Stage, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

| Historic Stage/Race | Total | Sex | | | |
|---------------------|-------|-------|---------------|--------|---------------|
| | | Male | | Female | |
| | | Cases | 5-Year RSR(%) | Cases | 5-Year RSR(%) |
| Local: | | | | | |
| White | 6,321 | 5,186 | 85.0 | 1,135 | 77.6 |
| Black | 854 | 672 | 75.1 | 182 | 67.5 |
| Regional: | | | | | |
| White | 4,988 | 3,874 | 50.6 | 1,114 | 50.0 |
| Black | 1,107 | 870 | 42.2 | 237 | 42.1 |
| Distant: | | | | | |
| White | 411 | 333 | 19.5 | 78 | 15.5 |
| Black | 106 | 84 | 20.1 | 22 | ~ |

~ Statistic not displayed due to less than 25 cases.

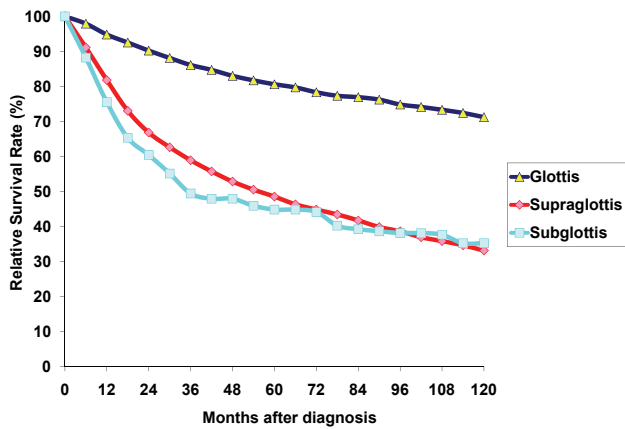
Table 8.7 presents 5-year relative survival rates as a function of site, sex, and race. For glottic tumors, white males fared best with 82% survival. For supraglottic tumors, white females had the best 5-year relative survival (53%).

In Table 8.8 and Figure 8.4 the survival of patients with glottic cancer as a function of morphologic stage at diagnosis is shown. Localized tumors accounted for 67.3% of glottic tumors followed by regional (28.7%), unstaged (2.9%) and distant (1.2%). At each time point shown relative survival varies by stage with the highest relative survival for localized disease and the lowest for distant disease at diagnosis. The median observed survival for patients with localized

disease at presentation was greater than 120 months, while patients with regional tumors had a median survival of 63 months, and those with distant disease 18 months.

In Table 8.9 and Figure 8.5 the survival of patients with supraglottic cancer as a function of morphologic stage at diagnosis is shown. Localized tumors account for 30.4% of glottic tumors, regional for 61.1%, distant for 5.5% and unstaged for 3.0%. At each time point shown relative survival decreases from diagnosis at localized to distant stage. The median observed survival for patients with localized disease at presentation was 73 months, regional disease was 36 months, and for distant disease was 11 months.

Figure 8.3: Cancer of the Larynx: Relative Survival Rates (%) by Subsite, Ages 20+, 12 SEER Areas, 1988-2001



DISCUSSION

Cancer of the larynx is closely related to tobacco and alcohol use. It remains primarily a disease of white men, although the number of women with this disease is increasing. For example, DeRienzo, Greenberg, and Fraire (4) found that the male-to-female ratio was 5.6 to 1 for the years of 1959-1973 and 4.5 to 1 for 1974-1988. In the population reported here, the male-to-female ratio in 1988-1998 decreased to 4 to 1. Small differences in relative survival by race were observed in this data. However, other researchers (5) have shown that these racial disparities disappear after controlling for other prognostic factors, including: treatment delay, type of therapy, and quality of care.

The vast majority (>95%) of tumors are of squamous cell origin. The overall prognosis is good and sub-site survival rates are much better for patients with glottic cancer than supraglottic or subglottic. This difference in survival may be due to the fact that the larynx is anatomically and clinically divided into these three distinct subsites. Anatomically, the glottis has much fewer lymphatic channels and vascular support than either the supraglottis or subglottis. Clinically, patients with glottic cancer will develop symptoms, such as hoarseness, earlier in the course of their disease than patients with tumors of the supraglottis or subglottis. The paucity of lymphatic and vascular supply and the development of symptoms earlier in the course of glottic cancer may explain why patients with glottic tumors generally present with local, rather than regional, disease. For all sub-sites, survival was strongly related to morphologic extent of disease at the time of diagnosis. Survival was also related to the degree of differentiation; as the degree of differentiation decreased survival worsened.

It would be informative to be able to include in analyses of larynx cancer survival host factors like comorbidity (6, 7) and performance status (8); socioeconomic factors like income and education; and tumor biology factors like p53 and epidermal growth factor receptor. However, many of these variables are not routinely found in medical records and are not generally part of the SEER analytic files.

Table 8.7: Cancer of the Larynx: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Race, Primary Site and Sex, Ages 20+, 12 SEER Areas, 1988-2001

| Primary Site/Race | Total | Male | | Female | |
|---------------------|-------|-------|---------------|--------|---------------|
| | Cases | Cases | 5-Year RSR(%) | Cases | 5-Year RSR(%) |
| Glottis | | | | | |
| White | 6,849 | 5,887 | 82.2 | 962 | 78.0 |
| Black | 956 | 830 | 72.8 | 126 | 69.9 |
| Supraglottis | | | | | |
| White | 3,956 | 2,765 | 48.5 | 1,191 | 52.7 |
| Black | 798 | 533 | 36.9 | 265 | 45.7 |
| Subglottis | | | | | |
| White | 163 | 118 | 46.5 | 45 | 37.7 |
| Black | 35 | 25 | 30.3 | 10 | ~ |

~ Statistic not displayed due to less than 25 cases.

Table 8.8: Cancer of the Glottis: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

| Historic Stage | Cases | Percent | Relative Survival Rate (%) | | | | | |
|----------------|-------|---------|----------------------------|--------|--------|--------|--------|---------|
| | | | 1-Year | 2-Year | 3-Year | 5-Year | 8-Year | 10-Year |
| Total | 8,160 | 100.0 | 94.8 | 90.2 | 86.1 | 80.6 | 74.8 | 71.2 |
| Localized | 5,489 | 67.3 | 98.9 | 96.5 | 93.5 | 89.5 | 84.8 | 82.0 |
| Regional | 2,338 | 28.7 | 87.0 | 77.5 | 70.9 | 61.3 | 52.9 | 46.8 |
| Distant | 95 | 1.2 | 60.0 | 40.5 | 37.0 | 34.3 | 25.3 | 22.2 |
| Unstaged | 238 | 2.9 | 91.7 | 85.4 | 80.9 | 77.0 | 68.1 | 67.9 |

Table 8.9: Cancer of the Supraglottis: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

| Historic Stage | Cases | Percent | Relative Survival Rate (%) | | | | | |
|----------------|-------|---------|----------------------------|--------|--------|--------|--------|---------|
| | | | 1-Year | 2-Year | 3-Year | 5-Year | 8-Year | 10-Year |
| Total | 4,920 | 100.0 | 81.8 | 66.8 | 58.9 | 48.5 | 38.6 | 33.1 |
| Localized | 1,494 | 30.4 | 90.8 | 81.9 | 75.4 | 64.1 | 52.0 | 44.5 |
| Regional | 3,008 | 61.1 | 80.6 | 62.7 | 54.1 | 43.8 | 34.5 | 29.7 |
| Distant | 270 | 5.5 | 49.6 | 31.7 | 22.4 | 15.4 | 12.0 | 9.8 |
| Unstaged | 148 | 3.0 | 76.3 | 59.4 | 54.9 | 45.8 | 35.9 | 30.6 |

Figure 8.4: Cancer of the Glottis: Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

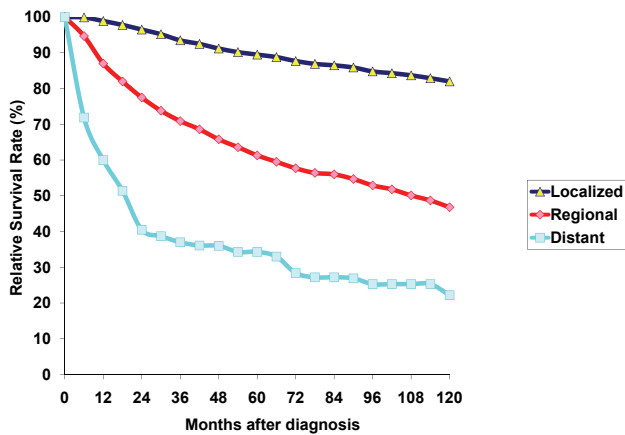
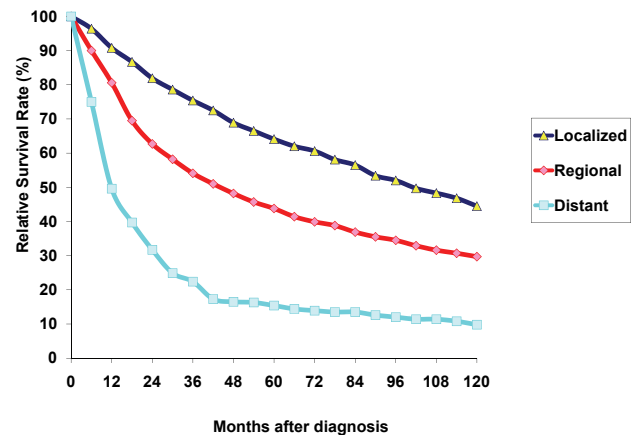


Figure 8.5: Cancer of the Supraglottis: Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001



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