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Survival outcomes in elderly patients with untreated upper aerodigestive tract cancer

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Abstract

Background—This study is an evaluation of survival in patients with upper aerodigestive tract (UADT) cancer who did not receive guideline-directed therapy.

Methods—The National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) database was examined to identify patients with invasive cancer of the UADT. Patients were classified as “untreated” if they received neither surgery nor radiotherapy. Kaplan-Meier observed survival estimates were computed and stage-specific actuarial estimates of relative survival were computed.

Results—Of 3589 untreated patients, 13.7% were black, compared to 9.5% white, and 9.2% all other races ($p < 0.0001$). Patients with Stage IV disease were more likely to be untreated than those with Stage I disease (11.9% vs 3.8%, $p < 0.0001$). Median survival was 39 months for treated patients and 4 months for untreated patients.

Conclusion—The median survival for untreated patients was 4 months. Stage, race, and primary site were independently associated with untreated status.

Keywords

Head and Neck Cancer; Survival; Epidemiology; Palliative Care; SEER

Introduction

Many factors are involved in making treatment recommendations for patients diagnosed with upper aerodigestive tract (UADT) cancer. Treatment outcome data based on primary tumor location and stage is an important piece of information that patients, their families, and

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physicians use in developing a plan. The first decision patients must make is whether they wish to have curative treatment or engage in a palliative regimen. This decision is especially relevant for older patients, whose life expectancy without cancer is shorter. Older patients also may have comorbidities that impact their ability to complete and recover from rigorous curative treatment.¹ Finally, as with younger patients, older patients' wishes about health and quality of life, and how best to maintain them, are an important part of treatment selection. As treatment options are weighed, many patients wish to know what their course would be like if they do not choose to have curative treatment. Several reports describe survival outcomes after curative treatment for UADT cancer, but little is known about survival outcomes in patients who choose not to receive guideline-based curative treatment.²⁻³

The objective of this study was to provide patients and clinicians with data regarding expectations for survival for elderly patients with UADT cancers who do not receive curative treatment. We also sought to characterize the patients that have chosen that pathway.

Methods

This study did not require approval from the University of Iowa Institutional Research Board as it was not considered Human Subject Research. We analyzed data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) cancer registry program.⁴ Patients diagnosed with cancer at the following subsites between 1983 and 2011 were identified: oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx. We included patients age 70 and older at the time of diagnosis with microscopically confirmed invasive squamous cell carcinoma whose vital status was actively followed by a SEER registry, and excluded cases entered into registry databases only through death certificates.

Demographic and disease characteristics including age, gender, race, primary site of disease, and derived American Joint Committee on Cancer (AJCC) tumor stage were examined.⁵ For each case, we recorded delivery of cancer-directed surgery of the primary site and any form of radiotherapy. As all guideline-directed curative therapy for cancers at these sites includes either surgery, radiotherapy, or both, patients who received neither surgery nor radiotherapy were classified as "untreated." Patients were defined as "treated" if they received surgery, radiotherapy, or both.

Characteristics of the treated and untreated cohorts were compared using Chi-square analysis for categorical variables and t-tests for continuous variables. Kaplan-Meier survival estimates were computed for treated and untreated patient cohorts to calculate median survival for each group. This computation was repeated for the cohort of patients who had no other prior or concurrent cancers reported in SEER.

To adjust for differences in age, sex, race, and calendar year distribution between the two cohorts, we calculated stage-specific actuarial relative survival estimates. Relative survival compares observed survival with that expected from an age-, year-, sex-, and race-matched cohort of the U.S. population (for example, a relative survival of 50% at 12 months for a cohort means that the observed survival for those patients at 12 months is 50% of that

expected for a cohort comprising a group of individuals with the same age, sex, and race in the same years as the study cohort). Computation was performed according to the method described by Dickman using U.S. expected survival life tables and the Ederer II method. Stage-specific relative survival was calculated for the untreated group.⁶⁻⁷

Results

We identified 36,954 patients diagnosed with UADT cancer between 1983 and 2011. 32,245 patients were classified as treated; 3589 (9.7%) patients were untreated. Treatment status was unknown in 1120 and these patients were excluded from subsequent analysis. Of the 35,834 patients whose treatment status was known, there was no difference in the proportions of male and female patients who were untreated, 10.0% and 10.1%, respectively ($p=0.58$).

Stage at presentation was associated treatment status, as shown in Table 1. Treatment status was statistically associated with stage at presentation. However, there was no clear trend toward lower likelihood of treatment at higher stage; stage II patients had the highest rate of no treatment at 12.6%. Race was also significantly associated with treatment status, as shown in Table 1, with blacks having the highest proportion of patients untreated. Primary site was also significantly associated with treatment status, with a smaller proportion of tumors at pharyngeal sites treated than those at oral cavity or laryngeal sites, as shown in Table 1. On multivariate logistic regression, stage, primary site, and race all remained statistically significant predictors of untreated status, with higher stages associated with progressively higher adjusted odds of untreated status.

The median observed survival for treated patients was 39 months, while the median observed survival for untreated patients was 4 months (Figure 1). When evaluating only patients whose index head and neck cancer was their only cancer, we identified 29,787 patients, of which 3245 (10.9%) were untreated. In this cohort, median observed survival remained 4 months. When analysis was limited to years 1983–1999, the median observed survival for untreated patients was also 4 months. Observed survival increased to 5 months for untreated patients diagnosed from 2000–2011. The Kaplan-Meier survival estimates were statistically significantly different between the 1983–1999 and 2000–2011 groups ($p=0.012$). Stage-specific relative survival estimates for untreated patients are shown in Figure 2; the majority of untreated Stage 1 patients survived at least 5 years post-diagnosis, whereas all other stages had median survival times between 4 and 8 months. Table 2 shows 1-year relative survival in untreated and treated patients.

Discussion

Treatment of UADT cancers presents great difficulty to patients. Surgical treatment can result in pain, disfigurement, and limitation of swallowing and communication, in addition to the risk of perioperative complication. A nonsurgical approach is likewise associated with high risk of both acute- and long-term morbidity.⁸ Patients diagnosed with cancer are therefore faced with deciding between life-extending but morbidity-inducing curative regimens and palliative management, in which maximizing quality of life is the primary

goal. Clinicians must facilitate the decision-making process by framing the choice in the context of the patient's overall situation and by providing critical information to the patient and family.

Patients who choose to forego curative treatment for a newly diagnosed UADT cancer do so with considerations other than their expected survival in mind. However, the survival data described in this study are important for several reasons. First, hearing that the median survival without treatment is 4–5 months provides specific detail about the gravity of the cancer diagnosis. Second, providing a quantitative description of prognosis allows patients to think more specifically about how to handle affairs should they choose no treatment. Third, and most importantly, specific prognostic information allows them to explore their own thoughts about end-of-life care, and thereby engage in a more considered planning process.

One surprising result was the outcomes of untreated Stage I patients. As expected, the vast majority receive treatment, as these tumors are generally amenable to therapy with low morbidity. However, we found that the median relative survival was not reached during the 5 years of analysis. Some patients may have had tumors small enough that biopsy resulted in no residual tumor. For Stage I patients, 70% relative survival at 1 year may be substantially greater than they might otherwise believe.

Another surprising finding was the proportion of with Stage II cancer patients who did not have treatment. One hypothesis to explain this result is that curative treatment for Stage II cancers is more difficult than that for Stage I cancers, but symptoms at presentation may not be tremendously worse, so that the balance is tipped away from treatment.

Our finding that black patients were less likely to have curative treatment, even when accounting for then effect of stage with multivariate analysis, raises the possibility of an important disparity that should be investigated further with a patient-level analysis.

There are limited descriptions in the literature of outcomes for UADT cancers which are untreated. In a retrospective analysis of nearly 800 Brazilian patients who elected no treatment of their head and neck cancer, the median observed survival was 4 months; the maximum reported survival was 4 years.⁹ That study categorized the reasons for no treatment, which were advanced untreatable tumor in 75%, poor health in 6%, and personal choice for 19%. On multivariate analysis, the only factor which predicted longer survival was performance status. In another retrospective analysis of 200 untreated H&N cancer patients from the United Kingdom (10% of all the H&N patients evaluated during the period of study), the median survival of the group was just over 3 months.¹⁰ The only significant predictor of survival was performance status.

The results of these prior studies of untreated H&N cancer patients are very similar to those reported in this study, with median 4-month survival for untreated H&N cancer. When the analysis is limited to the years 2000–2011, the median survival rose from 4 to 5 months. The statistically significant 1-month increase in survival from the 1983–1999 group to the 2000–2011 group may be related to current practices in palliative treatments. This study is unique by the size of the patient population, and the number of untreated patients in a variety of

clinical stages. In addition, use of a population-based database for this analysis allows inclusion of patients independent of any particular treatment center, thereby eliminating a potential bias related to treatment at a center large enough to assemble an institution-based cohort. It is important to note that the median survival reported in this study came about while excluding patients under age 70. We elected to study older patients because their natural life expectancy is shorter; therefore, the association between curative treatment and length of life is diminished so that the decision to receive such treatment is one that merits consideration.

Results should be interpreted with consideration of a few study limitations. We defined treatment status based on SEER variables related to surgery and radiotherapy, as these are the components of curative treatment for upper aerodigestive tract cancer. We could not distinguish patients who received definitive radiotherapy from those that received palliative radiotherapy; this imprecision would artifactually lower the median survival of the treated cohort in our analysis. The SEER database does not provide information on why guideline-based therapy was or was not undertaken (i.e. comorbidities, personal choice, access to care, etc.) We could also not analyze the use of palliative chemotherapy or “targeted” agents. Systemic therapy is not considered curative by itself, but it may bring about tumor regression and longer survival. Lack of this specific information somewhat limits the ability to directly apply this information to individual patient counseling. Finally, an analysis of the motivations of patients and clinicians in not choosing curative therapy would be relevant, but would require a prospective cohort design.

Conclusion

This population-based analysis showed that 10% of patients diagnosed with UADT cancer at age 70 or above do not receive guideline-supported curative treatment. Patients with oral cavity and larynx cancers were more likely than those with cancers at a pharyngeal site to receive treatment, and the proportion of patients receiving treatment differed based on stage at presentation. Accounting for the effects of other analyzed factors, black race was a risk factor for not receiving treatment. The median observed survival in the untreated cohort was 4 months. These findings provide important information to patients and families engaged in the difficult process of setting goals after a cancer diagnosis is made.

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Figure 1.
Observed Survival, treated and untreated patients.

Figure 2.
Survival of untreated patients stratified by cancer stage. UADT=upper aerodigestive tract.
Miss = missing stage

Table 1

Distribution of treatment status by patient and tumor characteristics

	Treated (%)	Untreated (%)	p
Sex			0.58
Female	11001 (89.9)	1241 (10.1)	
Male	21244 (90.0)	2348 (10.0)	
Stage			<.0001
Stage I	8268 (96.2)	324 (3.8)	
Stage II	4275 (87.4)	246 (12.6)	
Stage III	3372 (92.4)	276 (7.6)	
Stage IV	9908 (88.1)	1336 (11.9)	
Unknown stage	6422 (82.0)	1407 (18.0)	
Race			<.0001
White	27916 (90.5)	2934 (9.5)	
Black	2363 (86.3)	374 (13.7)	
Other	1844 (90.8)	187 (9.2)	
Unknown race	122 (56.5)	94 (43.5)	
Primary site			<.0001
Oral cavity	10964 (91.1)	1064 (8.9)	
Oropharynx	6857 (87.4)	988 (12.6)	
Larynx	11500 (88.0)	998 (8.0)	
Hypopharynx	2181 (84.4)	403 (15.6)	
Nasopharynx	743 (84.5)	136 (15.5)	

Table 2

1-year relative survival for treated and untreated patients

	Untreated	Treated
Stage I	70.6	97.1
Stage II	39.1	85.5
Stage III	27.9	75.9
Stage IV	19.5	64.1
Missing stage	42.8	84.4