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Individualized Estimation of Conditional Survival for Head and Neck Cancer Patients

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Abstract

Survival for cancer patients is usually only reported as survival from time of diagnosis. For patients who survive 1 or more years after diagnosis, however, their survival probability changes over time, and is more accurately depicted by conditional survival. The specific aim of this project was to build a survival regression model and web-based tool to make individualized estimates of conditional survival for head and neck cancer patients based on tumor and patient characteristics. Using data from the Surveillance, Epidemiology, and End Results (SEER) database, we built a prediction modeling tool that can estimate prognosis for head and neck cancer patients who have already survived a period of time after diagnosis. We believe that having more accurate prognostic information may empower both patients and clinicians to be able to make more appropriate decisions regarding follow-up, surveillance testing, and future treatment.

Keywords

Proportional Hazards Models; Models; Statistical; Regression Analysis; survival modeling; head and neck cancer

Background

A cancer patient's prognosis is usually only estimated at the time of diagnosis. Survival probability, however, changes over time, and estimates made at diagnosis are no longer applicable after a patient has survived for a period of time after diagnosis and treatment. Conditional survival (CS) is a more accurate estimate of prognosis because it accounts for the continuously changing hazard rates over time¹. CS estimates can be helpful for patients and providers who seek more accurate prognostic estimates to help guide health-related decisions^{2–4}. In our previous work, we demonstrated how conditional survival changes over time for head and neck cancer patients⁵. In this follow-up study, we constructed a survival

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Competing interests

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regression model from these data to enable estimation of CS for individual patients. Using this regression model, we built an interactive web-based prediction tool that can provide customized CS predictions for head and neck cancer patients who have already survived a time period following diagnosis and treatment.

Methods

CS is derived from the concept of conditional probability in biostatistics. CS can be calculated from traditional Kaplan-Meier or actuarial life table survival data. The mathematical definition of CS¹ can be expressed as follows: $CS(y|x)$, is the probability of surviving an additional y years, given that the person has already survived x years. Let $S(t)$ be the traditional actuarial life table survival at time t . CS can be expressed as:

$$CS(y|x) = \frac{S(x+y)}{S(x)}$$

We analyzed patients from the Surveillance, Epidemiology, and End Results (SEER) database (April 2010 release) diagnosed with head and neck cancer between 1995 and 2003 with follow-up through 2007. Patients with site code “oral cavity and pharynx” were selected.

A Cox proportional hazards (CPH) semi-parametric model was constructed using these data. The primary outcome variable was overall survival, conditional upon 0 to 5 years already survived. Patient covariates included were age, race and gender. Tumor characteristics included were tumor site, SEER summary stage, and grade. All covariates were converted to binary variables, except for age, which was modeled as a continuous variable and fitted to a smoothed restricted cubic spline function. The model was internally validated for both discrimination and calibration using bootstrap correction with 100 resamples. Discrimination was evaluated using the concordance index (C-index), which is the probability that given a pair of randomly selected patients, the model correctly predicts which patient will fail first.

The CPH regression model was incorporated into a web-browser based software tool. Users can enter specific tumor and patient characteristics, and the tool will calculate a customized conditional survival curve specific to that individual patient.

This research study was determined to be exempt from Institutional Review Board (IRB) approval by the Oregon Health & Science University IRB.

Results

A total of 35,027 head and neck cancer patients were included in the analysis. Ten year actuarial survival data were used to calculate 5-year observed CS in categories of stage, age, gender and race. Figure 1 shows 5-year CS by SEER summary stage, and depicts how CS changes with each additional year survived. Patients with more advanced regional disease (i.e., with both direct extension and positive lymph nodes) had lower 5-year CS than patients with localized disease, at the time of diagnosis (34% vs 64%) and at five years out from diagnosis (67% vs. 74%). As time elapses from diagnosis, however, the differences in prognoses between early stage and advanced stage narrows. Patients aged 60 years and over at diagnosis had lower CS than those under 60 years, both at diagnosis (39.5% vs. 62.5%) and at five years from diagnosis (56.7% vs. 83.2%). For all stages of disease, men had slightly lower 5-year survival than women, both at diagnosis (48.6% vs. 50.9%) and after 5 years from diagnosis (69.9% vs. 72.1%).

A CPH model was built and all covariates were found to be statistically significant prognostic factors in this multivariate analysis. The C-index was 0.70 indicating good discrimination. The calibration curve showed good agreement between predicted and observed outcomes.

An interactive web-based prediction tool was built from the CPH survival model (Figure 2). The user enters specific information about a patient, including time already survived, and the tool estimates the likelihood that the patient will survive up to an additional 5 years. The interactive nature of the tool allows the user to see how a patient's prognosis often improves with additional time survived since diagnosis. This web-based prediction tool is available for public use and can be found at <http://skynet.ohsu.edu/nomograms>.

Discussion

It is important to remember that the accuracy of this prediction tool is dependent upon the limitations of the historical SEER data. For example, if the model predicts a worse outcome for certain ethnic groups, this may be a reflection of historical patterns of socioeconomic disparities, and not necessarily an unalterable poor prognosis. This prediction tool should always be used in conjunction with other clinical indicators of prognosis.

In conclusion, we have built a web-based interactive prediction tool can be used by patients and providers to make individualized estimates of updated prognosis for patients who have already survived up to 5 years after diagnosis. Using this tool, patients and providers can more accurately quantify changes in prognosis over time. This information is potentially of great interest to patients, clinicians, and researchers, and can be used within the context of patient care. We believe that more accurate estimation of CS will permit improved risk assessment and ultimately lead to better care for head and neck cancer survivors.

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Figure 1.

Comparison of 5-year conditional overall survival by SEER summary stage for head and neck cancer patients. Each bar represents the likelihood that the patient will survive an additional 5 years, given that s/he has already survived a certain number of years since diagnosis. Error bars depict 2 times the standard error of each estimate. (Abbreviations: LN = Lymph Nodes, Direct Ext = Direct Extension)

Head & Neck Cancer

After your patient has already survived X months, what is their updated prognosis?

Enter the patient details below and the number of months since diagnosis, and this tool will calculate the patient's conditional survival, i.e., the likelihood of surviving additional years given that they have already survived a period of time.

Age: 65	Site: Oropharynx
Sex: Male	Stage: Regional-Lymph Nodes
Race: White	Grade: Grade II: Moderately Differentiated

Probability of surviving additional years given 24 months already survived: Calculate

Figure 2.

Online survival prediction calculator for making customized estimates of conditional overall survival for a head and neck patient with the specific parameters given. In this example, each bar represents the likelihood that this patient will survival additional years (0–5 yrs), given that the patient has already survived 24 months since diagnosis. This browser-based tool is available at <http://skynet.ohsu.edu/nomograms>.