Available online at www.sciencedirect.com

ScienceDirect

EJSO xx (2016) 1–6

EJSO the Journal of Cancer Surgery

www.ejso.com

Comparing a thyroid prognostic nomogram to the existing staging systems for prediction risk of death from thyroid cancers

K.A. Pathak [a,b,*], P. Lambert [a], R.W. Nason [a,b], T. Klonisch [b]

[a] CancerCare Manitoba, Winnipeg, Manitoba, Canada
[b] Canada University of Manitoba, Winnipeg, Manitoba, Canada

Accepted 13 May 2016
Available online ■ ■ ■

Abstract

Objective: Thyroid prognostic nomogram can be applied across different histological types for predicting the individualized risk of death from thyroid cancer. The objective of this study was to compare the strength of our recently published thyroid prognostic nomogram with 12 existing staging systems to predict the risk of death from thyroid cancer.

Method: This study included 1900 thyroid cancer patients, from a population based cohort of 2296 patients, on whom adequate staging information was available. Competing risk sub-hazard models were used to compare 12 pre-existing prognostic models with the nomogram model. Their relative strengths for prediction of patients' individualized risks of death from thyroid cancer were compared using Akaike information criterion (AIC), delta AIC, and concordance index. R version 3.2.2 was used to analyze the data.

Results: Our cohort of 450 males and 1450 females included 1796 (93.4%) differentiated thyroid cancers. Amongst the compared models, thyroid prognostic nomogram model appeared to be better than other models for predicting the risk of death from all non-anaplastic thyroid cancer (concordance index = 94.4), differentiated thyroid cancer (concordance index = 94.1) and papillary thyroid cancer (concordance index = 94.7). The difference from next best staging systems was most pronounced in non-anaplastic thyroid cancer (delta AIC = 114.8), followed by differentiated thyroid cancer (delta AIC = 35.6) and papillary thyroid cancer (delta AIC = 8.4).

Conclusions: Thyroid prognostic nomogram model was found to be better than the other models compared for predicting risk of death from thyroid cancer.

Keywords: Prognosis; Model; Survival; Thyroid neoplasm; TNM

Introduction

Thyroid cancer is the fastest growing cancer in Canadian Cancer Statistics 2015 with an estimated age standardized incidence rate (ASIR) of 14.9/10,000 in 2015. ASIR has been increasing at the rate of 6.3% per year in males since 2001 and by 4.4% per year in females (2005–2010).[1] It is the most common cancer in 15–29 year age group (16% of all cancers) and second most common cancer in 30–49 year age group (10% of all cancers).[1] Various staging/prognostic scoring systems have been used to predict oncological outcome of thyroid cancer.[2–19] Most of these are applicable only to the differentiated thyroid cancers[6–19] and provide stratified group risks rather than individualized risks. A nomogram, on the other hand, can be applied across different histological types to generate numerical probability of individual's clinical outcome, based on his/her risk assessment. We recently published a thyroid prognostic nomogram with excellent discrimination as demonstrated by high concordance index (0.92) and a very good calibration.[2]

This study was aimed to compare the strength of a thyroid prognostic nomogram with 12 commonly used staging/risk stratification systems, to predict the risk of death from thyroid cancer in a population based thyroid cancer cohort.

* Corresponding author. CancerCare Manitoba, 675 McDermot Avenue, Winnipeg R3E 0V9, Canada. Tel.: +1 204 787 8040; fax: +1 204 7872768.
E-mail address: apathak@cancercare.mb.ca (K.A. Pathak).

http://dx.doi.org/10.1016/j.ejso.2016.05.016
0748-7983/

Patients and methods

Study cohort

The Manitoba thyroid cancer cohort consists of all 2306 consecutive thyroid cancers diagnosed in 2296 patients, registered in Manitoba Cancer Registry, from January 1, 1970 to December 31, 2010. Sixty patients who were initially diagnosed by autopsy or death certificate, 76 patients with anaplastic thyroid cancer with extremely high case fatality rate, and 10 familial medullary thyroid cancers (MTC) where the oncological outcome is largely determined by their specific gene mutations, were excluded from this study. We also excluded 123 patients who did not have treatment with radical intent and 38 patients who were followed up in Manitoba health care system for less than a year. We reviewed individual electronic and paper records of the remaining 1989 patients and selected 1900 patients for this study on whom we had adequate information on patient demographics, tumor characteristics and completeness of tumor resection required for staging by 12 commonly used staging/risk stratification systems.[20] Ethics approval for this study was obtained from the Research Ethics Board at the University of Manitoba and the treatment details of these patients were obtained from CancerCare Manitoba, the tertiary cancer care center for the province of Manitoba with a catchment population of about 1.2 million. Patient demographics, extent of disease at initial presentation, the treatment modalities employed, pathology details, cancer recurrences during the follow-up, and the final oncological status as of July 1, 2015 were recorded. All patients who migrated out of province during the study period (considered lost to follow up), were censored at that point in time.

Statistical methods

The patient characteristics, the extent of disease at presentation and the tumor histology were recorded along with the treatment modalities, the patterns of failure and the final oncological outcome. The data were managed using SPSS for Windows version 23·0 (SPSS Inc., Chicago, IL). After checking for normality assumption, the mean and standard deviation were used to express normally distributed data (such as the age) and the median with interquartile range (IQR) was used for non-normally distributed data (such as the follow-up). A p-value <0.05 (two-sided) was considered to indicate statistical significance and 95% confidence intervals were used to express reliability in the estimates.

The effects of age at diagnosis, patient's gender, T, N and M categories, the histological type, and the presence of post treatment gross residual disease on the risk of death by disease were evaluated by competing risk analysis[21] to assess the competing influence of other causes of mortality, such as death due to a second primary tumor or non-cancer deaths. Cumulative incidence function (CIF) was used to describe the probability of death using proportional hazards regression model to directly model the sub-distribution of a competing risk.[22] R version 3.2.2 was used to analyze the data, using the packages of Hmisc to construct restricted cubic splines, and the packages of riskRegression and prodlim to run competing risk models. Restricted cubic splines were used to account for the non-linear relationship between age and the outcomes, using the default 3 knots. The discrimination capability of the models was evaluated by concordance index at 10 years. Concordance indices (c-index) were produced using only one of the 20 complete datasets after multiple imputations.

Akaike information criterion (AIC) was used to compare different prognostic models that are used for stage grouping/risk stratification of thyroid cancer. AIC is defined as $AIC = -2LL + 2m$, where LL is the maximized log-likelihood and m is the number of parameters in the model (degrees of freedom).[23,24] Delta AIC was calculated to compare the models. It is defined as $Delta\ AIC(\Delta_i) = AIC_i - minAIC$, where AIC_i is the AIC value for model i and min AIC is the AIC value of the best model identified by the lowest AIC.[25]

Results

Our study group of 1900 patients (450 males and 1450 females) had a follow up of 22,287 patient-years. The mean age of the patients was 46.99 $\pm$ 16.96 years and the papillary thyroid cancer (PTC) was the most commonly observed histological type in 1533 (80.68%) patients, followed by follicular carcinoma (FTC) in 193 (10.16%) patients, Hürthle cell in 70 (3.68%), poorly differentiated carcinoma in 39 (2.05%), and medullary carcinoma in 65 (3.42%) patients. TNM classification as well as stage/class/risk group distribution of patients with non-anaplastic thyroid cancer, differentiated thyroid cancer of follicular cell origin and papillary thyroid cancer is summarized in Table 1. Total thyroidectomy was performed in 1047 patients (55.10%) and 982 patients (54.68%) with differentiated thyroid cancers; 717 (73.01%) of these received adjuvant radioactive iodine. Sixty (3.16%) patients had post treatment residual disease. All patients with unresectable macroscopic residual disease in the neck at the time of surgery following total thyroidectomy or those at a high risk of disease recurrence; such as those with T3/T4 tumors, regional and distant metastasis received radioactive iodine for differentiated thyroid cancer (DTC). Use of external beam radiation therapy was limited to unresectable macroscopic residual disease.

During the median follow up of 11.59 years (inter-quartile range = 7.13–19.24 years), 181 (9.53%) patients had clinical/radiological evidence of recurrent disease after at least 6 months following an initial successful treatment.

Please cite this article in press as: Pathak KA, et al., Comparing a thyroid prognostic nomogram to the existing staging systems for prediction risk of death from thyroid cancers, Eur J Surg Oncol (2016), http://dx.doi.org/10.1016/j.ejso.2016.05.016