OPINION

Preoperative prediction of incomplete resection in non-small cell lung cancer

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ABSTRACT

After incomplete (R1-R2) resection, patients with stage I to stage III Non-Small Cell Lung Cancer (NSCLC) have a poor prognosis. With the use of preoperative patient, tumor, and treatment-related characteristics, our study attempted to create a prediction model to calculate the likelihood of an incomplete resection.

Patients with NSCLC who underwent surgical surgery without neoadjuvant therapy were chosen from a Dutch national cancer database. Analysis was done on thirteen potential predictors. A prediction model was developed using multivariable logistic regression. The American National Cancer Database was used for external validation, after which the model was modified. After internal and external validation, the model's discriminatory power and calibration were established. Histology, cT and cN stages, the length of surgery, and open versus thoracoscopic technique were independent predictors. Following internal confirmation, the resultant corrected C statistic. A C statistic was produced by applying the external data set of patients with incomplete resection in patients. The nomogram in both cohorts had a satisfactory overall fit, according to calibration. The capacity to forecast a patient's specific likelihood of an incomplete resection in those with stage I to stage III NSCLC who are planning to have it is provided by a nomogram that has received worldwide validation. Alternative therapeutic approaches may be considered in cases of high predicted risks of incomplete resection, whereas low risks justify the use of surgical techniques even more.

Key Words: *Tuberculosis; Undernutrition; Lung cancer; Interventional pulmonology*

INTRODUCTION

The most common malignancy diagnosed worldwide is lung cancer. Non-Small Cell Lung Cancer (NSCLC) accounts for the majority of lung cancer diagnoses and cancer-related deaths in the Western world. For patients with stage I or stage II illness, resection is the standard of therapy. The 5-year survival rates for stage I and stage II diseases following surgical therapy. The remaining no metastatic patients have locally progressed (stage III) illnesses and are comprised of a range of initial tumor sizes and nodal severities. Only a small percentage of stage III patients are thought to be respectable, and the majority of them get contemporaneous or subsequent chemoradiation, which is linked to roughly 5-year overall survival rates. The goal is to execute a radical (R0) resection on patients who are healthy enough for surgical therapy.

A patient's prognosis is worse if they had an incomplete (R1-R2) resection than if they had a complete resection. When considering overall survival following resection, hazard ratios for mortality have been recorded for R1-R2 resections as opposed to an R0 resection. It would be extremely valuable to be able to estimate the likelihood of a complete resection before surgery using preoperative factors.

The goal of this study was to develop and internally and externally validate a prediction model with the preoperative patient-, tumor-, and treatment-related factors that would enable the prediction of a patient's unique probability of an incomplete resection by using

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distinct large national databases of stage I to stage IV cancer patients. The Institutional Review Board of the University Medical Center Utrecht gave its approval to this observational study. Because the National Cancer Database (NCDB) database had all patient information deidentified, its usage was exempt from Institutional Review Board review. We used a nationwide database of patients with NSCLC who were diagnosed and only included patients who underwent surgical therapy from the Netherlands Cancer Registry, which is run by the Netherlands Comprehensive Cancer Organization. In-depth information about the patient, tumor, and therapy features can be found in the Netherlands Cancer Registry database. Based on data from electronic medical records, the Pathological Anatomical National Automated Archive (Pathologisch Anatomisch Landelijk Geautoma-tiered AR chief), the national registry of hospital discharge diagnoses, and diagnosis-treatment combinations, trained independent data managers in the Netherlands register every newly Diagnosed Cancer Case (DTC). These data are converted into standardized and uniform data sets. Age under 18, the cM1 stage, the CT is or cT0, neoadjuvant chemotherapy or preoperative radiotherapy, or both, carcinoid histology, and a delay from diagnosis to resection of more than days were all exclusion criteria. Neoadjuvant treatment patients were excluded in order to increase population homogeneity and because of the lack of data on restaging. We employed an American national cohort of lung cancer patients from the NCDB who underwent operations for the purpose of external validation. About one-third of the population of the United States is represented in the NCDB database, which contains deidentified data on patient demographics, tumor characteristics, and patient survival. The American Cancer Society and the American College of Surgeons' Commission on Cancer collaborated on the NCDB initiative. The exclusion standards were uniform. Age, sex, history of malignancy, lateralization (left or right sided), tumor location (upper lobe, lower lobe, and other [middle lobe, main bronchus, or overlapping locations]), histology, differentiation grade, clinical T stage, and N stage according to the American Joint Committee on Cancer, Edition, and extent of surgery (categorized as sub lobar [wedge or segmental resection]) were the variables examined. The variable was translated to cT stage according to the Edition when possible for incidence years for which data regarding CT stage were only available according to the Edition. Patients who were diagnosed with cT3 tumors were unable to do this, so the variable was treated as missing as a result. In order to compare this amended data set with the recorded SVIG-TB data. Using the Related Samples McNamara Change Test, the percentage of missing data in the SVIG-TB and Patient Record Review data was compared. Using Fisher's exact test for categorical variables and T-test for continuous variables, patients' characteristics linked to more missing values in SVIG-TB data were then retrieved. of hospital stay by MUST categorization. Without any further criteria, incomplete resection was only specified in the development set as microscopic incomplete resection (R1) or macroscopic incomplete resection (R2). Unspecified residual tumors or gross or microscopic residual tumors in the resection margins were both considered partial resections in the external validation data set. Depending on the normality of the data distribution, continuous variables are represented as mean SD or medians with interquartile ranges. The unpaired t-test or Mann-Whitney U test was used, respectively, to compare differences in continuous variables between patients with R1 to R2 resection and those with R0 resection. With the c2 test and Mann-Whitney U test, differences in nominal and ordinal categorical variables were respectively evaluated. The Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) statement was followed in all phases of the statistical analysis and reporting. For the clinical variables, logistic regression was used. The number of incomplete resections was adequate to allow for rough variables following the variable-per-event rule of thumb, hence no constraints were placed on these variables. We obtained Odds Ratios (ORs) and Confidence Intervals (CIs). Prior to modeling, multicollinearity was evaluated using Spearman correlations, and the Variance Inflation Factor (VIF) was used in the initial modeling stage. A VIF of more than or a correlation coefficient of greater than were both seen as indicators of multicollinearity. The variables with the highest clinical relevance were retained in the model in the event of multicollinearity. Because we hypothesized that the likelihood of an incomplete resection could differ depending on the histologic types and surgical approach depending on the tumor stage and nodal status, potential interactions between histology and overall stage, surgical approach with overall stage, and surgical approach with CN stage and CT stage were evaluated. Data that were missing were thought to have vanished at random. Missing values were imputed multiple times using chained equations, resulting in the creation of new data sets. The imputation process includes all of the stated predictors, significant interaction terms, and the result. These data sets were combined with all modeling phases. All variables were included in the initial modeling step, following which they were all removed using a stepwise backward selection method based on the Akaike information criteria. The C statistic was used to evaluate the model's discriminative capacity. Internal validation was done using bootstrap resamples of each imputed data set, repeating all modeling processes and removing superfluous variables in the process. As a result, the optimism and shrinkage factors could be estimated, allowing the intercept, b-coefficients, and C statistic of the final model to be corrected. In subsequent studies, the corrected intercept and b-coefficients were employed. By comparing anticipated and observed probabilities in octiles, the model's calibration was evaluated. The NCDB cohort underwent external validation using the revised model from the development set. With the help of calibration plots, calibration performance was evaluated. Based on the variance in the incidence of incomplete resections between the cohorts, the intercept of the logistic regression model was then adjusted. For the final model in both the development set after optimism correction and for the intercept-updated model generated from external validation, a nomogram was produced. The final model was composed of histology, CT stage, cN stage, surgical technique, and extent after backward stepwise selection. Following internal validation, the apparent C statistic and the corrected C statistic both showed that the final model had strong discriminative power. The b-coefficients and intercept were adjusted for optimism. Over the range of observed probabilities, the model's overall calibration was good. The ultimate model is shown as a nomogram.

Low-, intermediate-, and high-risk score subgroups were created for the development cohort for scores more than and greater than, respectively, for which the estimated probabilities of R1 to R2 resection were,, and, and correspondingly. The observed probabilities

and, respectively, agreed with these probabilities. Low-risk, intermediate-risk, and high-risk score subgroups were formed for the validation cohort for scores greater than to, and greater than, respectively, for which the projected probabilities of R1 to R2 resection were, and respectively. Additionally, these probabilities agreed with the observed probabilities in each case. The outcome's logit did not violate the linearity assumption, demonstrating appropriate goodness of fit. External validation revealed that the created models anticipated probability of full resection was lower than the observed probability, which was consistent throughout the whole risk spectrum (i.e., not particular to low- or high-risk groups). Based on the variation in full resection incidence between the cohorts, the model's intercept was modified. The model was re-calibrated so that expected and observed probability lined up. The C statistic that is produced when the final model is applied to the external validation set. An example instance is given to demonstrate how to use the nomogram. In patients with newly diagnosed stage, I to III NSCLC, a globally validated nomogram is provided that allows for individual preoperative prediction of the probability of full resection. In carefully chosen patients, there is a high likelihood of total resection. No adenocarcinoma histology, greater CT stage, clinical lymph node metastases, length of surgery, and an open surgical approach all indicate an elevated risk of incomplete resection. Complete excision has been proven to improve survival in numerous studies. Although adenocarcinoma histology influenced the completeness of resection in a favorable way, no pertinent references were found on histology's ability to predict the completeness of resection. A nomogram was created and validated based on the factors of histology, CT stage, cN stage, the extent of surgery, and surgical technique to better predict the incompleteness of resection in NSCLC patients. In stage I to III NSCLC patients who are candidates for surgical treatment, the nomogram permits pretreatment assessment of the individual chance of a full resection. Following internal and external validation, the adjusted C statistics showed that the final model had a strong discriminative ability. Overall, a substantial proportion of complete resections were seen in these patients. If there is a significant likelihood of incomplete resection, more extensive surgery or alternate therapeutic approaches such as induction chemotherapy or final chemoradiotherapy without surgery should be considered.