Journal of Infection ■■ (2018) ■■–■■

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevierhealth.com/journals/jinf

Development and validation of a prognostic score to predict tuberculosis mortality

Duc T. Nguyen, Edward A. Graviss *

Houston Methodist Hospital Institute, 6670 Bertner Ave, Houston, TX 77030, USA

ARTICLE INFO

Article history:
Accepted 19 February 2018
Available online

Keywords:
TB risk score
Prognosis
Elderly
Meningeal TB
TB-CXR
HIV infection

ABSTRACT

Objective: To develop and validate a simple prognostic scoring system to predict the mortality risk during treatment in tuberculosis patients.
Methods: Using data from the CDC's Tuberculosis Genotyping Information Management System of TB patients in Texas reported from 01/2010 to 12/2016, age ≥ 15 years and having an outcome as "completed" or "died", we developed and validated a prognostic mortality scoring system-based logistic regression beta-coefficients.
Results: The developmental and validation cohorts consisted of 3378 and 3377 patients, respectively. The score used 9 demographic and clinical characteristics, which are usually available at the patient's initial visits to a healthcare facility. Prognostic scores were categorized into three groups that predicted mortality: low-risk (<15 points), medium-risk (15–18 points), and high-risk (>18 points). The model had excellent discrimination and calibration with an area under the receiver operating characteristic curve of 0.82 and 0.80, and a non-significant Hosmer–Lemeshow test $P = 0.514$ and $P = 0.613$ in the developmental and validation cohorts, respectively.
Conclusion: Our validated TB prognostic scoring system, which used demographic and clinical characteristics available at the patient's initial visits, can be a practical tool for health care providers to identify TB patients with high mortality risk so that appropriate treatment, medical supports and follow-up resources could be appropriately allocated.

Introduction

Tuberculosis (TB) is one of the diseases with the highest morbidity and mortality. In 2015, approximately 10.4 million new TB cases with 1.4 million HIV-negative and 0.4 million HIV-positive individuals died of the disease worldwide.[1] Although TB mortality in the United States (U.S.) has decreased in recent years, the disease claimed 493 deaths in 2014.[2] One of the states having the highest TB burden in the U.S., Texas, also had TB as the disease having the highest standardized mortality ratio (SMR) relative to the national reference between 2001 and 2010 with 679 deaths.[3] Texas had a TB rate of 4.9 per 100,000 population in 2015, an increase of 4.3% compared to that in 2014.[4]

Rapid diagnosis and early treatment, as well as appropriate prognosis, especially in the patient's initial visit to a health care facility, are crucial tools for clinicians and health care workers to successfully manage individuals who have contracted TB. Many guidelines have been developed to improve TB diagnosis, prognosis, and treatment outcome.[5–8] Multiple risk factors have also been identified that are associated with TB morbidity and mortality.[1,4,9,10] Even though at least two TB risk scoring systems have been developed,[11,12] there is no currently standardized scoring system, validated with large population-based data, to promptly provide the prognosis for TB patients' outcome from their initial visits. The current study's main objective was to develop and validate a prognostic scoring system using a large population-based surveillance dataset to predict TB mortality during treatment, which is applicable prior to microbiologic and or laboratory confirmation.

Methods

Study population

In this study, we used the de-identified surveillance data on demographic and clinical characteristics of all confirmed TB patients from the state of Texas (U.S.) reported to the National TB Surveillance System. The dataset was downloaded from the Centers for

Funding: None.
* Corresponding author. Department of Pathology and Genomic Medicine, Houston Methodist Research Institute, Mail Station: R6-414, 6670 Bertner, Houston, TX 77030.
E-mail address: eagraviss@houstonmethodist.org (E.A. Graviss).

https://doi.org/10.1016/j.jinf.2018.02.009

Disease Control and Prevention (CDC) supported TB Genotyping Information Management System (TBGIMS) website. The inclusion criteria included: (1) confirmed TB cases in the state of Texas, U.S. in the National TB Surveillance System (NTSS) from 01/2010 through 12/2016 (based on official case count date); (2) age ≥15 years old; and (3) had documented treatment outcome in the dataset as either "completed" or "died". Patients age under 15 years old or having outcome coding other than as "completed" or "died" (such as "adverse", "lost", "moved", "other", "refused", or "unknown") were excluded from the analyses. A sensitivity analysis was done to compare the difference in demographic and clinical characteristics between the excluded and included patients. TB cases in the dataset were identified and verified by the local and state TB program staff using the CDC's TB case definition,[13] which included either positive *Mycobacterium tuberculosis* culture ($n = 5244$), positive nucleic acid amplification (NAA) test ($n = 107$), positive acid-fast bacilli (AFB) smear ($n = 31$), and verified clinical cases ($n = 1373$).

Statistical analysis

The dataset was randomly divided into two cohorts with a ratio of 50/50: developmental and validation cohorts. The developmental cohort was used to create the prognostic scoring system. The performance of the scoring system was then assessed in the validation cohort.

Demographic and clinical data were reported as median and interquartile range (IQR) for continuous variables, and as frequencies and proportions for categorical variables. Differences across groups were compared using the Chi-square test. Univariate and multiple logistic regression models were used to determine the contribution of potential prognostic variables to the patient outcome. Variables having a P value <0.2 in univariate logistic regression were investigated further in multiple logistic regression models using the Bayesian model averaging (BMA) method to identify significant risk factors for death.[14,15] Significant risk factors were assigned weighted-points that were proportional to their β regression coefficient values. The risk scores were calculated for each individual patient in the cohort. Patients were categorized in deciles of risk score and then collapsed into three groups which were significantly distinct in predictive risk for mortality: low (<10% mortality), medium (10%–20% mortality), and high risk (>20% mortality). Mortality was then calculated for each risk group. The discrimination of the predictive model was evaluated by the area under the receiver operating characteristic (ROC) curve (AUC). Differences in the AUC between the developmental and validation cohorts were compared using the Chi-square test. The model's good calibration (predictive accuracy) was determined by a non-significant Hosmer–Lemeshow goodness of fit test as well as the similarity in the mortality differences (delta) between high-risk and low-risk groups across the cohorts. Multiple logistic regression analyses with bootstrapped standard errors were also used to compare the odds of death across different risk groups. All the analyses were performed on Stata version 14.2 (StataCorp LP, College Station, TX). A P value of <0.05 was considered statistically significant.

Results

Characteristics of development and validation cohorts

A total of 8421 confirmed TB adult cases from Texas were reported in the National TB Surveillance System database from 01/2010 through 12/2016. After excluding 1666 patients (1014 with missing outcome status and 652 with an outcome of other than "completed" or "died"), 6755 patients were used for the analysis and randomly divided by Stata's randomization program into two cohorts at a ratio of 50/50: the developmental (3378 patients) and validation (3377 patients) cohorts (Fig. 1). Sensitivity analysis indicated that with the exception of male gender and meningeal TB, which are in a higher proportion in the 1666 excluded patients, there was no other significant difference in demographic and clinical characteristics between the excluded and included groups (data not shown).

The demographic and clinical characteristics of the developmental and validation cohorts are reported in Table 1. There was no significant difference between the two cohorts in all the characteristics under investigation, which included demographics, medical history, tuberculosis disease site, chest radiograph, specimen smear and culture, HIV status, multi-drug resistance, and clinical outcome (Table 1). The data of the 3378 patients in the developmental cohort was used in developing the prognostic mortality prognostic scoring system.

Development of the prognostic mortality prognostic score system

Univariate logistic regression analyses were used to identify potential risk factors associated with mortality (Table 2).

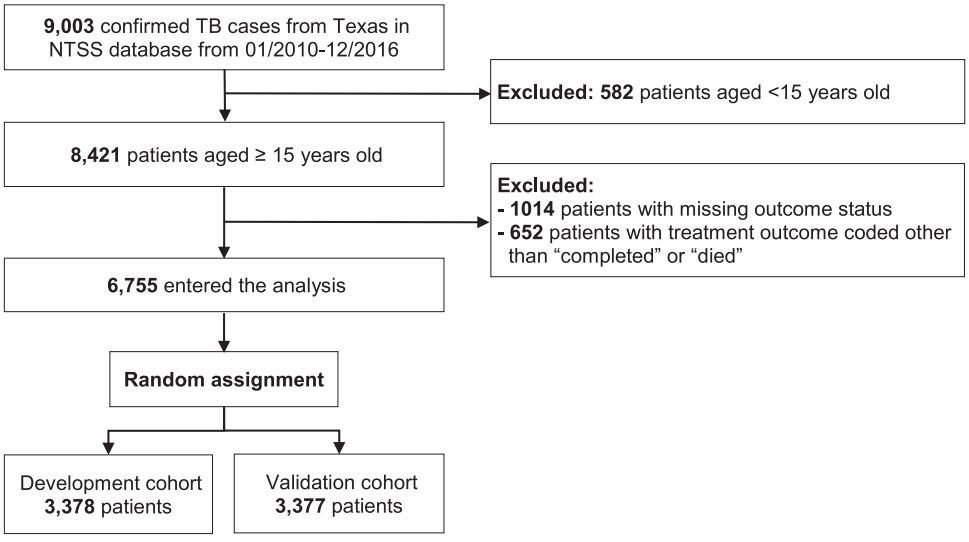

Fig. 1. Flowchart of the study population. NTSS, National Tuberculosis Surveillance System.