Automated Drug-Resistant TB Screening: Importance of Demographic Features and Radiological Findings in Chest X-Ray

Feng Yang
Lister Hill National Center for Biomedical Communications
National Library of Medicine, National Institutes of Health
Bethesda, MD 20894, USA
feng.yang@nih.gov

Hang Yu
Lister Hill National Center for Biomedical Communications
National Library of Medicine, National Institutes of Health
Bethesda, MD 20894, USA
hang.yu@nih.gov

Karthik Kantipudi
Office of Cyber Infrastructure and Computational Biology
National Institute of Allergy and Infectious Diseases, National Institutes of Health
Bethesda, MD 20894, USA
karthik.kantipudi@nih.gov

Alex Rosenthal
Office of Cyber Infrastructure and Computational Biology
National Institute of Allergy and Infectious Diseases, National Institutes of Health
Bethesda, MD 20894, USA
alexr@niaid.nih.gov

Darrell E Hurt
Office of Cyber Infrastructure and Computational Biology
National Institute of Allergy and Infectious Diseases, National Institutes of Health
Bethesda, MD 20894, USA
darrellh@niaid.nih.gov

Ziv Yaniv
Office of Cyber Infrastructure and Computational Biology
National Institute of Allergy and Infectious Diseases, National Institutes of Health
Bethesda, MD 20894, USA
zivrafael.yaniv@nih.gov

Stefan Jaeger
Lister Hill National Center for Biomedical Communications
National Library of Medicine, National Institutes of Health
Bethesda, MD 20894, USA
stefan.jaeger@nih.gov

Abstract—Tuberculosis (TB) is a global disease caused by the bacillus Mycobacterium tuberculosis. In recent years, great progress has been made in care and control of drug-sensitive TB, whereas drug-resistant TB continues to be a worldwide public health problem that takes a heavy toll on both patients and the health care system. Early detection of drug resistance during a patient’s first visit is very important because it enables appropriate drug treatment and thus reduces the period of infectiousness. However, discrimination between drug-resistant TB (DR-TB) and drug-sensitive TB (DS-TB) using imaging and readily available demographic data is still an open problem. In this paper, we investigate the possibility of automatic discrimination between DR-TB and DS-TB with demographic and radiological findings from chest X-rays (CXRs) using machine learning techniques as well as the importance of such features for classifier training. We use a dataset of 1311 DR-TB cases and 1311 DS-TB cases from 10 countries, collected from the NIAID TB Portals program (https://tbportals.niaid.nih.gov). We first perform a two-step preprocessing, which consists of feature quantitation and missing data imputation. Seven demographic features and 25 radiological features are selected from the dataset. Then, we train a random forest (RF) model to evaluate the ability to differentiate between DR-TB and DS-TB. An importance index calculated from the RF model is used to analyze the feature importance with respect to the discrimination task. The importance index from the RF model shows that the top ten important factors for discriminating between DR-TB and DS-TB are: number of daily contacts, BMI, patient type, education, medium density infiltrate, medium density stabilized fibrotic nodules, low ground glass density infiltrate, pleural effusion percentage of hemithorax involved, multiple nodules, small nodules. Ten-fold cross-validation using the RF model shows that automatic discrimination between DR-TB and DS-TB achieves an average accuracy of 75% and an average AUC value of 83%, when using the top ten features. Our study suggests that automatic discrimination between DR-TB and DS-TB with demographic and radiological features is possible.

Keywords—Tuberculosis (TB), drug resistance, random forest, differentiated diagnosis; demographic features; radiological findings

I. INTRODUCTION

Tuberculosis (TB), caused by the bacillus Mycobacterium tuberculosis, is a serious worldwide health issue with an estimated 10 million people infected and 1.5 million deaths each year [1]. In recent years, great progress has been made in care and control of drug sensitive TB [2], whereas drug resistant TB continues to be a worldwide public health problem [3]. In 2019, there were an estimated 10 million TB cases; approximately half a million cases are resistant to rifampicin, of which 78% are multidrug-resistant TB (MDR-TB) [1]. Drug-resistant TB is a growing public health concern since it requires more complex treatment than drug-sensitive TB and incurs more costs. Early detection of drug resistance is very important, as it helps with decision making, enables appropriate drug treatment, and reduces the period of infectiousness. However, discrimination between drug-resistant TB (DR-TB) and drug-sensitive TB (DS-TB) using imaging and readily available demographic data is still an open problem.

Previous works have shown evidence that certain clinical features can potentially aid in identification of DR-TB, such as prior treatment [4]–[8], positive sputum smear microscopy [5], history of drug injection [6], gender [6], [9], and age [7], [8]. Few works have dealt with radiological findings from chest imaging to identify the type of TB, DR-TB or DS-TB. Icksan et al. [10] reported that the MDR-TB group are more likely to have large-size lesions than DS-TB group. Wang et al. [11] found that
A. predictors for DR-TB. Our previous work [14] found that the mediastinal lymphadenopathy, presence of other non-TB failed at the end of the most recent course of treatment [18]. DR-TB patients, acquired from 10 countries.

radiological annotations are not biased towards a single to financial constraints and the size of the TB portals CXR the pleural effusion percentage of the hemithorax involved. Due abnormalities, the overall percentage of abnormal volume, and who has previously been treated for TB and whose treatment of TB caused by reinfection). A failure case represents a patient was declared cured or completed treatment at the end of the most case refers to a patient who has never been treated for TB, or has taken anti-TB drugs for less than one month.  A relapse laboratory tests, treatment period, treatment status and outcome. A new case refers to a patient who has previously been treated for TB or has taken anti-TB drugs for less than one month. A relapse case refers to a patient who has previously been treated for TB, was declared cured or completed treatment at the end of the most recent course of treatment, and is now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection). A failure case represents a patient who has previously been treated for TB and whose treatment failed at the end of the most recent course of treatment [18]. Radiological findings include chest radiography patterns such as nodules, cavities, infiltrates and collapses, the presence of mediastinal lymphadenopathy, presence of other non-TB abnormalities, the overall percentage of abnormal volume, and the pleural effusion percentage of the hemithorax involved. Due to financial constraints and the size of the TB portals CXR dataset, radiological features are obtained using a single experienced radiologist-reading per image. The whole dataset was annotated by multiple radiologists from the countries contributing data to the program. Consequentially, the radiological annotations are not biased towards a single radiologist. The 2622 patients include 1311 DS-TB and 1311 DR-TB patients, acquired from 10 countries.

B. Feature preprocessing

We perform a two-step preprocessing for demographic and radiological features. It consists of feature quantitation and missing data imputation. Feature quantitation indicates converting text features into numeric features. Missing data for a demographic feature is replaced by the mean value of other non-missing values under the same feature, while missing data for a radiological feature is assigned a special group number. For example, the radiological feature under the category Overall Percentage of Abnormal Volume will be assigned four values after feature quantitation and missing data imputation: 1 (0), 2 (<50%), 3 (>50%) and 4 (missing data).

Seven demographic features and 25 radiological features are selected by removing those whose missing data is more than 40% and by removing the country of origin from demographic features. Since almost 80% patients comes from five countries (Belarus, Georgia, India, Ukraine, and Kazakhstan), training on the country of origin may result in biased classification.

C. Random forest classifier

Based on the selected demographic and radiological features, we train a machine learning classifier, a Random Forest (RF) model [19], to discriminate between DS-TB and DR-TB. We illustrate the pipeline of our machine classification in Fig. 1. To compare the contributions of different features for classifying DR-TB vs DS-TB, we train the RF classifiers using different feature combinations.

D. Importance measure

Each tree in a RF model is built from a random sample of the data, and not all observations are used to construct a specific tree. The observations that are not used to construct a tree are called out-of-bag (OOB) observations of this tree. In a RF model, each tree is built from a different sample of the original data, so each observation is “out-of-bag” for some of the trees.

Assuming that our RF model includes M decision trees H={h₁, h₂, …, hₘ}. The importance index of a given predictor Xᵢ is calculated using the following four steps.

Step 1: Use the decision tree hₘ to predict its OOB observations. We refer th input matrix as Xₘ th (feature matrix), and output matrix as Yₘ, then the prediction error Err₁ can be calculated as the mean square error (MSE) between the predicted values Yₘ and real values Y:

\[ \text{Err₁} = \text{mean} (Yₘ - Y)^2. \]  (1)

Step 2: Permute values for the feature Xᵢ (the i-th column of the feature matrix) and use decision tree hₘ to predict the OOB observations. Then, the prediction error Err₂ can be calculated as:

\[ \text{Err₂} = \text{mean} (Yₘ^P - Y)^2, \]  (2)
\[ E_{r2} = \text{mean} \left( Y'_m - Y \right)^2 \]  

Step 3: The importance index of predictor \( X_i \) on decision tree \( h_m \) is calculated as: \( MSE_m = E_{r2} - Err1 \).

Step 4: The importance index of predictor \( X_i \) on the RF model is given by:

\[ \alpha = \frac{1}{M} \sum MSE_m. \]

\( \alpha > 0 \) means \( X_i \) is important since changing its order makes the error larger; \( \alpha = 0 \) indicates that the order of \( X_i \) is not important since the MSE does not change; \( \alpha < 0 \) suggests that the variable can have a detrimental impact on the classification since changing its order makes the error smaller (substituting the feature with noise is better than the original feature; hence, the feature is worse than noise).

III. EXPERIMENTAL RESULTS

Figure 1 shows the importance index calculated using Eq. (3) on seven demographic and 25 radiological features. We see that the top ten important factors for classifying DR-TB and DS-TB are: number of daily contacts, BMI, patient type, education, medium density infiltrate, medium density stabilized fibrotic nodules, low ground glass density infiltrate, pleural effusion percentage of hemithorax involved, multiple nodules, small nodules.

To investigate the possibility of automatically differentiating between DR-TB and DS-TB and to evaluate the contribution of specific features, we trained RF models using the following combinations: 1) seven demographic features, 2) 25 radiological features, 3) 32 demographic and radiological features, and 4) top 10 important features. The results in Table 1 show that 1) demographic features have more influence on the RF model than radiological features; 2) the RF classifiers using top 10 features and using 32 features achieve very close performance, with an average AUC value of 83% and an average accuracy of 75%. Figure 2 shows the ROC curves for RF-based classifier using the top 10 features.

Table 1 RF classifier performance with ten-fold cross validation.

<table>
<thead>
<tr>
<th>RF model features</th>
<th>AUC</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 demog. features</td>
<td>64.89% ±2.52%</td>
<td>72.16% ±1.88%</td>
<td>76.05% ±4.13%</td>
<td>71.39% ±2.22%</td>
<td>72.67% ±1.48%</td>
</tr>
<tr>
<td>6 demog. without patient type</td>
<td>77.11% ±2.47%</td>
<td>72.16% ±2.78%</td>
<td>77.33% ±4.11%</td>
<td>66.59% ±3.07%</td>
<td>69.94% ±2.41%</td>
</tr>
<tr>
<td>25 radiol. features</td>
<td>64.89% ±3.81%</td>
<td>60.79% ±3.36%</td>
<td>68.65% ±3.68%</td>
<td>52.94% ±5.10%</td>
<td>59.39% ±3.07%</td>
</tr>
<tr>
<td>32 features</td>
<td>82.86% ±3.49%</td>
<td>75.03% ±0.05%</td>
<td>78.33% ±5.25%</td>
<td>69.72% ±4.40%</td>
<td>72.20% ±3.09%</td>
</tr>
<tr>
<td>Top 10 features</td>
<td>82.55% ±2.64%</td>
<td>75.17% ±3.36%</td>
<td>77.58% ±4.36%</td>
<td>72.77% ±4.23%</td>
<td>74.04% ±3.76%</td>
</tr>
</tbody>
</table>

Note: demog. indicates demographic, radiol. indicates radiological.


Fig. 3. ROC curves for ten-fold cross validation using random forest classifier based on the top 10 features.

IV. DISCUSSION AND CONCLUSION

In this paper, we investigated the importance of demographic and radiological features in discrimination between DS-TB and DR-TB and the possibility applying machine learning to discrimination between DR-TB and DS-TB by incorporating both features.

We select balanced DR-TB and DS-TB cases to avoid the bias of unbalanced dataset on machine classifier training and to avoid the unpredictable effects of synthetic data from
augmentation methods. It should be noticed that about 80% of the patients come from five countries (Belarus, Georgia, India, Ukraine, and Kazakhstan). That is, our machine classifier learns drug-sensitive and drug-resistant features primarily from five countries, and thus the classification performance will likely decrease when we use it to identify DR-TB from other countries or when we perform a country-level evaluation.

We observe from Table 1 that patient type plays an important role in discriminating between DR-TB and DS-TB, with specificity decreasing around 5% when removing patient type from the training features. This is probably due to the fact that most of the patients with patient types of Failure (95%) and Relapse (83%) are drug resistant.

Experimental results show that automated discrimination between DR-TB and DS-TB using a RF model achieves an AUC value of 83% and an accuracy of 75% with the top 10 demographic and radiological features. Our study suggests that automatic discrimination between DR-TB and DS-TB is possible by utilizing both demographic features and radiological features.

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