The Validity of Classic Symptoms and Chest Radiographic Configuration in Predicting Pulmonary Tuberculosis*

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Objective: Patients admitted to the pulmonary isolation service to rule out tuberculosis (TB) were prospectively studied to identify predictors of smear-positive TB.

Methods: History of symptoms—cough, sputum production, fever, weight loss, night sweats, hemoptysis, anorexia, and dyspnea; medical history—TB, tuberculin skin test (TST) status, TB contact; and social factors—crowding index, history of incarceration or living in a shelter, and employment status were obtained in face-to-face interviews. Chest x-rays (CXRs) were scored as typical, atypical, or negative. Serial morning sputa were collected.

Results: Complete data were collected on 101 patients; 44 had pulmonary TB; 33 patients were smear positive and considered infectious; 11 patients were smear negative but culture positive. There was no difference between TB and non-TB patients with respect to HIV status and social risk factors. Significant differences were found between patients who were smear positive for TB and smear negative with respect to cough, sputum, and typical CXR (79%, 76%, and 79% sensitivity, respectively). Eleven patients without TB had an atypical CXR and denied cough, sputum, and weight loss. Only one patient with TB presented this way.

Conclusion: Even in high-risk populations, symptoms of cough, sputum, weight loss for less than 2 weeks, and the absence of a typical CXR are strong negative predictors for TB.

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Key words: diagnosis; predictive model; sputum acid-fast bacilli smear; tuberculosis

The nationwide epidemic of tuberculosis (TB) has created an urgent mandate for the rapid diagnosis and effective treatment of patients with this disease, especially those with pulmonary TB who are responsible for infection transmission.

The Centers for Disease Control and Prevention (CDC) have issued guidelines on the prevention of TB transmission in the workplace. These guidelines emphasize the need for a hierarchy of controls, the most important being the early identification of patients with active TB. Because of its protean clinical and radiographic manifestations, the American Thoracic Society and CDC have recommended that “pulmonary tuberculosis should always be included in the differential diagnosis of persons with pulmonary signs or symptoms and appropriate diagnostic measures should be instituted.” Yet evaluating every patient with respiratory disease of unknown etiology in an isolation room is beyond the means of any health-care institution. Health-care providers in hospital emergency departments and clinics must rely on routine history, physical examination, chest x-ray (CXR), and possibly initial sputum smears to decide if the patient requires isolation, treatment, and further expensive diagnostic testing.

In most hospitals, the initial decision to isolate the patient in expensively engineered negative pressure rooms is still made based only on the history, physical, and initial CXR. Those hospitals that have very few patients who are at high risk for TB, and who have a large number of these rooms can afford to isolate almost anyone at risk. In hospitals such as our own with very large numbers of patients at risk, and very few isolation rooms, it becomes important to develop negative predictors for TB among high-risk patients in order to better triage these limited resources.

Materials and Methods

Setting

This study was conducted at Cook County Hospital (CCH), a large, public, urban hospital that serves the population groups that have been most severely affected by the TB epidemic. CCH is at the front line of the TB epidemic. The state of Illinois has suffered the second largest increase (6.5%) in cases in the United States and

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Chicago ranks third among all US cities in percentage increase (5.9%) of new cases. CCH bears the distinction of having the largest burden of TB of any institution in the state. In 1993, 195 of the 802 new cases of TB reported in the city of Chicago were diagnosed at CCH. Of these 195 new cases, 11 (6%) had multidrug-resistant TB. Five hundred twenty-three new patients with HIV were treated in 1993 and of these patients had HIV-associated TB. One percent of all hospital admissions were for TB and more than 2% were to rule out TB.

This study prospectively evaluated a subset of the inpatient population that was at high risk for TB and evaluated the predictive value of symptoms and CXR findings for the presence of TB.

Subjects

From September 1, 1993 to January 9, 1994, 208 consecutive patients were referred by physicians in the Emergency Department, wards, and clinics of the hospital to the pulmonary TB service for suspected TB. The pulmonary isolation service has administrative control of isolation beds and consists of an on-call resident and fellow who perform the initial evaluation and decide on the need for respiratory isolation. All patients were reevaluated by a board-certified pulmonologist the following morning. One hundred thirty-seven patients believed to be at risk of having pulmonary TB based on symptoms, medical and social risk factors, and CXR findings were isolated. Thirty-six patients were excluded from the study due to a history of active TB diagnosed within the last year (n=22), respiratory failure (n=4), signing out against medical advice resulting in incomplete sputum collection (n=7), or contaminated cultures (n=3). Complete data were collected on 101 patients.

Methods

Face-to-face interviews were conducted using a well-constructed, standardized questionnaire eliciting symptoms and duration of cough, sputum production, fever, weight loss, night sweats, hemoptysis, anorexia, and dyspnea. Patients were considered to have positive cough, sputum, tactile fever, anorexia, dyspnea, and drenching night sweats if these symptoms were present for 2 weeks or more; less than this was coded as negative for the analysis. Weight loss was defined as positive if it was greater than 4.5 kg or 10% of ideal body weight within the last 6 months. Hemoptysis was recorded as positive if it occurred even once.

A history of previous TB, TB treatment, and tuberculin skin test (TST) status was obtained. Social history, including history of incarceration or residing in a shelter for the homeless within the last year, employment, smoking, substance abuse, injection drug use, and number of rooms and persons in the home was obtained. Height, weight, and maximum temperature in the last 24 h were also obtained.

CXR were reviewed by two pulmonologist investigaors (R.C., S.M.) independently and blinded to the patient’s name and clinical information. The CXRs were divided into four zones: above the clavicles, upper, middle, and lower zones. The CXRs were scored as "typical" —the presence of nodular, alveolar, or interstitial infiltrates predominantly affecting the zones above the clavicles or upper zones, "atypical"—any other pattern, and "negative"—normal CXR, or inactive process.

Spontaneously expectorated or if the patient had a nonproductive cough, induced sputa, were collected every morning for up to 6 days. Sputum induction was performed using 0.45% NaCl via air-powered nebulizer for 15 min. Inspection of conventional auramine-hodamine fluorochrome smear and standard mycobacterial cultures were performed on Lowenstein-Jensen slants and Middlebrook 7H10 media. Statistical analysis was performed using χ² analysis, with a two-tailed Fisher’s Exact Test for categorical variables. Group comparisons were determined using χ² analysis by determining sensitivity, specificity, and positive and negative predictive values and by calculating odds ratios.

RESULTS

Of the 101 patients, 44 were found to have pulmonary tuberculosis. Of these 44, 33 were smear positive on at least one specimen and 11 were smear negative but culture positive. Table 1 shows characteristics of study subjects. Demographic breakdown revealed that 75% of patients were African-American, 5% white, 15% Hispanic, and 5% Asian; 11% were female and 89% were male. There were no significant demographic differences between TB and non-TB populations.

Of the 57 patients who did not have Mycobacterium tuberculosis, 5 had Mycobacterium kansasii and 4 had Mycobacterium avium complex cultured from respiratory secretions. For the purposes of analysis, these nine patients were considered non-TB. HIV test results were available on 54 patients; 29 of these patients tested HIV positive, and 20 of these had CD4 counts available.

Symptoms of cough, sputum production, weight loss, and a typical CXR were significantly more frequent in patients with TB (Table 2), with an even stronger association noted for patients with smear-positive TB (Table 3).

In univariate analysis, there was no significant difference between TB and non-TB patients with respect to symptoms of fever, night sweats, dyspnea, anorexia, and hemoptysis for smear- or culture-positive patients. There was also no significant difference between these groups in the frequency of risk factors of alcohol, smoking, injection drug use, employment status, substance abuse, residence in a shelter, incarceration, history of TB, TB treatment, or TST status. Analysis of CXR findings did show significant differences between TB and non-TB patients in the frequency of a typical CXR (p<0.001). This test had good negative predictive value for TB (75%), especially smear-positive TB (85%). Very few TB patients had a normal CXR, and no patients who were smear positive...
had a normal CXR in this series. When symptoms of cough, sputum, and weight loss are combined with CXR interpretation, the negative predictive value for having TB is quite strong. While 11 patients without TB had an atypical or normal CXR and had less than 2 weeks of cough, sputum, and weight loss, only 1 patient with TB presented this way.

We also looked at differences between patients with TB who were known HIV positive (n=13) vs those who were known HIV negative (n=9). We found no significant difference in symptoms and social factors. It was interesting to note that 46% (six) of patients with HIV-associated TB had atypical or normal CXRs compared with only 11% (one) of patients with TB who were HIV negative (p=0.10) (Table 4). When the HIV-positive TB patients were divided into two groups based on CD4 counts greater or less than 200, 83% of patients with low CD4 counts had nontypical CXRs compared with just 20% of patients with CD4 counts greater than 200 (p=0.06) (Table 5).

### Table 2—Symptoms and CXR Configuration Associated With Culture-Positive TB (Total n=101)

<table>
<thead>
<tr>
<th></th>
<th>TB (n=44) (%)</th>
<th>Non-TB (n=57) (%)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30 (69)</td>
<td>27 (47)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>14 (31)</td>
<td>30 (53)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Sputum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>29 (66)</td>
<td>25 (44)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>15 (34)</td>
<td>32 (56)</td>
<td>0.027*</td>
</tr>
<tr>
<td>Weight loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32 (73)</td>
<td>34 (60)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12 (27)</td>
<td>23 (40)</td>
<td>0.17</td>
</tr>
<tr>
<td>Typical CXR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32 (73)</td>
<td>21 (37)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>No</td>
<td>12 (27)</td>
<td>36 (63)</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05 was considered statistically significant; se=sensitivity; sp=specificity.

### Table 4—CXR Configuration in Patients With Known HIV Status (Total n=22)*

<table>
<thead>
<tr>
<th></th>
<th>HIV-Positive TB (n=13)</th>
<th>HIV-Negative TB (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR Configuration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Atypical or normal</td>
<td>6 (46)</td>
<td>1 (11)</td>
</tr>
</tbody>
</table>

*p=0.10, Fisher's Exact Test.

### Table 5—CXR Configuration in Patients With HIV-Associated TB by CD4 Count (Total n=11)*

<table>
<thead>
<tr>
<th></th>
<th>CD4 &lt;200 (n=6)</th>
<th>CD4 &gt;200 (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR Configuration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Atypical or normal</td>
<td>5 (83)</td>
<td>1 (20)</td>
</tr>
</tbody>
</table>

*CD4 counts were unavailable on two patients with HIV-associated TB. p=0.06, Fisher’s Exact Test.

### Discussion

The CDC’s recommendations for isolation of patients are quite broad and result in the isolation of large numbers of patients, straining the resources of many institutions. Our data showed significant negative predictive values in the range of 85% for classic symptoms and CXR configuration that may help triage these beds. Only one patient with TB (2%) had an absence of the three strongest predictors.

We are unaware of other published studies that have systematically evaluated the clinical, demographic, and radiographic characteristics of patients at high risk for pulmonary TB using those data to construct a predictive model which would distinguish patients with and without the disease. Such a model could consist of a combination of these characteristics and would need to have a sufficiently high specificity and negative predictive value in order to be useful, allowing safe admission to a nonisolation area.

Several studies describe the clinical and radiographic manifestations of patients with pulmonary TB,10-13 but very few compare these patients with others thought to be at risk for pulmonary TB but who are found not to have that disease. A recent retrospective study10 of patients with respiratory specimens culture positive for Mycobacterium tuberculosis showed that patients with pulmonary TB were more likely than control subjects to have a CXR with cavitory or apical infiltrates typical of pulmonary TB, a positive TST, a history of weight loss, diabetes, or recent contact with TB, and to be foreign born. The low prevalence of pulmonary TB and the retrospective nature of the study precluded the identification of more useful predictors of the presence or absence of pulmonary TB.

There is reason to believe that a TB predictive model can be constructed. The CXR is integral to the development of a meaningful TB score. While many radio-
graphic presentations have been described, including normal studies (that have been reported in 6% to 18% of HIV-infected patients with pulmonary TB\textsuperscript{14-17}), at least 80% of patients with pulmonary TB have one of five different radiographic patterns. In a prospective study of 188 consecutive non-AIDS patients seen at Los Angeles County/University of Southern California Medical Center, 85% had either a typical pattern consisting of alveolar, interstitial, or cavity infiltrates in the upper lung fields, or a miliary pattern.\textsuperscript{18} Similarly, 80% or more of HIV-infected patients with pulmonary TB have an upper lobe infiltrate, hilar adenopathy, cavitation, pleural effusion, or a miliary pattern on CXR.\textsuperscript{19,20} The presence or absence of the sentinel symptoms of TB will add significant predictive value to CXR in developing a TB risk score, especially since CXR loses sensitivity in populations with advanced immunosuppression. Data on symptoms from this and other studies could be added to CXR in the construction of the TB risk score. While a low TB score might not have clinically significant negative predictive value for smear-negative culture-positive pulmonary TB, it could reliably predict the absence of smear-positive pulmonary TB. This would be of great value in the management of limited isolation resources.

Our data show a significant correlation between symptoms of cough, sputum, and weight loss and smear-positive TB with lesser, but still significant predictive value for smear-positive and smear-negative TB combined. A significant weakness of this study was the relatively small sample size that made multivariable analysis impossible. A further study with a larger sample size is warranted.

This study population had a high TB prevalence rate (44%) that reflects the patient population at our hospital and the necessity of isolating only those at highest risk due to the relatively small number of isolation rooms. These indicators may not have the same sensitivity and specificity in populations with a lower prevalence of TB.

**CONCLUSION**

The absence of the sentinel symptoms of 2 weeks of cough sputum, weight loss, combined with the absence of a typical CXR are still extremely useful predictors of the absence of infectious TB. More than 10% of our patients, who denied cough, sputum, and weight loss and had atypical CXRs, may not have required isolation—a potential savings of valuable resources.

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