Performance of the Xpert MTB/RIF Assay on Nonrespiratory Specimens and Accuracy of This Assay for Detection of Rifampin Resistance in a Low-Prevalence Setting

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With interest, we read the paper “Integrating the Xpert MTB/RIF Assay into a Diagnostic Workflow for Rapid Detection of Mycobacterium tuberculosis in a Low-Prevalence Area” by Deggim et al. (1). Based on the failed detection of Mycobacterium tuberculosis complex (MTB) by the Xpert assay (GeneXpert; Cepheid, Sunnyvale, CA) in 3 of 4 culture-positive nonrespiratory specimens, the authors concluded that such specimens may not be suitable for Xpert testing, in particular for paucibacillary samples. Furthermore, they questioned the Xpert assay’s accuracy of detection of rpoB mutations associated with rifampin (RIF) resistance, because in 2 of 18 MTB culture-positive specimens, RIF resistance was wrongly identified. Since these conclusions were based on only a few specimens, we analyzed our own data.

Between October 2010 and August 2013, we investigated 29 nonrespiratory specimens by the Xpert MTB/RIF assay and cultured these specimens by use of the Bactec MGIT 960 system (Becton, Dickinson, Sparks, MD) and Loewenstein-Jensen solid medium (as the standard method for detection of MTB). The 29 nonrespiratory specimens included various biopsy specimens (\(n = 21\)), fluid specimens (\(n = 7\)), and a wound swab sample (\(n = 1\)), obtained from 28 patients. The Xpert results compared with those of culture are displayed in Table 1.

Cultures of 18 of the 29 specimens grew MTB. In 17 out of these 18 (94.9%) culture-positive specimens, the Xpert assay correctly detected MTB (Table 1). Ten of the 17 Xpert-positive specimens were smear negative, as was the one sample in which Xpert failed to detect MTB. For an additional 6 specimens, the Xpert result was positive, but culture remained negative. Since 5 of these 6 specimens came from patients who had had tuberculosis in the past and our in-house PCR (2) confirmed MTB DNA in all 6 of these samples, we consider these results of the Xpert assay true positives.

Furthermore, we checked the accuracy of the Xpert results for RIF resistance with the results obtained by conventional drug susceptibility testing using the Bactec MGIT 960 system (our gold standard) in 94 Xpert assay-positive samples from which a cultured MTB isolate was available. These 94 MTB samples came from 48 respiratory and 17 nonrespiratory specimens as well as 24 Bactec MGIT 960 and 5 Middlebrook 7H10 agar cultures. Thirty-three percent (16/48) of the respiratory samples and 59% (10/17) of the nonrespiratory specimens were smear negative. The Xpert assay indicated in 92% (60/65) of the respiratory and nonrespiratory specimens the presence of very low and low levels of MTB DNA, respectively. One smear-negative bronchoalveolar lavage fluid specimen was excluded, because the Xpert assay reported that RIF resistance was indeterminate due to a “very low” level of MTB DNA available in this sample. Thus, 93 out of 93 (100%) RIF results by the Xpert assay, including 14 samples with rpoB mutations associated with RIF resistance, could be confirmed by conventional drug susceptibility testing.

To date, there is no standardized Xpert protocol for the detection of MTB in nonrespiratory specimens. This flaw might contribute to various results after performance of the Xpert assay in different laboratories (3, 4). In contrast to the results of Deggim et al., our data on larger numbers indicate that the Xpert MTB/RIF assay can perform reliably also on paucibacillary nonrespiratory specimens, which is in accordance with the results of other authors (3, 4). Furthermore, in our hands, the Xpert assay accurately detected RIF susceptibility or resistance in both respiratory and nonrespiratory specimens, despite low or very low levels of MTB DNA, as well as on liquid and solid cultures. These results were obtained in similar low-prevalence and low-multidrug-resistance settings within Switzerland.

<table>
<thead>
<tr>
<th>Xpert assay result</th>
<th>Growth of MTB</th>
<th>No growth of MTB</th>
<th>Total no. of specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTB detected</td>
<td>17</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>MTB not detected</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Total no. of specimens</td>
<td>18</td>
<td>11</td>
<td>29</td>
</tr>
</tbody>
</table>

**TABLE 1 Results of the Xpert assay for 29 nonrespiratory specimens compared with culture results**

REFERENCES


