Journal of Infection (2013) **67**, 369—377

BIAA British Infection Association

www.elsevierhealth.com/journals/jinf

REVIEW

Commercial MPT64-based tests for rapid identification of *Mycobacterium tuberculosis* complex: A meta-analysis

Xiaomao Yin [a], Lei Zheng [a], Li Lin, Yarong Hu, Fen Zheng, Yanwei Hu, Qian Wang*

Department of Laboratory Medicine, Nanfang Hospital, Southern Medical University, No. 1838, North of Guangzhou Road, Baiyun District, Guangzhou 510515, PR China

Accepted 15 June 2013
Available online 22 June 2013

KEYWORDS
Mycobacterium tuberculosis complex;
Nontuberculous mycobacteria;
MPT64;
Immunochroma tographic test

Summary *Objective:* We did a systematic review and meta-analysis of published studies to evaluate the accuracy of commercial MPT64-based immunochromatographic tests for rapid identification of *Mycobacterium tuberculosis* complex.
Methods: We identified studies by searching Pubmed, BIOSIS Previews and Web of Science, and included studies using predetermined inclusion criteria. The data were pooled using the DerSimonian-Laird random effects model.
Results: A total of 28 studies were included in the final analysis. Pooled estimates were 97% (confidence interval [CI] 96—97%) for sensitivity and 98% (CI 98—99%) for specificity. The summary receiver operating characteristic curve showed an area of 0.9968 and a Q* of 0.98. Subgroup analysis showed that test accuracy did not depend on commercial kit, reference test and medium.
Conclusions: Commercial MPT64-based immunochromatographic tests are highly sensitive and specific for rapid identification of *M. tuberculosis* complex. They are good alternatives to biochemical test and molecular assays. Nevertheless, additional studies are required in setting with high prevalence of *mpt64* mutations or high contamination of cultures.

* Corresponding author. Tel./fax: +86 20 61641007.
E-mail addresses: nfyyWangQian@163.com, lunwentongxun@163.com (Q. Wang).
[a] Xiaomao Yin and Lei Zheng contributed to this study equally.

0163-4453/$36
http://dx.doi.org/10.1016/j.jinf.2013.06.009

Introduction

Members of the *Mycobacterium tuberculosis* complex (MTC) are the causative agents of tuberculosis (TB), which is still a matter of serious public health concern.[1] Nontuberculous mycobacteria (NTM) are a major cause of opportunistic infections in immunocompromised individuals.[2] Therefore, the ability to identify MTC isolates and differentiate them from NTM is very important for the selection of antimicrobial therapy and patient management.

Few current methods for the identification of MTC could completely satisfy the demands on rapidity, cost-effectiveness and simplicity. Biochemical technique, the conventionally used method, is time-consuming and cumbersome. Other methods such as gas—liquid chromatography, high-performance liquid chromatography and nucleic acid amplification-based methods allow rapid and accurate identification of mycobacteria.[3] However, chromatography method requires expensive equipment and skilled personnel, and molecular biology methods such as AccuProbe are laborious and expensive for routine use.[4]

Recently, a novel immunochromatographic test (ICT) based on the detection of MPT64 has been developed for rapid identification of MTC and has shown promise.[5] MPT64-based ICT is relatively easy to perform and only requires the type of laboratory infrastructure that is needed for routine mycobacterial cultures. The turnaround time of this method is 15 min for liquid culture and 30 min for solid culture. So far, 3 commercial MPT64-based ICT kits have been introduced for rapid identification of MTC, including Capilia TB assay (TAUNS, Numazu, Japan), SD Bioline Ag MPT64 rapid assay (Standard Diagnostics, Yongin, South Korean) and BD MGIT TBc ID test (Becton Dickinson, Sparks, USA).[5] The principles of these commercial kits are identical and described as follows.

MPT64, which is described as MPB64 for *Mycobacterium bovis*, is a 24 kDa protein secreted by MTC during bacterial growth. It is highly specific for MTC, including *M. tuberculosis* (MTB), *Mycobacterium africanum*, *M. bovis* and some substrains of *M. bovis* bacilli Calmette-Guerin (BCG).[6] The MPT64 antigen in liquid or solid media could be detected by using anti-MPT64 monoclonal antibody and lateral-flow technique. The color band in test zone indicates the existence of MPT64 and the growth of MTC. So strains with positive ICT results are finally identified as MTC.

A multi-center study has shown that the sensitivity of this method was 94.8% and the specificity was 100%.[3] However, some subsequent studies found that clinical MTB isolates were falsely identified as NTM because of *mpt64* gene mutations.[7–9] This weakness may influence the performance of MPT64-based ICT and there may be some differences in accuracy between 3 commercial kits. Thus, we conducted a systematic review and meta-analysis on the performance of commercial MPT64-based ICTs for the identification of MTC.

Methods

Search strategy and selection criteria

We searched the following electronic databases: Pubmed (1999—2012), BIOSIS Previews (2000—2012) and Web of Science (2000—2012). All searches were up to 22 November 2012. The search terms included "Tuberculosis, *M. tuberculosis*, *M. bovis*, mycobacteria, nontuberculous mycobacteria, MPT64, MPB64, Capilia TB, SD Bioline, MGIT TBc, identification, differentiation, confirmation, detection, diagnosis, evaluation, performance." We restricted our search to reports published in English. In addition, we searched the reference lists of some primary studies and several previously published reviews on mycobacteria identification tests.

We included studies that met the following predetermined inclusion criteria: (1) original data were presented; (2) commercial not in-house MPT64-based ICT was evaluated; (3) at least one accepted reference standard (biochemical method or molecular methods such as AccuProbe MTC, GenoType MTBC and DNA sequencing) was used; (4) cultures in liquid media or on solid media were tested; (5) total number of strains tested and positive/negative results were reported, so calculation of true positives (TP), true negatives (TN), false positive (FP) and false negative (FN) is allowed. The following studies were excluded: (1) case reports, editorials, letters, reviews and conference abstracts; (2) studies performed with in-house MPT64-based ICT; (3) studies not compared the assay with a reference standard; (4) studies not performed according to the manufacturers' instructions.

Citations were screened independently by two reviewers (XY and LL). Titles and abstracts were screened for relevance and any citations identified by either reviewer were evaluated further by review of full-text reports. Disagreements between the reviewers were resolved by consensus. A list of excluded studies and full reasons for exclusion are available from the authors on quest.

Data extraction and quality assessment

One reviewer (XY) assessed the final set of included articles and extracted data from all the reports using a piloted data extraction form. A second reviewer (LL) independently assessed data from a subset of the included studies to check accuracy in data extraction. The inter-rater agreement obtained from the checked studies was 100%. Data retrieved from the reports included calendar period of the study, country in which the study was conducted, methodological quality, brand of commercial MPT64-based ICT kit, reference standard method used, sample size, outcome data (sensitivity and specificity as determined by comparison with the reference standard).

We used the QUADAS criteria for assessment of quality of diagnostic studies to assess quality characteristics that were judged to be important for this review[10]: (1) study design (cross-sectional versus case-control); (2) collection of specimens (consecutively/randomly versus neither); (3) interpretation of the test results with reference standard results and vice versa (single/double blind versus unblinded); (4) verification of the test results with the reference standard (complete versus partial/differential).

Data synthesis and meta-analysis

TP, FP, TN and FN were taken directly from the source reports. If the information was not available, these values were calculated from the data that were provided in the