Microbial Drug Resistance

Diagnostic Accuracy of Pyrazinamide Susceptibility Testing in *Mycobacterium tuberculosis*: A Systematic Review with Meta-Analysis

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Abstract

Introduction: Pyrazinamide (PZA) susceptibility testing plays a critical role in determining the appropriate treatment regimens for multidrug-resistant tuberculosis. We conducted a systematic review and meta-analysis to evaluate the diagnostic accuracy of sequencing PZA susceptibility tests against culture-based susceptibility testing methods as the reference standard.

Methods: We searched the MEDLINE/PubMed, Embase, and Web of Science databases for the relevant records. The QUADAS-2 tool was used to assess the quality of the studies. Diagnostic accuracy measures (*i.e.*, sensitivity and specificity) were pooled with a random-effects model. All statistical analyses were performed with Meta-DiSc (version 1.4, Cochrane Colloquium, Barcelona, Spain), STATA (version 14, Stata Corporation, College Station, TX), and RevMan (version 5.3, The Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark) software.

Results: A total of 72 articles, published between 2000 and 2019, comprising data for 8,701 isolates of *Mycobacterium tuberculosis* were included in the final analysis. The pooled sensitivity and specificity of the PZA sequencing test against all reference tests (the combination of BACTEC mycobacteria growth indicator tube 960 (MGIT 960), BACTEC 460, and proportion method) were 87% (95% CI: 85–88) and 94.7% (95% CI: 94–95). The positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and the area under the curve estimates were found to be 12.0 (95% CI: 9.0–16.0), 0.17 (95% CI: 0.13–0.21), 106 (95% CI: 71–158), and 96%, respectively. Deek's test result indicated a low likelihood for publication bias ($p = 0.01$).

Conclusions: Our analysis indicated that PZA sequencing may be used in combination with conventional tests due to the advantage of the time to result and in scenarios where culture tests are not feasible. Further work to improve molecular tests would benefit from the availability of standardized reference standards and improvements to the methodology.