

Using harmonised results of different tests for a single biomarker in test accuracy meta-analysis

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Background: Evaluating the performance of a biomarker is challenging when different tests exist for measuring the same marker. Along with other sources of heterogeneity in systematic reviews of diagnostic test accuracy (DTA) studies, this can further influence and confound the results of meta-analysis.

Aims: We here propose a strategy to combine multiple tests to measure the same marker in a single meta-analysis. We apply this strategy to a meta-analysis of DTA studies of the Enhanced Liver Fibrosis (ELF) test, used in non-alcoholic fatty liver disease patients.

Methods: Our systematic search in five databases identified ten studies. Two different ELF tests were proposed, each using a different formula, expressed on a different scale. We initially conducted two meta-analyses, accounting for the multiple thresholds (diagmeta package in R). We then (1) evaluated, in a separate study of 502 samples, the presence of a linear relationship between the results of the tests. We (2) used the regression equation to obtain harmonized test results and (3) performed a single meta-analysis, combining the results from all nine studies.

Results: Eight studies used one formula (Siemens) and two used another (Guha). The first meta-analysis of the eight studies resulted in an “optimal” threshold (maximum Youden) of 9.30, for a sensitivity of 0.75 (95%CI 0.59; 0.87) and a specificity of 0.81 (95%CI 0.68; 0.90). After checking the linearity (R²: 0.995) and mapping the results on the same scale (Figure 1A), a meta-analysis of all ten studies was possible. This resulted in an “optimal” threshold of 9.38 for a sensitivity of 0.72 (95%CI 0.70; 0.90) and a specificity of 0.79 (95%CI 0.66; 0.88) (Figure 1B).

Conclusion: Our three-step method allows the combination of multiple tests of the same marker in a single meta-analysis, facilitating the interpretation of the accuracy of using specific thresholds.

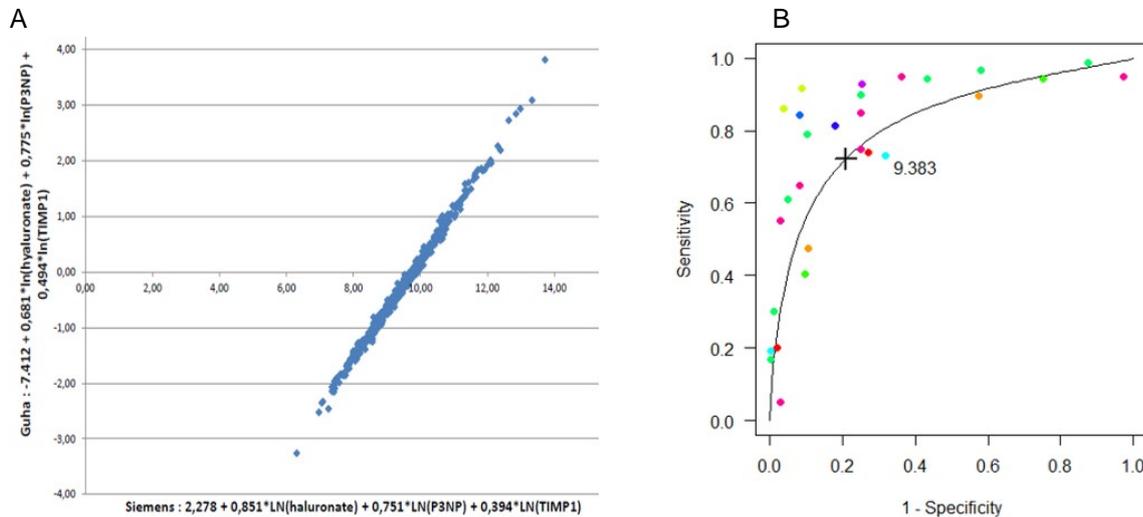


Figure 1: (A) Scatter plot of the correlation between two tests: Test 1: Siemens and Test 2: Guha. Using the regression formula of : Guha results = 0.8854*(Siemens results) - 8.6498. (B) Multiple thresholds sROC (mtsROC) curve based on the multiple thresholds model using homogenized thresholds. Circles represent information on sensitivity and specificity.

Keywords

Meta-analysis, accuracy studies, harmonization