Publication of the Month

September 09/09: Likelihood ratio for result intervals- more useful than the cutoff.

Cutoff-based test result evaluation is widely used in laboratories for all autoimmune tests. However, the pure result figure and its interpretation as positive or negative is of limited help in clinical evaluation. What is the clinical significance of a result of 20 U/ml if the test has a cutoff of 10 U/ml? Is the patient likely to have the disease? At last in tests for autoantibodies which are pathogenic the probability for the patient to have the disease depends on the antibody titer. In these cases the calculation of the positive and negative likelihood ratios (LRs) provides a much better tool for evaluating the clinical impact of the test result than the pure cutoff. The publication presented shows this using the example of ANCA tests.

For refreshment purposes:

$$\text{number of } \frac{\text{true positives/ true positives + false negatives}}{\text{false positives/ false positives + true negatives}} = \text{pos. LR} = \frac{\text{sensitivity}}{\text{1 - specificity}}$$

$$\text{number of } \frac{\text{false negatives/ true positives + false negatives}}{\text{true negatives / false positives + true negatives}} = \text{neg. LR} = \frac{\text{false negative rate}}{\text{true negative rate}}$$

Useful tests have large positive LRs and on the other side negative LRs close to 0. Example: a positive diagnostic LR of 5.0 means that for every 1% of false positive subjects, 5% of the diseased subjects will test as positive. A negative LR of 2.5 means that for every one false negative, 2.5 true negatives are observed.

Vermeersch P, Blockmans D, Bossuyt X

Use of likelihood ratios can improve the clinical usefulness of enzyme immunoassays for the diagnosis of small-vessel vasculitis

Clin Chem 2009;55 (10): in press

The calculation presented is based on 37 consecutive patients with newly diagnosed small vessel vasculitis and 285 consecutive control individuals who were suspected to have vasculitis, but turned out to have other diseases. Sera from these two groups were analyzed using indirect immunofluorescence (IIF) on human granulocytes as well as enzyme immunoassays (EIA) from three different suppliers.

The data demonstrates that the likelihood ratio for small vessel vasculitis increases with antibody concentration and that the positive likelihood ratio is much higher for EIAs than for IIF. The lower positive likelihood ratio observed with IIF is due to the lower specificity of this assay compared to EIA. However, also between different EIAs substantial differences are obvious and point to a different clinical usefulness of these tests.

In conclusion, the publication illustrates how the use of likelihood ratios for different test-result intervals can improve the clinical usefulness of EIA testing for small vessel vasculitis. Clinical laboratories might consider providing likelihood ratios for test-result intervals and not only cutoff based positive/negative evaluation to improve clinical interpretation.