Online Supplementary Appendix

Brief tutorial on ROC analysis and clinical application of Bayes’ theorem

A Receiver Operating Characteristic (ROC) curve is obtained by calculating the sensitivity and specificity of every observed test value and plotting sensitivity (true positive results; ordinate) against 1–specificity (false positive results; abscissa). A test that perfectly discriminates between two groups would yield a curve coinciding with the left and top sides of the plot and having an area under the ROC curve (AUROC) of 1.0. A test that is completely useless would give a straight line from the bottom left corner to the top right corner and have an AUROC of 0.5. In addition, ROC analysis calculates sensitivity, specificity, likelihood ratios, and positive and negative predictive values for all possible threshold values of a given assay, and identifies the cut-off point with the best compromise between sensitivity and specificity. This is the cut-off which creates the smallest total number of false positive plus false negative results.

The positive likelihood ratio (LR +) of a test result is defined as “the probability of an individual with disease having a positive test” (true positive) divided by “the probability of an individual without the disease having a positive test” (false positive) and is calculated as follows: sensitivity / (1–specificity). The negative likelihood ratio (LR −) is defined as “the probability of an individual with disease having a negative test” (false negative) divided by “the probability of an individual without the disease having a negative test” (true negative), and is calculated as follows: (1–sensitivity) / specificity. The greater a LR + is, the more useful is the given test result to detect patients with the target disease. On the other hand, the smaller the LR − is, the more useful is the given test result to exclude the disease. By convention, LR + above 10 and LR − below 0.1 are taken as strong evidence to consider or rule out diagnosis in most circumstances.

Applying Bayes’ theorem, likelihood ratios can be used to calculate the probability of disease for individual patients. This is accomplished by combining the pre-test probability of disease with the likelihood ratio of the test result, either by direct mathematical calculation or by using Fagan’s nomogram. The mathematical calculation makes use of the odds rather than probability according to the equation: “pre-test odds x likelihood ratio = post-test odds”. The pre-test probability p1 can be converted to the pre-test odds with the formula: p1 / (1–p1) = pre-test odds. After calculation, the post-test odds ω can be converted back to a post-test probability with the equation: ω / (1 + ω) = post-test probability.

References