IVDR Performance Evaluation: ROC in absence of Gold Standard

Most of the diagnostic tests give accurate results in comparison with a gold standard method or a well-established standard procedure. In such scenario, all standard diagnostic accuracy estimates can be calculated such as sensitivity, specificity, false-positive rate, false-negative rate, positive predictive value, positive predictive value adjusted for known prevalence of the disease, negative predictive value, negative predictive value adjusted for known prevalence of the disease, false omission rate, false discovery rate, prevalence of the disease based on the data, proportion correctly classified, proportion incorrectly classified, confidence intervals for various rates, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio.

These estimates can be calculated when the diagnostic test results are dichotomous (for example: positive/ negative). But in certain scenarios, diagnostic test results may be in numerical values (for example fasting blood sugar, Total Cholesterol, etc.). In such cases, we need to derive a cutoff point to determine whether the subject is having a disease condition or not. To perform this analysis, the Receiver Operating Characteristic (ROC) curve will be used.

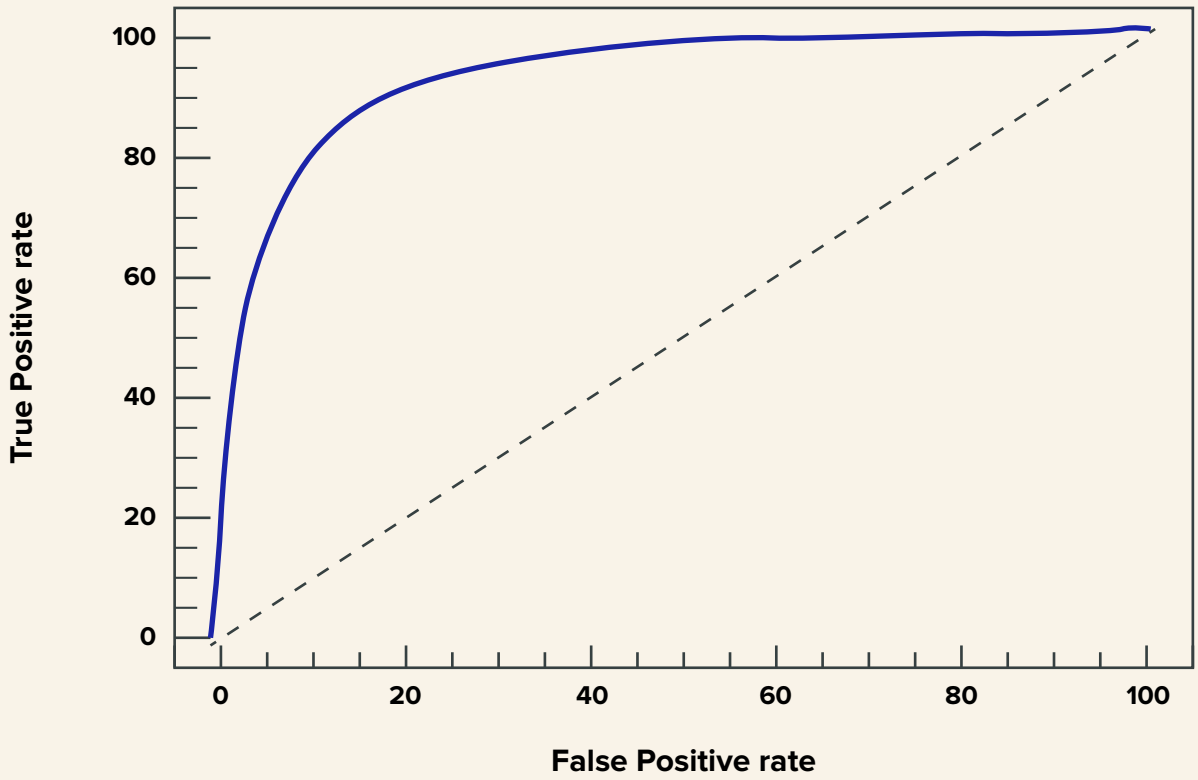
ROC curves are used to represent graphically the connection/trade-off between clinical sensitivity and specificity for every possible cut-off point for the diagnostic test result. Further, a gold standard or a well-established standard procedure may not exist for the diagnosis of a particular disease. In such cases, an imperfect reference standard can be used, because the subjects' disease condition is unknown. The objective of this paper is to review statistical methods to estimate a cutoff point when there is no gold standard.

As mentioned above, the absence of gold standard is a common challenge in diagnostic studies and hence there is a need for statistical methods to be used to estimate cutoff value for a diagnostic test. We can use Bayesian approach to estimate the probability of the unknown disease status via a latent class model. Latent Class Analysis (LCA) is a statistical method for identifying unmeasured class membership among subjects using categorical and/or continuous observed variables. We can estimate two indexes viz., area under curve (AUC) and integrated discrimination improvement (IDI) from this analysis when there is no gold standard.

Area under Curve: Receiver Operating Characteristic (ROC) curve is a probability curve and Area under Curve (AUC) represents degree or measure of separability. It tells how much a model is capable of distinguishing between classes. Higher the AUC, the better the model is to distinguish between patients with the disease and without the disease.

Integrated Discrimination Improvement (IDI): IDI is defined as the sum of the average increase in predicted probability among patients with the outcome and the average decrease in probability among patients without the outcome.

Receiver Operating Characteristic (ROC) curve: ROC curve is plotted with True Positive Rate (TPR) against the False Positive Rate (FPR) where TPR is on the y-axis and FPR is on the x-axis as shown below.



Thus by using the ROC curve, AUC and IDI, a diagnostic test cutoff point may be derived in the absence of a gold standard. The calculation procedures are beyond the scope of this paper.

To conclude, when there is no gold standard available, both area under the curve and integrated discrimination improvement statistics may be estimated and can decide the practical value of a new diagnostic test/procedure.

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