A meta-analysis comparing the prognostic accuracy of six diagnostic tests for prediction perioperative cardiac risk in patients undergoing major vascular surgery

Appendix

Summary receiver characteristics curves

Conventional receiver operating characteristic curves (ROC) graphically represent the true positive and false positive rates for a diagnostic test when the threshold for a positive test result is varied.[67] The area under the curve summarises the overall diagnostic performance of the test, with larger areas corresponding to a more discriminating test. Most reports of the performance of a diagnostic test provide only single estimates of the true positive (TP) and false positive (FP) rates for one fixed threshold value. A possible source of heterogeneity in a meta-analysis of a diagnostic test is the variability of threshold values across studies. Variability in TP and FP rates derived from published reports may represent different operating points on one common underlying ROC curve. Hence, pooling TP and FP rates from different sources would underestimate the diagnostic performance.[68]

Summary ROC (SROC) analysis assumes that part of the reported variability in test performance reflects the difference in the cut off points or positivity criteria used, and aims to adjust for these differences. SROC analysis also allows adjustment for important clinical covariates and for comparison between different types of tests.[69] In this case, a variable corresponding to the type of non-invasive testing used is entered into the regression equation. The differences in diagnostic performance of the tests are represented by the regression coefficients and can be interpreted after antilogarithm transformation as relative diagnostic odds ratios. They indicate the diagnostic performance of a test, with a value larger than 1 indicating better discriminatory power, whereas a value equal to 1 indicates no difference, and values below 1 indicate reduced discriminatory ability.[70]

First, the estimates of sensitivity (true positive rate) against the estimates of 1specificity (false positive rate) were plotted. If there was a positive relation between true positive rates and false positive rates (that is, both true positive and false positive rates increase), then this association was identified using the non-parametric Spearmen correlation test.[71] If the true positive rates and false positive rates were positively correlated, then summary ROC analysis was undertaken. In case of a negative correlation only summary point estimates that is, weighted

sensitivity and specificity of the test were given.

Construction of a summary receiver characteristics curve

The construction of a SROC curve requires that the number of true positive (TP), false positive (FP), true negative (TN), and false negative (FN) observations in each study be available.[69]

Computational steps involved in the construction of summary ROC curve

Computation of the difference (D) and the sum (S) of the logit transforms of TP and FP rates

$$D = \ln((TP+1/2)/(FN+1/2)) \ln((FP+1/2)/(TN+1/2))$$

$$S = \ln((TP+1/2)/(FN+1/2))+\ln((FP+1/2)/(TN+1/2))$$

where TP, FN, TN, and FP are corrected by one half to ensure that D and S would not be undefined if TP, FN, TN, or FP equals zero.

Computation of the asymptotic variance (VAR) of D

$$VAR (D) = ((1/TP+1.2)+(1/FN+1/2)+(1/TN+1/2)+(1/FP+1/2)$$

Weighted least square regression analysis, using weights proportional to the inverse of VAR (D)

In our study, the following equation was used to evaluate the prognostic accuracy of individual tests:

$$D = \alpha + \beta_s*S + \varepsilon$$

where D is the dependent variable from equation 3, α, β_s, are regression coefficients, S is the independent variable for equation 4, and ε is the error term.

The following equation was used for between-test comparisons to compare the prognostic accuracy of two tests:

$$D = \alpha + \beta_s*S + \beta_t*T + \varepsilon$$

where D is the dependent variable from equation 3, α, β_s, β_t are regression coefficients, S is the independent variable for equation 4, and T is a dummy variable indicating the type of test for between-test comparison (with T=0 for one test and T=1 for the other).

The regression lines were converted to the ROC space using the following formula:

$$TPRp = [1+e^{(intercept)/(1-slope)}*(1-FPR/FPR)^{(1+slope)/(1-slope)}]^{-1}$$

where TRPp is the predicted value of the TP rate for a given FP rate (FPR), the intercepts represents intercept of the regression line in the (S, D) space, and slope is the slope of this line.