# Chapter 41
# Performance Evaluation of Novel Diagnostic Tests (650 and 588 Patients)

## General Purpose

Both logistic regression and c-statistics can be used to evaluate the performance of novel diagnostic tests (see also Machine learning in medicine part two, Chap. 6, pp 45–52, Logistic regression for assessment of novel diagnostic tests against controls, Springer Heidelberg Germany, 2013, from the same authors). This chapter is to assess whether one method can outperform the other.

## Primary Scientific Question

Is logistic regression with the odds of disease as outcome and test scores as covariate a better alternative for concordance (c)-statistics using the area under the curve of ROC (receiver operated characteristic) curves.

## Example

In 650 patients with peripheral vascular disease a noninvasive vascular lab test was performed. The results of the first 10 patients are underneath.

| test score | presence of peripheral vascular disease (0 = no, 1 = yes) |
|---|---|
| 1,00 | ,00 |
| 1,00 | ,00 |

(continued)

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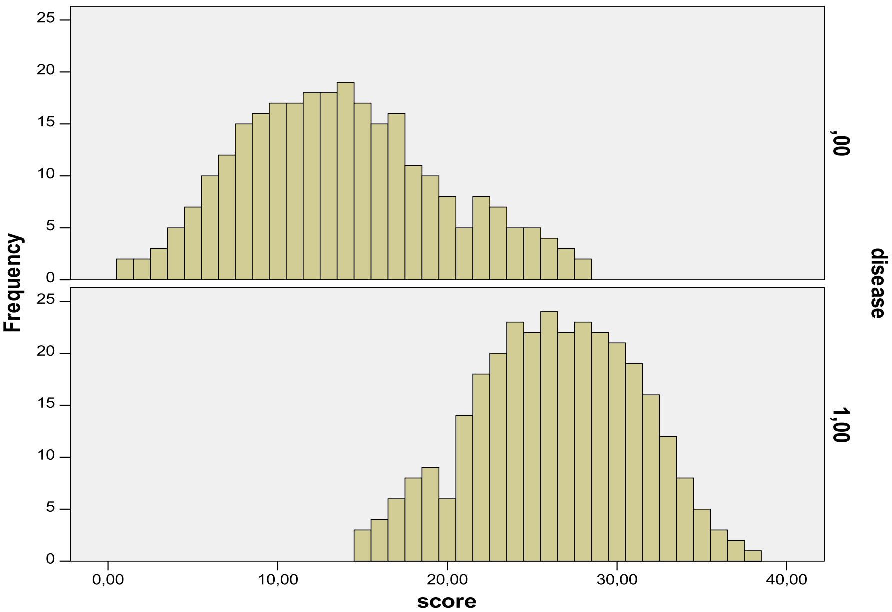
| test score | presence of peripheral vascular disease (0 = no, 1 = yes) |
|---|---|
| 2,00 | ,00 |
| 2,00 | ,00 |
| 3,00 | ,00 |
| 3,00 | ,00 |
| 3,00 | ,00 |
| 4,00 | ,00 |
| 4,00 | ,00 |
| 4,00 | ,00 |

The entire data file is in extras.springer.com, and is entitled “vascdisease1”. Start by opening the data file in SPSS.

**Then Command:**

Graphs....Legacy Dialogs....Histogram....Variable(s): enter "score"....Row(s): enter "disease"....click OK.

The underneath figure shows the output sheet. On the x-axis we have the vascular lab scores, on the y-axis “how often”. The scores in patients with (1) and without (0) the presence of disease according to the gold standard (angiography) are respectively in the lower and upper graph.



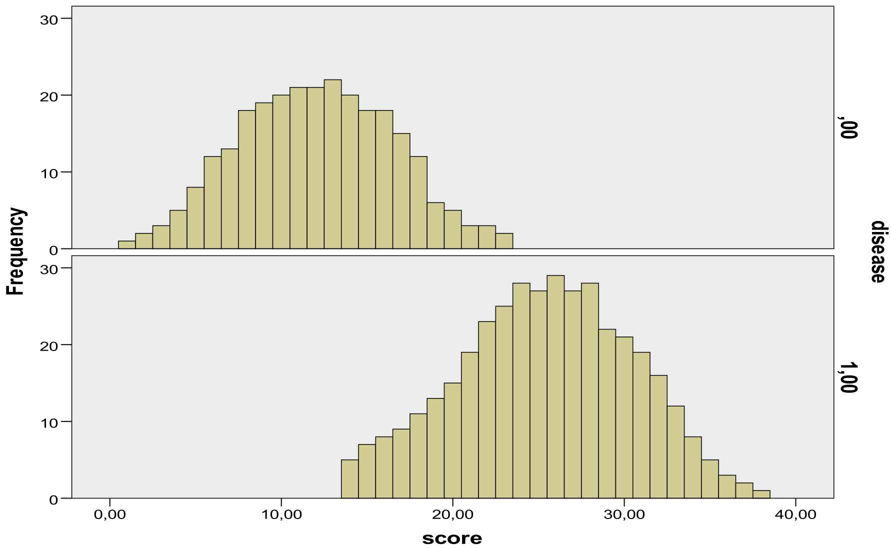
The second data file is obtained from a parallel-group population of 588 patients after the noninvasive vascular test has been improved. The first 10 patients are underneath.

| test score | presence of peripheral vascular disease (0 = no, 1 = yes) |
|---|---|
| 1,00 | ,00 |
| 2,00 | ,00 |
| 2,00 | ,00 |
| 3,00 | ,00 |
| 3,00 | ,00 |
| 3,00 | ,00 |
| 4,00 | ,00 |
| 4,00 | ,00 |
| 4,00 | ,00 |
| 4,00 | ,00 |

The entire data file is in extras.springer.com, and is entitled "vascdisease2". Start by opening the data file in SPSS.

**Then Command:**

Graphs....Legacy Dialogs....Histogram....Variable(s): enter "score"....Row(s): enter "disease"....click OK.



The above figure is in the output sheet.

The first test (upper figure) seems to perform less well than the second test (lower figure), because there may be more risk of false positives (the 0 disease curve is more skewed to the right in the upper than in the lower figure).

## *Binary Logistic Regression*

Binary logistic regression is used for assessing this question. The following reasoning is used. If we move the threshold for a positive test to the right, then the proportion of false positive will decrease. The steeper the logistic regression line the faster this will happen. In contrast, if we move the threshold to the left, the proportion of false negatives will decrease. Again, the steeper the logistic regression line, the faster it will happen. And so, the steeper the logistic regression line, the fewer false negatives and false positives and thus the better the diagnostic test.

For both data files the above analysis is performed.

**Command:**

Analyze…. Regression.…Binary logistic…. Dependent variable: disease…. Covariate: score.…OK.

The output sheets show the best fit regression equations.

Variables in the equation

| | | B | S.E. | Wald | df | Sig. | Exp(B) |
|---|---|---|---|---|---|---|---|
| Step 1[a] | VAR00001 | ,398 | ,032 | 155,804 | 1 | ,000 | 1,488 |
| | Constant | −8,003 | ,671 | 142,414 | 1 | ,000 | ,000 |

[a]Variable(s) entered on step 1: VAR00001

Variables in the equation

| | | B | S.E. | Wald | df | Sig. | Exp(B) |
|---|---|---|---|---|---|---|---|
| Step 1[a] | VAR00001 | ,581 | ,051 | 130,715 | 1 | ,000 | 1,789 |
| | Constant | −10,297 | ,915 | 126,604 | 1 | ,000 | ,000 |

[a]Variable(s) entered on step 1: VAR00001

Data file 1: log odds of having the disease = −8.003 + 0.398 times the score
Data file 2: log odds of having the disease = −10.297 + 0.581 times the score.

The regression coefficient of data file 2 is much steeper than that of data file 1, 0.581 and 0.398.

Both regression equations produce highly significant regression coefficients with standard errors of respectively 0.032 and 0.051 and p-values of $< 0.0001$. The two regression coefficients are tested for significance of difference using the z – test (the z-test is in Chap. 2 of Statistics on a Pocket Calculator part 2, pp 3–5, Springer Heidelberg Germany, 2012, from the same authors):

$$z = (0.398 - 0.581) / \sqrt{(0.032^2 + 0.051^2)} = -0.183 / 0.060 = -3.05,$$

which corresponds with a p-value of $< 0.01$.

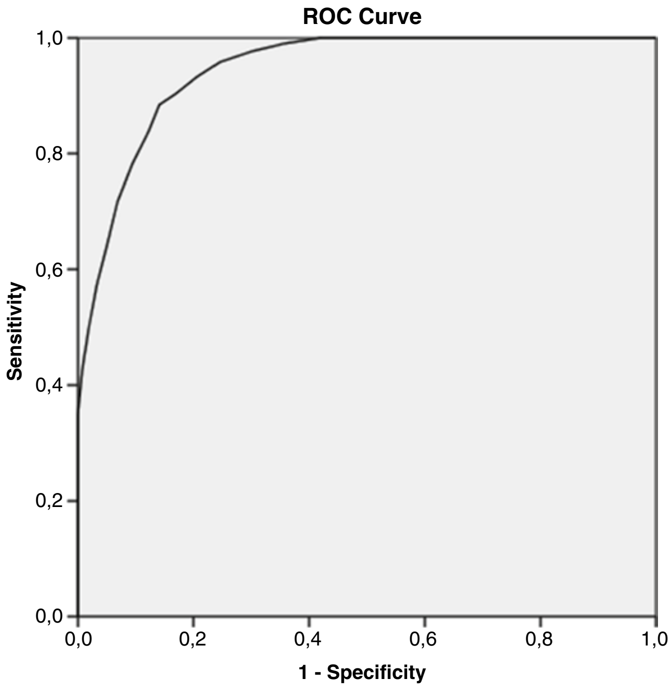
Obviously, test 2 produces a significantly steeper regression model, which means that it is a better predictor of the risk of disease than test 1. We can, additionally, calculate the odds ratios of successfully testing with test 2 versus test 1. The odds of disease with test 1 equals $e^{0.398} = 1.488$, and with test 2 it equals $e^{0.581} = 1.789$. The odds ratio = 1.789/1.488 = 1.202, meaning that the second test produces a 1.202 times better chance of rightly predicting the disease than test 1 does.

## *C-Statistics*

C-statistics is used as a contrast test. Open data file 1 again.

**Command:**

Analyze....ROC Curve....Test Variable: enter "score"....State Variable: enter "disease"....Value of State Variable: type "1"....mark ROC Curve....mark Standard Error and Confidence Intervals....click OK.

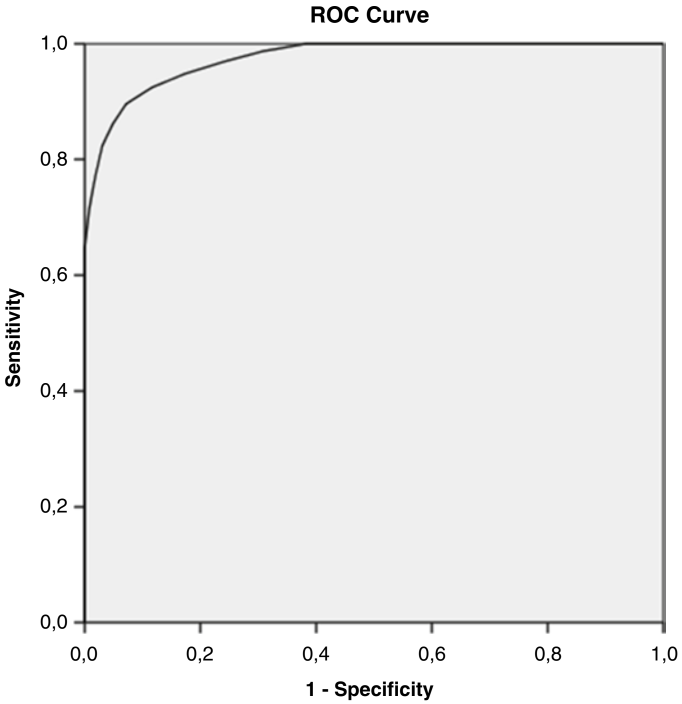



Diagonal segments are produced by ties.

| Area under the curve | | | | |
|---|---|---|---|---|
| Test result variable(s): score | | | | |
| | | | Asymptotic 95 % confidence interval | |
| Area | Std. error[a] | Asymptotic Sig.[b] | Lower bound | Upper bound |
| ,945 | ,009 | ,000 | ,928 | ,961 |

The test result variable(s): score has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased
[a]Under the nonparametric assumption
[b]Null hypothesis: true area = 0.5

Subsequently the same procedure is followed for data file 2.




Diagonal segments are produced by ties.

| Area under the curve | | | | |
|---|---|---|---|---|
| Test result variable(s): score | | | | |
| | | | Asymptotic 95 % confidence interval | |
| Area | Std. error[a] | Asymptotic Sig.[b] | Lower bound | Upper bound |
| ,974 | ,005 | ,000 | ,965 | ,983 |

The test result variable(s): score has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased
[a]Under the nonparametric assumption
[b]Null hypothesis: true area = 0.5

The Area under curve of data file 2 is larger than that of data file 1. The test 2 seems to perform better. The z-test can again be used to test for significance of difference.

$$z = (0.974 - 0.945) / \surd\left(0.009^2 + 0.005^2\right) = 2.90$$

$$p = < 0.01.$$

## Conclusion

Both logistic regression with the presence of disease as outcome and test scores of as predictor and c-statistics can be used for comparing the performance of qualitative diagnostic tests. However, c-statistics may perform less well with very large areas under the curve, and it assesses relative risks while in practice absolute risk levels may be more important

## Note

More background, theoretical and mathematical information of logistic regression and c-statistics is in Machine learning in medicine part two, Chap. 6, pp 45–52, Logistic regression for assessment of novel diagnostic tests against controls, Springer Heidelberg Germany, 2013, from the same authors.