Statistical properties of sensitivity and specificity in receiver operating characteristic analysis: a simulation study using real-world data

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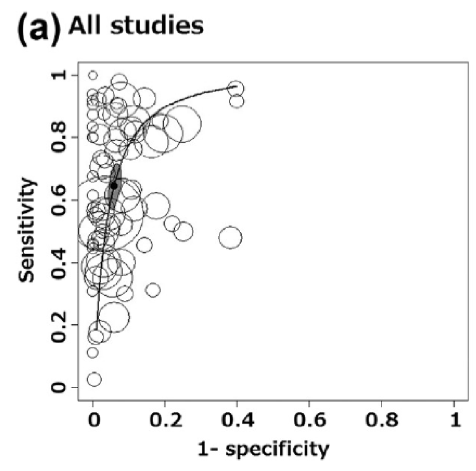
Background

- The receiver operating characteristics (ROC) curve is widely used for the diagnostic meta-analysis of infections.
- Generally, in ROC analyses, the sensitivity and specificity of the optimal cutoff value is analyzed from the ROC curve.
- Theoretically, in diagnostic tests, when the positive and negative predictive values are fixed, an increased proportion of patients with positive diagnostic tests causes higher sensitivity and lower specificity.
- We conducted a simulation study using real-world data to examine whether these statistical properties impacted the sensitivity and specificity of the optimal cutoff value.



Eguchi H, et al. Clin Microbiol Infect. 2017;23:907-915.

Research design & Methods

- We analyzed the 24-h glucose levels of 150 patients with type-2 diabetes to design 110 simulated patterns of ROC curves analyzed using logistic regression.
- To unify the simulated ROC curves with large area under the curve (AUC), we used multiple logistic regression analysis with two covariates stating that "realizing high glucose level and low glycemic variability can reduce hypoglycemia."

Covariates		Binary response variables										
		<80	<77	<74	<71	<68	<65	<62	<59	<56	<53	<50
Mean glucose level	Glycemic variability metrics 1	"1 mean glucose level × 10 glycemic variability metrics × 11 binary response variables = 110 patterns."										
	Glycemic variability metrics 2											
	Glycemic variability metrics 3											
	Glycemic variability metrics 4											
	Glycemic variability metrics 5											
	Glycemic variability metrics 6											
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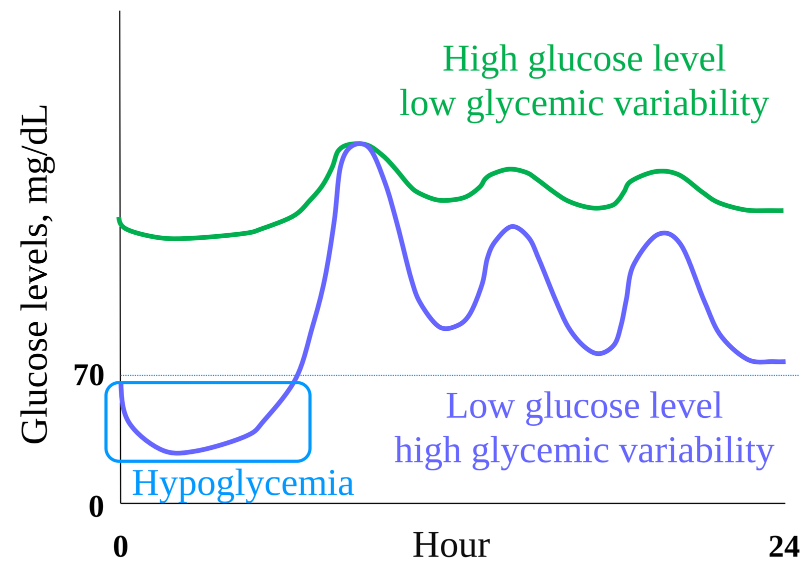
	Glycemic variability metrics 10											



- A covariate, the mean glucose level, was used uniformly for the evaluation of "high glucose level" whereas the other covariate, 10 glycemic variability metrics, was used for the evaluation of "low glycemic variability."
- Regarding the binary response variables evaluating hypoglycemia, we used 11 binary response variables of "absence of glucose levels <80, <77, <74…<53, <50 mg/dL.
- 110 simulated ROC curves were designed as "1 mean glucose level × 10 glycemic variability metrics × 11 binary response variables = 110 patterns."

- The "predictive values" in ROC analyzed using multiple logistic regression are applicable to "cutoff values" in ROC analysis using univariate logistic regression.

- We proposed a metric, "positive-proportion-index," corresponding to the "proportion of patients with positive diagnostic tests" in diagnostic tests, as "optimal predictive values ÷ sum of predictive values × 100" because predictive values, indicating probability that binary numbers which are 0 and 1 become 1, calculated as 1 ÷ (1 + exp(-"regression formulae")), are sure to be 0< predictive values <1.
- The lower optimal predictive value relative to the sum of predictive values indicates that a greater number of predictive values exceed the optimal predictive value.
- A lower "positive-proportion-index" corresponds to a higher "proportion of patients with positive diagnostic tests" in diagnostic tests.

Image	A	B	C
	0.2	0.3	0.4
	0.3	0.4	0.5
	0.4	0.5	0.6
	0.5	0.6	0.7
	0.6	0.7	0.8
Total	2	2.5	3
positive-proportion-index	25	20	16.7

Purple : optimal predictive value

Blue : applied to patients with positive diagnostic tests, in diagnostic tests

Red : applied to patients with negative diagnostic tests, in diagnostic tests

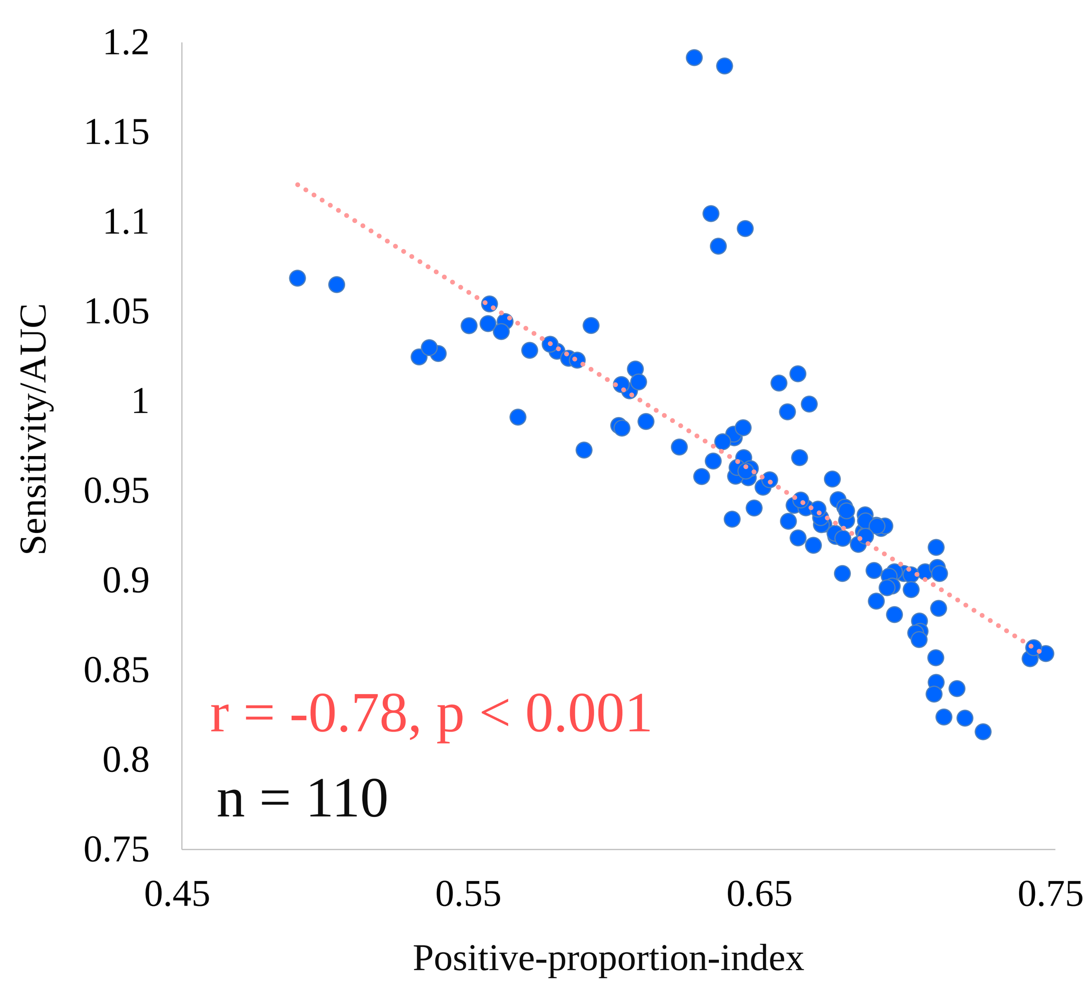
The lower optimal predictive value relative to the sum of predictive values indicates that a greater number of predictive values exceed the optimal predictive value.

- We analyzed a correlation between the "sensitivity of an optimal predictive value ÷ AUC" (sensitivity/AUC) or "specificity of an optimal predictive value ÷ AUC" (specificity/AUC) and positive-proportion-index.

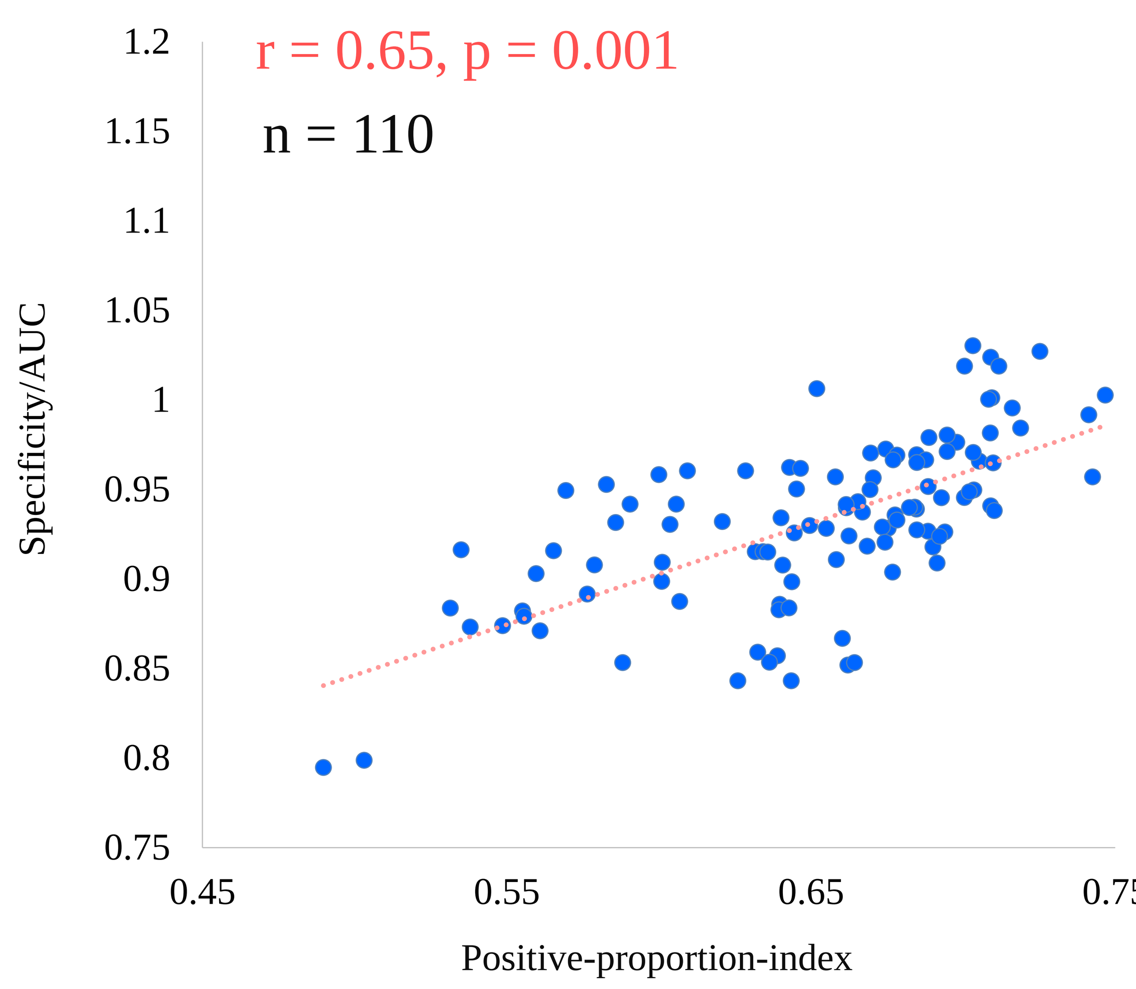
Results

Sample characteristics

n = 110	Mean ± standard deviation
Positive-proportion-index, %	0.65 ± 0.05
Sensitivity/AUC, %	95.5 ± 7.0
Specificity/AUC, %	93.2 ± 4.7
AUC, %	90.0 ± 5.3



Sensitivity/AUC significantly negatively correlated with positive-proportion-index.



Specificity/AUC significantly positively correlated with positive-proportion-index.

Discussion

- The results suggest that an interpreter of ROC analyses should pay attention to the optimal predictive value relative to the sum of predictive values.

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Conclusion

A lower optimal predictive value relative to sum of predictive values causes higher sensitivity and lower specificity for an optimal predictive value.