Short Comunications

Use of the ROC curves for the evaluation of the Guillain-Barré diagnostic methods

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ABSTRACT

Introduction: The ROC (Receiver Operating Characteristic) curves are widely used to compare methods in search of greater specificity and sensitivity in which they are selected.

Methods: For the diagnosis of Guillain-Barré, different methods were used, such as the clinical one, which is performed in routine or basic clinical laboratories, radial immunodiffusion and neurophysiological, which are not mutually exclusive. The total number of patients studied was 347 divided into two groups: a probable group formed by 31 patients and not probable formed by 316 patients. For the quantification of albumin by radial immunodiffusion in serum and cerebrospinal fluid NOR and LC Partigen® plates were used by Siemens (Marburg, Germany) and by agglutination with modified particles of HELFA latex (CIE, BioCubaFarma, Havana).

Results: The Guillain-Barré Syndrome rapid diagnostic latex agglutination test showed little difference between the areas under the curve contrasted with the method considered as reference. As the other tests were incorporated into the diagnosis by latex agglutination, the area under the curve was increased. The area under the curve of the latex agglutination method was 0.742, showing that the technique of agglutination in albumin latex in cerebrospinal fluid does not replace the simple radial immunodiffusion for the immunological diagnosis of Guillain-Barré Syndrome, but it does allow a diagnostic orientation as screening.

Conclusions: The latex agglutination test showed that it can be used for the rapid diagnosis of Guillain-Barré Syndrome.

Keywords: Guillain-Barré; ROC curves; latex agglutination test; diagnosis; sensitivity; specificity.

INTRODUCTION

Clinical researcher is often confronted with the question how accurate a particular laboratory test is capable of identifying a disease. The ability of a test to discriminate positive cases from normal cases is evaluated using Receiver Operating Characteristic (ROC) curve analysis[1-2]. ROC curves can also be used to compare the diagnostic performance of two or more laboratory or diagnostic tests[3]. When you consider the results of a particular test in two populations, one population with a disease, the other population without the disease, you will rarely observe a perfect separation between the two groups. Indeed, the distribution of the test results will overlap. For every possible cut-off point or criterion value you select to discriminate between the two populations, there will be some cases with the disease correctly classified as positive or true positive fraction but some cases with the disease will be classified negative or false negative fraction. On the other hand, some cases without the disease will be correctly classified as negative or true negative fraction, but some cases without the disease will be classified as positive or false positive fraction.

Guillain-Barré syndrome patients have increased in number during the recent years because of the appearance of new arbovirus like Zika virus in the America region and particularly in Cuba. In order to improve the early diagnosis of this syndrome in emergency it was necessary to select a method that should be fast, easy to perform and to have enough specificity to apply when a suspicious patient arrives at the hospital.

The aim of this paper is to apply ROC curve analysis to determine the best method or methods to improve the early diagnosis of Guillain-Barré syndrome.

METHODS

For the diagnosis of Guillain-Barré, different methods have been used, such as the clinical one, which is performed in routine or basic clinical laboratories, radial immunodiffusion and neurophysiological, which are not mutually exclusive. The total number of patients studied was 347 divided into two groups: a probable group formed by 31 patients and not probable formed by 316 patients.

For the quantification of albumin by radial immunodiffusion in serum and cerebrospinal fluid NOR and LC Partigen® plates were used by Siemens (Marburg, Germany) and by agglutination with modified particles of HELFA latex (CIE, BioCubaFarma, Havana).[4]

In order to find the best method or a combination of several methods that allow to diagnose more properly Guillain-Barré Syndrome is compared each method already mention individually and in combination of several ones. The best method applying ROC curves is the one that has a larger area under curve in the ROC curves because has the better specificity and sensibility.

Table 1. Contingency table. Outcomes of a test

Test	***Disease present***	***n***	***Disease absent***	***n***	***Total***
Positive	True positive	a	False positive	c	a+b
Negative	False negative	b	True negative	d	b+d
Total		a+b		c+d	

In order to understand much better ROC analysis it is important to take into account the following variables:

Sensitivity. Is the probability that a text result will be positive when the disease is present. It is the same as the true positive rate, expressed as a percentage: (a/a+b) x 100.

Specificity: Is the probability that a text result will be negative when the disease is not present. It is the same as true negative rate, expressed as a percentage: (d/c+d) x 100.

RESULTS

The Guillain-Barré Syndrome rapid diagnostic latex agglutination test showed little difference between the areas under the curve contrasted with the method considered as reference as seen in Figure 1.

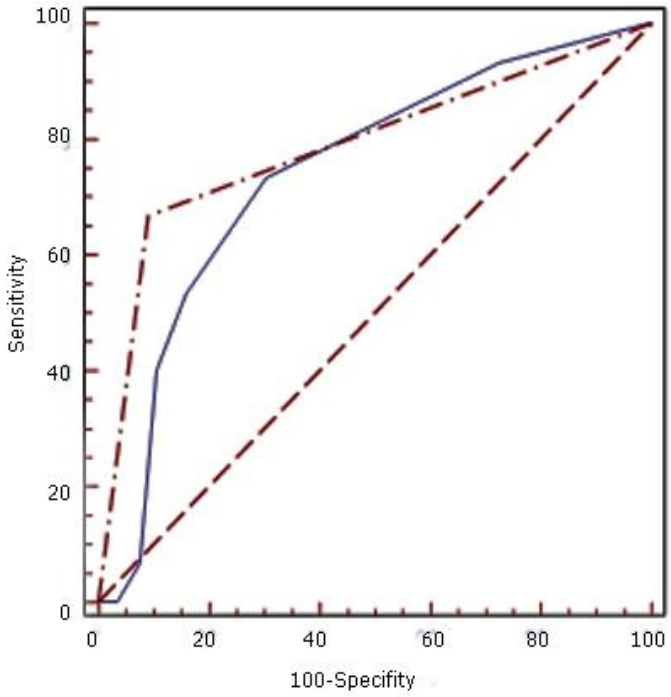


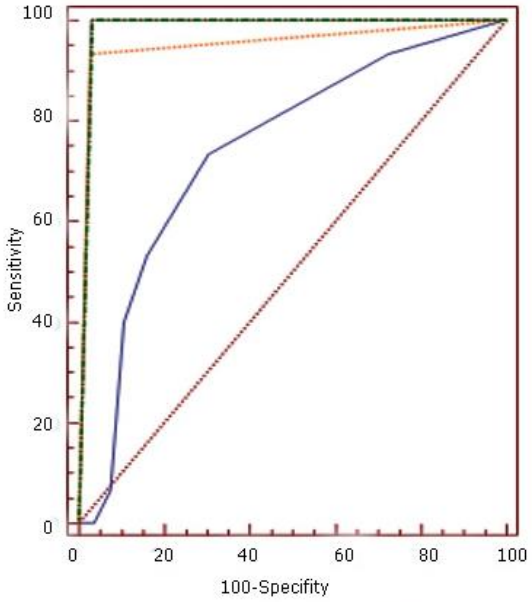
Fig. 1 Comparison between blood/ cerebrospinal fluid barrier dysfunction and the maximum latex agglutination .Maximum ( ) Barrier dysfunction ( )

The different area under the curves of the different methods it can be found in Table 2. The different diagnosis methods employed was compared. There are two methods: the clinical and the basic CSF analysis, both presumptive ones and the agglutination test and the immunological method that are certainty ones.

Table 2. Methods used for the diagnosis of GBS and latex agglutination

Methods	Area down the curve	Standard error	Confidence interval 95 %
Clinical	0.977	0.027	0.956-0.990
Basic CSF	0.985	0.022	0.966-0.995
Simple radial immunodiffusion	1.000	0.000	0.989-1
Neurophysiological	0.764	0.073	0.715-0.807
Latex agglutination	0.742	0.075	0.692-0.787

As the other tests were incorporated into the diagnosis by latex agglutination, the area under the curve was increased.



AC= area under curve. Maximum titulation (——)Sum of basic CSF methods and neuroimmunological method (AC=0,903) (– – –)Sum of basic CSF methods and neurophysiological methods (AC=0,871) (——)Sum of basic CSF methods, neuroimmunological method and neurophysiological methods (AC=0,919) (– – –)

Fig. 2. ROC curves comparison of the association of several tests already stablished with the latex agglutination.AC= area under curve.

The area under the curve of the latex agglutination method was 0.742; showing that the technique of agglutination in albumin latex in cerebrospinal fluid does not replace the simple radial immunodiffusion for the immunological diagnosis of Guillain-Barré Syndrome, but it does allow a diagnostic orientation as screening.

DISCUSSION

The value of the area under the ROC curve means that a randomly selected individual from the positive group can be interpreted as follows: An area of 0,90, for example, means that a random selected individual from the positive group has a test value larger than for a randomly chosen individual from the negative group in 90 % of the time.[5] When the variable under study cannot distinguish between the two groups, i.e. where there is no difference between the two distribution, the area will be equal to 0,5 (the ROC curve will coincide with the diagonal, When there is a perfect separation of the values of the two groups, not overlapping of the distribution the area under the curve, the area under the ROC curve equals 1 and the ROC curve will reach the upper left corner of the plot.

It is possible to compare statistically the difference between two or more areas under different ROC curve and it is employ to determine not only the best method, also if one method is better than the other ones.

When the ROC curve was analyzed there are small differences between the barrier dysfunction and the use of agglutination technique. It is an important fact in favor to use this method for the GBS diagnosis because this physiological finding is the basis of the diagnosis.[6,7]

The area under the curve showed for the agglutination technique is not better than the immunological methods and other ones but it will be useful for screening purposes.

In the same way that it is possible to employ different techniques jointly the area under the curve became better indicating that the specificity as well as the sensibility increased the GBS diagnosis.

The screening diagnostic test or quick diagnostic test has advantages and disadvantages. Among the advantages it can be found the possibility to decrease the diagnostic costs, the employ of people less qualified in the emergency, it is more easy to perform and it allow to perform more samples at the same time among other ones.

Among the disadvantages it can be mentioned that not always are flexible methods or there has not recognition in the international standards and there are qualitative methods, generally.

The application of ROC curve analysis was useful to determine the best method to improve the early diagnosis of Guillain Barré syndrome.

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