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PD2iCA as prognostic score of mortality in the intensive care unit

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Abstract

Background: PD2iCA (Point Correlation Dimension) is a nonlinear time-dependent algorithm used for risk evaluation of cardiac death due to arrhythmia or pump failure. Although there are studies that proves the usefulness of PD2iCA, its utility has not been determined in the intensive care unit (ICU)
Methods: This is a four months prospective cohort study of the utility of PD2iCA as prognostic score of mortality in the ICU. In each patient, the PD2iCA score was determined at time of admission following manufacturer's guides. Subsequently, in order to determine mortality, patients were followed during hospitalization in ICU and until 30 days after discharge from the unit. Sensitivity, specificity, negative predictive value, positive predictive value and relative risk were calculated.
Results: From August through December 2010 fifty seven patients were admitted to ICU. Nevertheless, fifty four patients completed the study. Thirty one patients were in the group with risk according to PD2iCA score, and 23 in the group without risk. The sensitivity of the test was 93.75% (95% CI, 78.76 to 100), specificity 57.89% (95% CI, 40.88 to 74.91), negative predictive value 95.65% (95% CI, 85.14 to 100), positive predictive value 48.39% (95% CI, 29.18 to 67.59) and relative risk 11.13 (95% CI, 1.58 to 78.31). The Chi-square and Fisher's Exact Tests gave p values less than 0.05.
Conclusions: We found that PD2iCA is useful to determine risk of death in the ICU. This diagnostic test is fast, and can be used routinely.

I. Introduction

There is experimental evidence for an association between alterations in sympathetic or vagal activity and propensity for lethal arrhythmias. As a result, many efforts have been made for the development of quantitative markers of autonomic function. Chiefly, the hearth rate variability (HRV) represents one of the most promising markers [1]. The analysis of the HRV gives us information about changes in cardiac autonomic function and performance [2]. Low indices of HRV are associated with an increased risk of ventricular arrhythmias and sudden arrhythmic death [2], [3]. For this reason, these indices are independent risk factors for mortality in patients with myocardial infarction and advanced cardiac heart failure [2], [4]. Additionally, the analysis of HRV is useful in the detection of diabetic neuropathy [1], [5].

Currently there are several indices of HRV; however, they are not widely used in clinical practice because there is not enough statistical data that proves their utility [2]. The majority of these indices are based in linear stochastic algorithms. Consequently, this type of algorithms presumes that the heartbeat variations are random and are distributed around a mean [2]. On the other hand, some indices are based on nonlinear deterministic models, which presume that heartbeat variations are caused physiologically; hence, this type of indices are more accurate [6].

PD2iCA (Point correlation dimension) is a nonlinear time-dependent algorithm developed by Vicor Technologies, Inc. PD2iCA is used for risk evaluation of cardiac death due to arrhythmia or pump failure [2]. Studies show that this method has: sensitivity= 96-100%, specificity= 58-85%, negative predictive value= 99% and positive predictive value= 20% [2], [7]. Also, a comparative test between linear and nonlinear algorithms suggests that PD2i is the best method [8]. However, there are not studies that prove the usefulness of PD2iCA in the ICU area.

This research has two objectives. First, determine the risk of death of patients in the intensive care unit (ICU) using PD2iCA. Second, determine if patients with risk survive during hospitalization in ICU and until 30 days after discharge from the unit.

II. Material and methods

We performed a prospective cohort study of the usefulness of PD2iCA as prognostic score of mortality in the ICU of the Hospital General de la Fuerzas Armadas N° 1, in Quito-Ecuador.

A. Patients

We include critically ill patients admitted to the ICU from August to December 2010. The inclusion criteria were an age ≥ 18 years old, men or women and the approval of the informed consent. Also, the accepted admission diagnoses were severe sepsis and septic shock, acute coronary syndrome (with or without ST elevation), cerebrovascular accident (ischemic or hemorrhagic) and severe trauma. We excluded patients with cardiac arrhythmia (auricular fibrillation) or lesions incompatible with life. Each pathology was treated according to institutional protocols.

Patients, during hospitalization in ICU and until 30 days after discharge from the unit, were followed in order to determine mortality. The follow up 30 days after discharge from ICU was made using clinical expedients or phone calls. Patients with lost to follow up were excluded from the final analysis. Furthermore, excluded were patients that died because of causes different from the admission diagnosis. Data were collected in records sheets that include name, contact information, diagnosis, PD2iCA score, and place, time and cause of death.

B. PD2iCA analysis

At the time of admission, in order to obtain the PD2iCA score, four electrodes were

placed in each patient: two in the mid clavicular line at the second intercostal space, and two in the mid clavicular line at the costal edge. The electrodes were connected to the PD2i Cardio Card (Model: CUSB, Nasiff Associates for Vicor Technologies, New York City, NY) which is linked to a computer. With the purpose to avoid noise that could affect the final analysis, the PD2i Cardio Card functions with battery, and is never connected to the electric main. A 1000 heartbeats or fifteen minutes of ECG analysis was made using the Point Correlation Dimension (PD2i) software (Vicor 2.0, Vicor Technologies, Inc., Boca Raton, FL). The cut-point to determine risk was established in 1.4 like in previous studies. In other words, a PD2iCA≤ 1.4 is considered a risk factor [9]. All technical specifications were followed according to manufacturer's guides [2], [7], [8].

C. Statistics

Initially, general descriptive statistics were obtained of the entire information. We calculated the risk of death in patients with positive (≤ 1.4) and negative (> 1.4) PD2iCA scores. Additionally, attributable fractions (among exposed and in the population) were calculated. The sensitivity, specificity, negative predictive value, positive predictive value and relative risk of the PD2iCA were obtained with a 95% confidence interval. In order to determine if there is association between mortality and a PD2iCA of risk, the Chi-square test was obtained with p values. Taking into account that the sample is small, we also made a Yates' correction. Moreover, we applied the Fisher's Exact Test. Finally, we made a ROC curve to determine the accuracy of the test, and to determine the ideal cut-point of PD2iCA for the patients of this study. All data were calculated using SPSS Statistics 17.0 and EPIDAT 3.1.

III. Results

A. Characteristics of patients

From August through December 2010 a total of 57 patients admitted to ICU had the inclusion criteria. However, three patients were excluded from the final analysis because of lost to follow up and cause of death different from the admission diagnosis. The entire cohort was composed of 19 women and 35 men. The mean age was 68.37 years old. Severe sepsis and septic shock was the most common diagnosis (32 patients). In contrast, severe trauma was the less frequent pathology (five patients). During hospitalization in ICU thirteen patients (24.1%) died, and during the follow up three (5.6%). As a result, the total mortality was 29.63%. PD2iCA score was positive for risk in 31 participants (57.4%). The main diagnosis in the group with risk was severe sepsis and septic shock (25 patients). On the other hand, the main diagnoses in the group without risk were severe sepsis and septic shock, and acute coronary syndrome (seven patients in each one). The general characteristics of the cohort are shown in table 1, and the characteristics of each group in table 2.

B. Association between PD2iCA and mortality

The risk of death in patients that have a PD2iCA score ≤ 1.4 was 0.483871. Similarly, the risk in patients with a negative PD2iCA score was 0.043478. Consequently, the risks difference was 0.440393 (95% CI, 0.25 to 0.64). The attributable fraction among the exposed was 0.910145 (95% CI, 0.37 to 0.99). Likewise, the population attributable fraction was 0.853261 (95% CI, 0.05 to 0.97).

With the intention to calculate sensitivity, specificity, negative predictive value, positive predictive value and relative risk, a contingency table was made (table 3). This table shows two variables: the risk factor (PD2iCA score) and the outcome (death).

The sensitivity was 93.75% (95% CI, 78.76 to 100), specificity 57.89% (95% CI, 40.88 to 74.91), negative predictive value 95.65% (95% CI, 85.14 to 100), positive predictive value 48.39% (95% CI, 29.18 to 67.59) and relative risk 11.13 (95% CI, 1.58 to 78.31). Furthermore, the Chi-square test was obtained, which result was 12.2817 (P= 0.0005) without correction. Applying the Yates' correction the value was 10.2604 (P= 0.0014). Moreover, in the case of Fisher's Exact Test the p values were 0.0003 and 0.0006 in the unilateral and bilateral analyses respectively.

The ROC curve (Fig. 1.) showed an area under the curve of 0.789 (P= 0.001; 95% CI, 0.656 to 0.921). The ideal cut-point obtained by this method was ≤ 1.26, which was related with: sensitivity 93.75% (95% CI, 78.76 to 100), specificity 68.42% (95% CI, 52.33 to 84.52), negative predictive value 96.30% (95% CI, 87.32 to 100), positive predictive value 55.56% (95% CI, 34.96 to 76), relative risk 15.00 (95% CI, 2.13 to 105.71) and false negatives 31.6%. The contingency table with the new cut-point is shown in table 4.

IV. Discussion

In this cohort study we determined the utility of the PD2iCA as a prognostic score of mortality in ICU. The groups of risk and no risk were similar in the proportion of male and female patients. In the same way, the two groups had similar frequencies in diagnoses. However, the median age was different; in other words, the group without risk had younger patients. Furthermore, mortality was lower in the group without risk, which is consistent with a good test.

The risk of death in patients with a positive PD2iCA score was higher in comparison with patients that had a negative score. In addition, the risks difference was 0.440393; hence, patients with a positive PD2iCA score had 44.04% more risk of death in comparison with individuals in the negative group. According to the attributable fraction among the exposed, 91.01% of the

deaths in the risk group were associated with a PD2iCA score ≤ 1.4. Also, the population attributable fraction shows that 85.33% of the deaths in all patients were related with PD2iCA. Moreover, Chi-square and Fisher's Exact Tests had p values less than 0.05. Thereupon, there is a statistically significant relation between PD2iCA score and death.

PD2iCA had high sensitivity (93.75%); as a result, this suggests that this test have a low false-negative rate, and it is useful as a screening test. The negative predictive value was 95.65%; thus, when a patient has a negative score, the probability of death is low. In the case of specificity and positive predictive value, the obtained percentages were low. Therefore, PD2iCA is not helpful as a confirmatory test. These findings were consistent with previous studies[2,8]. The relative risk was 11.13; consequently, patients with a positive score have eleven times more risk of death than patients with a negative score. Accordingly, the test was a good risk marker.

In relation to the ROC curve, the area under the curve is consistent with an accurate test in the risk classification. With the cut-point ≤ 1.26 the percentages of specificity and positive predictive values increased in 10.53% and 7.17% respectively. Likewise, the relative risk increased in 3.87 points. This finding suggest that possibly the cut-point must be changed in ICU patients. It is necessary to do more research in order to have a definitive answer to this question.

The sample size was small; for this reason, there is probability that the result can not be generalized. It is recommended to use larger sample size in future studies with the intention to obtain better results. On the contrary, the 95% confidence intervals and p values obtained were significant. As a result, all statistics analyses are reliable.

In future studies could be valuable to make comparisons between PD2iCA and other prognostic scores, to determine which one is superior in the clinical practice. Additionally, the

follow up time could be lager in posterior studies to have a better idea of the impact of this prognostic score in the future survival.

In conclusion, we found that PD2iCA is a useful test to determine risk of death in the ICU. Especially, to rule out risk of mortality in patients with a negative score. This diagnostic test is fast, and can be used routinely.

V. Figures and tables

TABLE I
CHARACTERISTICS OF THE STUDY PATIENTS

Total Number	54
Sex	
Male N° (%)	35 (64.8%)
Female N° (%)	19 (35.2%)
Median age	75
Mortality N° (%)	16 (29.6 %)
PD2iCA score	
Risk N° (%)	31 (57.4%)
No risk N° (%)	23 (42.6%)
Diagnosis	
Severe sepsis and septic shock N° (%)	32 (59.3%)
Acute coronary syndrome N° (%)	11 (20.4 %)
Cerebrovascular accident N° (%)	6 (11.1%)
Severe trauma N° (%)	5 (9.3%)

TABLE II
CHARACTERISTICS OF THE GROUPS OF RISK AND WITHOUT RISK

Characteristics	Risk	No risk
Sex		
Male N° (%)	18 (58.1%)	17 (73.9%)
Female N° (%)	13 (41.9%)	6 (26.1%)
Median age	77	59
Mortality N° (%)	15 (48.4%)	1 (4.3%)
Diagnosis		
Severe sepsis and septic shock N° (%)	25 (80.6%)	7 (30.4%)
Acute coronary syndrome N° (%)	4 (12.9%)	7 (30.4%)
Cerebrovascular accident N° (%)	2 (6.5%)	4 (17.4%)
Severe trauma N° (%)	0 (0%)	5 (9.3%)

TABLE III
CONTINGENCY TABLE WITH THE CUT-POINT ≤ 1.4

		Death		Total
		Yes	No	
PD2iCA	Risk	15	16	31
	No risk	1	22	23
Total		16	38	54

TABLE IV
CONTINGENCY TABLE WITH THE CUT-POINT ≤ 1.26

		Death		Total
		Yes	No	
PD2iCA	Risk	15	12	27
	No risk	1	26	27
Total		16	38	54

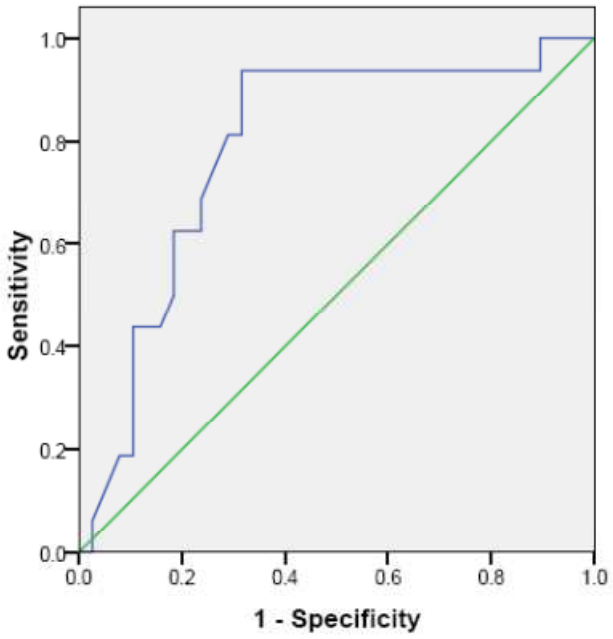

Fig. 1. ROC curve. This graphic shows values of sensitivity and false negatives (1-specificity) associated with different cut-points of PD2iCA.

VI. REFERENCES

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