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Determination of Global Registry of Acute Coronary Events score based on initial symptoms of coronary syndrome using multilayer perceptron

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ABSTRACT

Introduction: the GRACE scale estimates prognosis and mortality due to acute coronary syndrome.

Objective: to predict the GRACE score according to admission characteristics for acute coronary syndrome in a Peruvian hospital using multilayer perceptron.

Materials and methods: analytical and cross-sectional study of a secondary database of 106 patients from a Peruvian hospital admitted for acute coronary syndrome. The variables were GRACE score, heart rate, systolic blood pressure, left arm pain, neck pain, abdominal pain, age, and ST-segment elevation. Multilayer perceptron-type neural networks were used.

Results: The neural network had a relative error of 0.168 and 0.139 in training and testing, respectively. The scatter plot had a homogeneous distribution, with an R-squared of 0.847, indicating that 85% of the variation in the GRACE score can be explained by the GRACE score predicted by multilayer perceptron. The average GRACE score in patients without ST elevation was 104.74, while with ST elevation it was 142.14, similar to the GRACE score obtained using multilayer perceptron, where the average in the absence of ST elevation was 105.52, while with ST elevation it was 140.36.

Conclusions: the use of neural networks is efficient for the prediction of GRACE score based on symptoms and signs upon admission in patients with acute coronary syndrome.

INTRODUCTION

Cardiovascular diseases are the first cause of death in the world, having increased by 60% in recent decades, representing a significant socioeconomic load in all countries, with indirect costs estimated in 237 billion dollars per year and a projected increase to 368 billion dollars by 2035 at world level.[1,2] In Peru, more than 4 thousand people die by myocardial infarction.[3]

Acute coronary syndrome (ACS) is a condition coursing with decrease in coronary artery flow, affecting the function and vitality of the myocardium, causing the death of this tissue. It may course with ST-segment elevation (coronary total occlusion) associated to atherosclerotic plaque rupture, or without ST-segment elevation (coronary partial occlusion) associated to plaque erosion.[4] The symptoms of both types of ACS are similar, with chest pain standing out, experienced as oppression or sharp pain radiating to or located in the arm, shoulder, neck, back, upper abdomen or jaw, associated to nausea, diaphoresis and dyspnea.[5]

Scores have been developed to estimate prognosis and mortality by coronary syndrome, such as the Thrombolysis In Myocardial Infarction (TIMI), as well as the GRACE score (Global Register of Acute Coronary Events). In regard to the GRACE score, it assesses the risk of in-hospital mortality and 6 months after discharge, both in patients with and without ST-segment elevation. For this, it uses the markers of age, systolic blood pressure, heart rate, creatinine, elevated biomarkers (such as troponin), ST-segment changes, heart arrest during hospital stay and Killip classification for heart failure.[6] This score, developed from data from more than 100 countries, is a valuable resource for clinical decision-making in the short and long term.[7]

To obtain accurate estimations with the GRACE score, biochemical, hemodynamic and electrocardiographic markers are required, which are not always available in the short term because of the saturation of hospital services, which could generate a mild but significant time gap until obtaining the required variables to reach predictor results, so having a provisional datum may guide cardiologists or ER doctors to have a view to plan the management to follow (along with their clinical criteria), until the time when enough information is available to make new decisions. Generally, the earliest data available are physical symptoms, blood pressure and electrocardiographic pattern.

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In this regard, the development of possible predictor factors may benefit from using deep learning methods, capable of modeling complex relationships, flexible, and with the ability to solve complex problems. For this reason, the aim of this investigation was to predict the GRACE score according to the characteristics of admission due to acute coronary syndrome to a Peruvian hospital by multilayer perceptron.

MATERIALS AND METHODS

Design and population of the study

Analytical and cross-sectional study from a secondary database, belonging to Herrera-Castillo et al, from the article "Performance of the TIMI and GRACE scores in identifying the risk of death from acute coronary ischemic syndrome: a retrospective study in patients with chest pain at a Peruvian Hospital". The article has been added to the F1000research.com platform.[8] The population was made up by 106 patients admitted to the Regional Hospital José Alfredo Mendoza Olavarría of Tumbes, Peru, due to acute coronary syndrome (ACS), evaluated within 10 minutes of their clinical manifestations, including precordial pain within 48 hours before admission to the ER, being evaluated by the GRACE score. The total of the database population was 106 patients, using the whole population for this investigation. The characteristics of the population studied are included in *Table 1*.

TABLE 1.
Characteristics of the population studied

		Frequency	Percentage
Sex	Male	67	63,20
	Female	39	36,80
Older than 50 years	No	54	50,90
	Yes	52	49,10
ST elevation	No	70	66
	Yes	36	34
Precordial pain	No	3	2,80
	Yes	103	97,20
Left arm pain	No	28	26,40
	Yes	78	73,60
Neck pain	No	83	78,30
	Yes	23	21,70
Diaphoresis	No	63	59,40
	Yes	43	40,60
Abdominal pain	No	92	86,80
	Yes	14	13,20
Dyspnea	No	45	42,50
	Yes	61	57,50
Nausea	No	77	72,60
	Yes	29	27,40
Syncope	No	93	87,70
	Yes	13	12,30
HTN	No	46	43,40
	Yes	60	56,60
Hypercholesterolemia	Yes	44	41,50
	No	62	58,50
Diabetes	Yes	38	35,80
	No	68	64,20
Smoker	Yes	82	77,40
	No	24	22,60
Cardiac arrest	Yes	103	97,20
	No	3	2,80
Elevated biomarkers (troponin)	Yes	22	20,80
	No	84	79,20
Death	Yes	97	91,50
	No	9	8,50

Variables and measurements

The dependent variable was the GRACE score, which is a model applied to all coronary syndromes, estimating in-hospital mortality and within six months, based on the score that considers the following variables: age, heart rate, systolic blood pressure, creatinine in blood, heart arrest upon admission, ST-segment deviation in ECG, abnormal cardiac enzymes (troponin) and Killip classification.[9] The independent variables included as predictors in the multilayer perceptron neural network were: age (continuous, in years), systolic blood pressure (continuous, in millimeters of mercury), abdominal pain (categorical, yes and no), ST-segment elevation (categorical, yes and no), neck pain (categorical, yes and no), heart rate (continuous) and left arm pain (categorical, yes and no).

Statistical analysis

Multilayer perceptron neural networks were used. They are artificial neural networks constituted by several layers of interconnected neurons, analogous to biological neurons, and organized in three layers: input layer, one or more hidden layers, and an output layer. Each neuron of the hidden and output layers has a nonlinear activation function, enabling the perceptron to model complex relationships. The perceptron has the ability to perform classification, prediction and regression tasks. In a system that can learn by backpropagation from labeled data, adjusting the weights of connections during training. The neural network was trained to predict the GRACE score on the basis of age, systolic blood pressure, abdominal, neck and left arm pain, ST-segment elevation, and heart rate.

After obtaining the quantitative data predicted by the perceptron, a dispersion graph was carried out to determine the degree of linearity of distribution. The graph included the R2 coefficient of determination, which measures the accuracy of a statistical model to predict an outcome; in this case, to what extent the GRACE score variation can be explained by the GRACE score derived from the multilayer perceptron.[10] Finally, to supplement the dispersion graph findings, a table was made, where according to the presence or absence of ST-segment elevation, the GRACE

TABLE 2.
Outline of the neural network model to predict the GRACE score from clinical symptoms upon admission

Training (n=72)	Sum of square error	5.947
	Relative error	0.168
	Stopping rule used	1 consecutive step(s) with no error decrease
	Training time	0:00:00.01
Tests (n=36)	Sum of square error	2.195
	Relative error	0.139

TABLE 3.
Average of GRACE score based on clinical markers and average of GRACE score predicted by multilayer perceptron according to the presence of ST-segment elevation

	GRACE score (p<0,001)		GRACE score predicted by multilayer perceptron (p<0,001)	
ST elevation	**Average**	**SD**	**Average**	**SD**
No	104.74	29.593	105.52	26.659
Yes	142.14	37.037	142.36	30.629

SD: standard deviation

score average obtained in the hospital was compared with the GRACE score predicted by multilayer perceptron. This was done with the aim of observing whether the averages were similar in both types of scores. For the comparison of averages, a Student's t-test was applied. Data processing and analysis, including the neural network modeling, were made by the SPSS statistics 25™ software. The neural network training route was: analyzing → neural networks → multilayer perceptron, including the GRACE score as dependent variable, and age, abdominal, left arm and neck pain, systolic blood pressure, ST-segment elevation and heart rate as covariates.

Ethical considerations

The study was observational and data were taken from a secondary database; therefore, there was no intervention or use or manipulation of biological samples, using only clinical registries and anonymous data, freely provided by the author of the original database, under creative commons license, so that no evaluation was required by a committee on ethics. Supplementary information, including the database where the neural network training was made, was available through the following link: *https://figshare.com/articles/dataset/data_csv/23897043/1?file=41896686*

RESULTS

The neural network made its training with 72 patients; while the test was with 26. The sum of squares error was 5.947 and 2.195 in the training and the testing, respectively, and the relative error was 0.168 in training and 0.139 in the test *(Table 2).*

The neural network had 1 input layer with 7 units, 1 hidden layer with 3 units, and one output layer with one unit. The activation function of the hidden layer was by hyperbolic tangent; while the output layer activation function was identity. The variables, in descending error, were age, systolic blood pressure, abdominal pain, ST-segment elevation, neck pain, heart rate and left arm pain *(Figure 1).*

The dispersion graph between the GRACE score and the predicted value by multilayer perceptron, had a homogeneous distribution, with an R2 determination quotient of 0.847, indicating that 85% of the GRACE score variation, can be explained by the GRACE score obtained by symptoms and signs upon admission to the ER by acute coronary syndrome *(Figure 2).*

The average of the GRACE score in patients with no ST-segment elevation was 104.74; while in those with ST-segment elevation, it was 142.14. In regard to the GRACE score obtained by multilayer perceptron, the average in absence of ST elevation was 105.52; while it was 140.36 in those with ST elevation *(Table 3).*

DISCUSSION

The neural network model based on age, systolic blood pressure, abdominal pain, ST-segment elevation, neck pain, heart rate and left arm pain had a proper performance to predict the GRACE score. In this neural network,

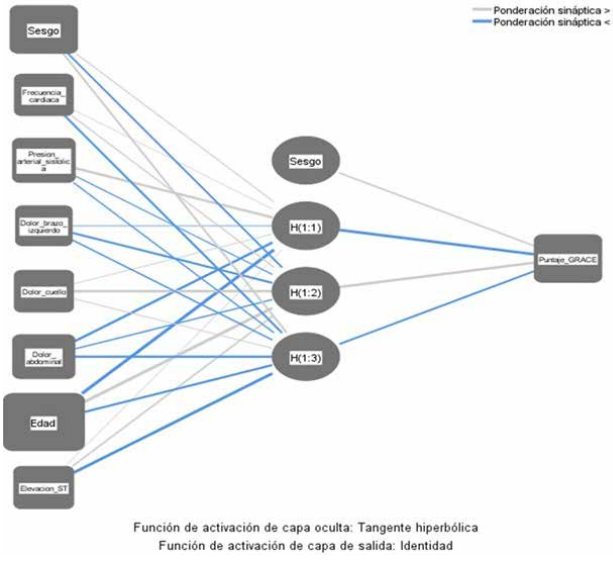

FIGURE 1.
Neural network structure of the multilayer perceptron type for the prediction of GRACE score according to symptoms and signs upon admission of patients with acute coronary syndrome

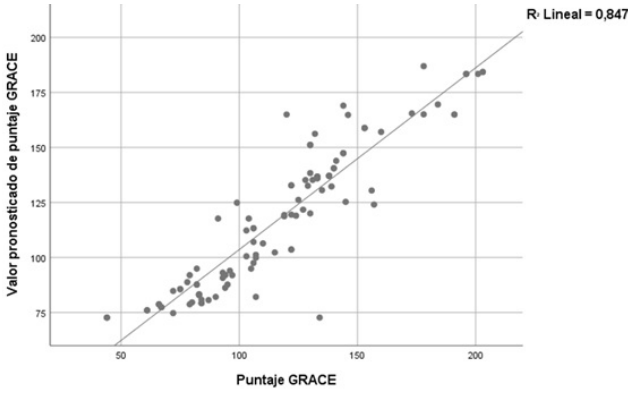

FIGURE 2.
Dispersion between the GRACE score and values predicted with multilayer perceptron for the GRACE score

besides including the parameters proper of the GRACE score, such as age, heart rate, blood pressure and ST-segment elevation, it also included characteristics associated to early symptoms of coronary syndrome, such as abdominal, neck and left arm pain. These symptoms had less weight for the neural network than age and blood pressure, but similar to heart rate and ST-segment elevation, being greater than left arm pain, which is a frequent symptom of acute coronary syndrome.

The contribution to the neural network by abdominal and neck pain suggests that its presence during the first stages of ACS are relevant predictors of severity. In terms of atypical presentations, previous studies have found that some types of pain, like abdominal pain, are associated to higher rates of morbidity and mortality, even when present in outpatients, often being underdiagnosed, as initially they may resemble gastrointestinal or respiratory symptoms, in some cases presenting as severe ear and throat pain.[11,12,13,14,15]

However, the pathophysiological foundations for a greater severity of atypical symptoms have not yet been clarified completely in medical literature, with risk factors known such as age, smoking history and hypertension.[16] However, it is known that craniofacial pain is a pain radiated from the vagus nerve, afferent from the heart, toward the somatic nerves, efferent to the head and neck, in a similar way to sympathetic and parasympathetic innervation linked to the level of the abdomen.[17,18] Possibly, the atypical extrathoracic presentation is a manifestation of an early extension of myocardial damage, adjacent to the infarcted area. However, it is necessary to develop studies to explain this phenomenon.

The neural network had an R2 quotient of more than 80%, indicating that the results are close to the GRACE score, which could be verified also when comparing the score averages according to the presence or absence of ST elevation, where the averages were virtually identical when compared with the GRACE values and when compared with the multilayer perceptron values. These results open a chance to implement artificial neural networks algorithms in emergency services, allowing to obtain fast estimations of the degree of severity of patients with acute coronary syndrome, until being able to have all biochemical and hemodynamic values available, which are part of the GRACE score criteria. In this regards, this trained neural network does not entail a replacement of severity scores validated at international level; however, it can be provisory supplement during the early stages of care of patients with acute coronary syndrome, during the time gap before obtaining all the elements that would allow cardiologists and emergency specialists to opt for TIMI or GRACE scores, mainly considering scenarios where ER services have a high flow of patients and low availability of staff and medical teams.

Between the limitations of this investigation, there were the facts that data was taken from a secondary database, so there could be information and classification biases. Moreover, about the variables related to abdominal and neck pain, there were no specifications available, such as the location of the abdomen or cervical region where pain occurred, or the time elapsed since symptoms appeared. Likewise, although using this neural network may suggest an immediate usefulness, it should be perfected in terms of the sample size of the study, which was 106 patients, so we invite cardiology researchers to develop trained models with a greater number of patients, if possible increasing the data of this trained network, which is made available.

To conclude, the neural network based on age, systolic blood pressure, abdominal pain, ST-segment elevation, neck pain, heart rate and left arm pain had a good performance to predict the GRACE score in patients admitted to a Peruvian hospital due to acute coronary syndrome. Its implementation could orient about severity score until the elements that make up the GRACE score criteria are available, allowing physicians to have a tool to supplement clinical criteria and the management to follow during the early stages of care by acute coronary syndrome. However, studies are required with a higher population number to improve the prediction of the neural network model.

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