ORIGINAL ARTICLE

A Machine Learning Algorithm for Risk Prediction of Acute Coronary Syndrome (ANGINA)

Predicción de riesgo de sufrir un síndrome coronario agudo mediante un algoritmo de machine learning

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ABSTRACT

Background: Chest pain represents one of the most common reasons for consultation in emergency medical services (EMS). A diagnostic strategy using objective and subjective information about the characteristics of chest pain has not been identified yet.
Objective: The aim of this study was to evaluate the performance of a machine learning classifier as a tool for prediction of the risk for non-ST-segment elevation acute coronary syndrome (ACS) in patients consulting an EMS due to chest pain.
Methods: A total of 161 patients consulting the EMS due to chest pain were analyzed. Both objective and subjective variables about the characteristics of chest pain were recorded using a machine learning classifier.
Results: Mean age was 57.43±12 years, 72.7% were men and 17.4% had prior cardiovascular disease. Acute coronary syndrome was present in 57.8% of cases with an incidence of 29.8%. Among the latter 35% required percutaneous coronary intervention and 9.9% myocardial revascularization surgery during a 30-day follow-up period. A Random Forest Classifier was used as model of classification, with an area under the ROC curve of 0.8991, sensitivity of 0.8552, specificity of 0.8588 and accuracy of 0.8441. The most significant predictors in the model were weight (p = 0.002), age (p = 5.011e-07), pain intensity (p = 3.0679e-05), systolic blood pressure (p = 0.6068) and the subjective characteristics of pain (p = 1.590 e-04).
Conclusions: Machine learning classifiers are a useful and effective tool to predict an acute coronary syndrome at a 30-day follow-up period.

Key words: Machine learning - Myocardial infarction - Technology.

RESUMEN

Introducción: Las consultas por dolor torácico son frecuentes en los servicios de emergencias médicas (SEM). Aún no se ha identificado una estrategia diagnóstica que utilice tanto los datos objetivos como los subjetivos del dolor.
Objetivos: Evaluar un clasificador de machine learning para predecir el riesgo de presentar un síndrome coronario agudo (SCA) sin elevación del segmento ST, en pacientes que consultan a un SEM con dolor torácico.
Material y métodos: Se analizaron 161 pacientes que consultaron al SEM con dolor torácico. Se registró mediante un clasificador de machine learning las variables objetivas y subjetivas de caracterización del dolor.
Resultados: La edad promedio fue de 57,43 ± 12 años, 72.7% eran de sexo masculino y 17.4% presentaban enfermedad cardiovascular previa. El 57,8% presentaba un síndrome coronario agudo con una incidencia de IAM de 29,8%, de los cuales requirieron revascularización por ATC el 35%, y CRM el 9,9% en el período de seguimiento a 30 días. Como modelo de clasificación se utilizó un Random Forest Classifier que presentó un área bajo la curva ROC de 0,8991, sensibilidad de 0,8552, especificidad de 0,8588 y una precisión de 0,8441. Las variables predictoras más influyentes fueron peso (p = 0,002), edad (p = 5,011e-07), intensidad del dolor (p = 3,0679e-05), tensión arterial sistólica (p = 0,6068) y características subjetivas del dolor (p = 1,590e-04).
Conclusiones: Los clasificadores de machine learning son una herramienta útil a fin de predecir el riesgo de sufrir un síndrome coronario agudo a 30 días de seguimiento.

Palabras clave: Machine learning - Síndrome coronario agudo - Tecnología.

INTRODUCTION

Undifferentiated chest pain represents one of the most common reasons for consultation at the emergency medical services (EMS), and its frequency has increased over the past decades. This information implies a challenge for the medical team in terms of making a quick and effective diagnosis, as in many cases, doctors must decide whether to continue with a more thorough

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evaluation of the patient's condition in the hospital setting or to discharge the patient and continue the evaluation on an outpatient basis, which entails a high risk associated with underdiagnosis of serious diseases and, consequently, an ominous clinical outcome.

Several strategies and diagnostic algorithms have been analyzed to reduce these risks. The validated diagnostic tools currently available (as the HEART score) consider only part of the subjective data related to chest pain obtained from the anamnesis by the treating physician, and there are many medical interpretations of the same clinical condition based on the experience of the medical team involved. (1, 2) Therefore, there is currently no single diagnostic method capable of linking the objective data of patients with the subjective data derived from the anamnesis, thereby synthesizing the information obtained into a risk prediction algorithm.

We believe that in the era of digital technology and with the advent of artificial intelligence and machine learning algorithms, a risk score classifier using these technologies can be a useful tool to predict the occurrence of an acute coronary syndrome (ACS) in patients who spontaneously attend the EMS with undifferentiated chest pain.

OBJECTIVE

The aim of this study was to demonstrate the ability of machine learning classifiers to diagnose and predict an ACS in patients who spontaneously consult the EMS with undifferentiated chest pain, during a 30-day follow-up period.

METHODS

A prospective, observational study was conducted in a center specialized in cardiology in the Autonomous City of Buenos Aires between August 2018 and April 2019.

Inclusion criteria

- Patients > 18 years
- Patients with undifferentiated chest pain
- Feasibility to complete the 30-day follow-up period
- Having signed an informed consent form

Exclusion criteria

- Patients with electrocardiogram (ECG) with ST-segment elevation.
- Patients with hemodynamic instability or arrhythmias at the time of consultation.

The data obtained from a cohort of 161 patients attending the EMS due to undifferentiated chest pain were analyzed. During the triage stage of chest pain, the objective variables and the subjective variables collected by the treating physician during the diagnostic anamnesis were recorded using a machine learning classifier integrated into a portable digital device (tablet or smartphone).

a. Patient's objective variables:

1. Age
2. Sex
3. Weight
4. Height
5. Hypertension
6. Dyslipidemia
7. Diabetes with or without insulin requirement.
8. Smoking (current smoker or within the last month) and former smoker (having quit smoking for more than 1 month).
9. Family history of cardiovascular diseases-
10. Systolic and diastolic blood pressure
11. Heart rate
12. Positive signs on physical examination: third heart sound, bilateral crackles.

b. Subjective variables obtained:

1. Characteristics of chest pain: sharp, crushing, burning, stabbing, penetrating.
2. Intensity: chest pain intensity was measured using a visual analogue scale with a score ranging from 1 to 10 (where 1 was "minimum intensity" and 10 "maximum intensity").
3. Pain duration and number of episodes in the last 24 hours; pain increase or decrease associated with exertion.
4. Pain relief with nitrates.
5. Pain associated symptoms: diaphoresis, dizziness, tenesmus, palpitation, nausea, breathlessness.
6. Pain intensity changes with: chest movements, arm movements, by applying pressure on the pain area, cough, inspiration.
7. Evaluation of pain perception by means of a continuous visual scale, which was reported by the patient on the digital device following instructions of the treating physician.
8. Site of chest pain identified by the patient by means of a touch-sensitive body diagram integrated into the digital device, following the instructions of the treating physician.

History of cardiovascular disease, percutaneous coronary interventions (PCI), coronary artery bypass graft surgery (CABGS) and acute coronary syndrome (ACS) with or without ST-segment elevation was also recorded.

The classification system using the machine learning algorithm was developed in cooperation with the company Sigmind LAB, which developed and implemented a digital backup system with the aim of ensuring the privacy and confidentiality of data obtained through the use of the algorithm through an encrypted access, only accessible by the study team of researchers.

The Scikit-Learn tool was used to implement the Random Forest Classifier of 150 estimators as a predictive model. (7) Random Forest is a classifier, that is, an algorithm that predicts output values from input data. In this case, the model utilized predicts whether a patient will develop an event based on the data entered into the digital device (patient's objective and subjective data). Thus, the algorithm is trained with labeled data, i.e. the algorithm is provided with input data and its corresponding output data; or variable to be predicted. Using this data processing, when the training process ends, the algorithm is capable of generating the modeled prediction as data that it has never seen, or test data.

Overfitting may occur in machine learning algorithms. We used cross-validation to prevent overfitting, a strategy extensively described in the literature. In this study, we used a 10-fold cross-validation. Cross-validation means splitting the labeled data (dataset of patients' data and the variables to predict) in a number of k-folds. Then, k-1 folds are considered (i.e. 90% of the patients participating in the protocol) as the training set.

After algorithm training, the testing stage is performed, in order to predict whether the patients not used as training set (those of the remaining fold) will generate or not an event. Since we have the actual value of whether each patient in the fold used as test set had an event or not, we obtain an actual value that is similar to how the trained algorithm would perform with data from new patients. This process is repeated k times, taking each time another fold as test set. The resulting performance is the mean obtained from the k repetitions of all the folds. The implementation used can be accessed at the following link: https:

//scikitlearn.org/stable/modules/generated/sklearn.ensemble.RandomForestClassifier.html

Patients were followed-up for 30 days from index consultation and were contacted by telephone calls or in person to analyze the occurrence of events.

The following events were analyzed:

- Cardiovascular mortality. Mortality due to acute myocardial infarction (AMI), stroke, ventricular arrhythmia or sudden death of unclear cause.
- ST-segment elevation or non-ST segment elevation AMI according to the fourth universal definition of AMI.
- ACS: a composite of myocardial infarction and unstable angina.
- Percutaneous trasnluminal coronary angioplasty (PTCA)
- Coronary artery bypass graft surgery (CABGS)

The adjudication of events was done in person or using the information from the electronic medical record (EMR) and by a phone call made by one of the study investigators.

Statistical analysis

The mean value for each measure of performance was reported. Continuous variables had normal distribution and were compared using Student's t test.

Before the implementation of the algorithm, an initial stage of verification was carried out in order to evaluate preventable errors of the classifier, understanding the model and assessing the feasibility of using the digital system by the EMS physicians. Those patients analyzed during the initial testing stage (n=20) were excluded from the subsequent analysis.

Ethical considerations

All the patients signed an informed consent approved by the institutional Ethics Committee.

The investigators implemented measures to protect the confidentiality of all the information according to the Argentine Personal Data Protection law 25,326. These data were only available to the investigators of the ANGINA study and the members of the teaching, ethics and research committee, as required. The study was conducted following national ethical standards (CABA law Nº 3301 about Protection of Human Subjects in Health Research) and the recommendations of the Declaration of Helsinki, among others.

RESULTS

Data from 161 patients consulting the EMS with undifferentiated chest pain were analyzed. Mean age was 57±12 years and 72.7% were men. Hypertension was present in 51.5% of the patients, 14.2% had diabetics, 51.5% had dyslipidemia and 14.3% were smokers. During the interview, 18% of the patients reported a family history of cardiovascular disease and 17.4% presented a previous coronary event (23.6% PCI, 5% CABGS).

Among the patients analyzed, 57.8% (n=93) presented an acute coronary syndrome, with an incidence of AMI of 29.8% (n=48), 35% (n=56) of which required PCI and 9.9% (n=16) underwent CABGS. There were no deaths during follow-up (Table 2).

The area under the ROC curve of the machine learning model, with the use of a Random Forest algorithm as classifier, was 0.8991, with a sensitivity of 0.8552, specificity of 0.8588 and accuracy of 0.8441, considering patients with ACS during follow-up as positive class (Figure 1).

The most significant predictors for the model were, in order of importance: weight (p=0.002), age (p=5.011e-07), pain intensity (p=3.0679e-05), and perception of pain evaluated through a continuous visual scale (p=1.590 e-04). All the variables mentioned were statistically significant after correction with the Bonferroni test for multiple comparisons.

DISCUSSION

The present study, showed that the use machine learning classifiers is a useful and effective tool to predict an acute coronary syndrome in patients who spontaneously consult the EMS with undifferentiated chest pain.

Technology is part of our lives, and not only as a facilitator of ludic activities, but also for health care and wellbeing. Over the past decades, many strategies re-

Table 1. Baseline population characteristics.

Variable	Value
Age, years	57 ± 12
Hypertension, n	93 (51.5%)
Smoking habits, n	23 (14.3%)
Dyslipidemia, n	93 (51.5%)
Family history, n	29 (18%)
Male gender, n	117 (72.7%)
Diabetes, n	23 (14.2%)
Previous coronary event, n	28 (17.4%)
Previous percutaneous transluminal coronary angioplasty, n	38 (23.6%)
Previous CABGS, n	8 (5%)

CABGS: Coronary artery bypass graft surgery

Table 2. Cardiovascular events at a -30 days follow-up period.

Events	n (%)
Acute coronary syndrome	93 (57.8%)
AMI	48 (29.8%)
PTCA	56 (35 %)
CABGS	16 (9.9 %)

AMI: Acute myocardial infarction. PTCA: Percutaneous transluminal coronary angioplasty.. CABGS: Coronary artery bypass graft surgery.

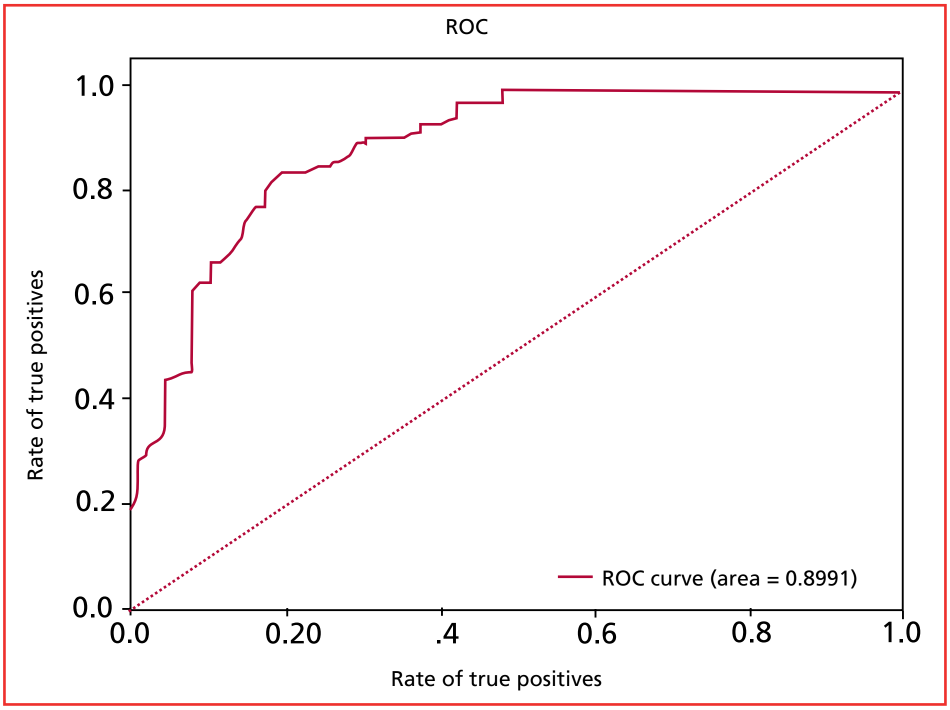

Fig. 1. Area under the ROC curve of the Random Forest Classifier

lated to the prevention and early diagnosis of diseases have been implemented through digital devices such as smartphones, tablets and smart watches, which are nowadays widely spread, accessible and used by different age groups.

This evolution includes methods based on the processes of artificial intelligence and machine learning, understood as the ability of a computer system to acquire their own knowledge by extracting patterns from a large volume of raw data. (8)

Different studies have demonstrated the benefit of machine learning classifiers to predict an ACS in patients with chest pain. VanHouten et al. obtained 20,078 variables used by the conventional diagnostic algorithms for ACS from a multicenter registry and analyzed them using elastic net and random forest algorithms. (9) The Random Forest classifier obtained an AUC of 0.848 and of 0.849 in the validation set, outperforming the TIMI and GRACE risk scores. (10, 11)

The AUC in our machine learning model is similar, but the main difference is that data was prospectively collected in our case.

These algorithms have also proved to be efficient in predicting long-term cardiovascular events. Weng et al. demonstrated the effectiveness of machine learning classifiers to predict cardiovascular events in a population without known history of cardiovascular disease during a 10-year follow-up period , being more effective and accurate than many clinical risk prediction algorithms recommended by the current clinical practice guidelines. In this way, these classifiers identify those patients who could benefit from an early preventive treatment. (12)

We consider that the use of these machine learning algorithms can be very useful in our setting, mainly due to the high demand of health care professionals and the high interobserver variability for making a diagnosis according to the medical experience acquired. Machine learning algorithms could thus be used to complement medical care through their ability for risk stratification, thus allowing more time to focus on the most serious diseases. They could also be an additional tool for the correct interpretation of complementary test results and to predict the outcome when used together with current conventional strategies. (13-16)

Artificial intelligence classifiers based on machine learning algorithms do not come from remote and inaccessible places. In our country, they have already been used in the field of public health. Scavuzzo et al. used neural networks, a machine learning algorithm, to identify and predict those regions with the highest concentration of Aedes aegypti mosquito eggs to implement prevention strategies against dengue. (17)

Study limitations

Firstly, the potential bias in data collection is a limitation of our predictive algorithm as the patients were evaluated in the emergency department by cardiologists in a center only specialized in cardiology. However, most of the data collected had dichotomous answers, which should reduce this potential bias.

Secondly, the number of clinical events in our study was significant and implies a positive predictive value greater than a negative predictive one.

We acknowledge that a study comparing our algorithm with the traditional such as HEART, GRACE or TIMI risk scores would be useful. Future studies will analyze these data.

Future investigations

This work is included in a program that has the following predefined steps:

1. Validation of the machine learning algorithm used in other populations from public and private hospitals, with doctors belonging to the medical emergency services of different subspecialties.
2. Optimise the algorithm based on all the information obtained T to improve its predictive and prognostic ability.
3. Development of an application for public use.

As far as we know, this is the first study in our country that demonstrated the usefulness of machine learning classifiers in cardiovascular disease, as a useful element in the diagnosis of acute coronary syndrome.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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