Narrative review

Machine learning for risk assessment and diagnosis of heart failure

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Abstract
Congestive heart failure has become a growing public health problem. Reducing the high cost of congestive heart failure is challenging, as it progresses silently for years before diagnosis, especially in people with high cardiovascular risk and who do not control predisposing factors. New technological advances such as artificial intelligence offer solutions to these problems. Therefore, in this narrative review we determine the application of machine learning for risk identification and diagnosis of heart failure. The search was carried out in English and Spanish in the databases PubMed, HINARI, Google Scholar and Elsevier with the following MeSH terms: «Artificial intelligence», «Machine Learning», «Algorithm», «Cardiology», «Heart Failure», «Heart Failure/diagnosis», and «Heart Failure/prevention and control». We considered original articles, meta-analyses, literature reviews, and systematic reviews, including both cases and controls, published within the last seven years. No artificial intelligence was used in the preparation of this document. Artificial intelligence allows for risk assessment of heart failure and facilitates its timely diagnosis through the analysis of cardiac imaging techniques.

Keywords
Machine Learning, Heart Failure, Cardiac Imaging Techniques, Artificial Intelligence, Deep Learning.

Resumen
La insuficiencia cardíaca congestiva se ha vuelto un problema de salud pública que aumenta cada año. La reducción del alto costo que esta conlleva se ve limitada por su desarrollo silente durante años antes del diagnóstico, especialmente en personas con alto riesgo cardiovascular y sin control de los factores de riesgo. Nuevos avances tecnológicos como la inteligencia artificial ofrecen soluciones a estas situaciones. Por tanto, en esta revisión narrativa se propone determinar la aplicación del aprendizaje automático para la identificación de riesgo y diagnóstico de insuficiencia cardíaca. La búsqueda se efectuó en inglés y español en las bases de datos PubMed, HINARI, Google Académico y Elsevier con los siguientes términos MeSH: «Artificial intelligence», «Machine Learning», «Algorithm», «Cardiology», «Heart Failure», «Heart Failure/diagnosis», y «Heart Failure/prevention and control». Se incluyeron artículos de revisión bibliográfica, casos y controles, artículos originales, revisiones sistemáticas con metaanálisis de 2018 a 2024, en los idiomas inglés y español. No se utilizó inteligencia artificial en la elaboración de este documento. La inteligencia artificial permite estratificar el riesgo de insuficiencia cardíaca y facilita su diagnóstico oportuno a través del análisis de técnicas de imagen cardíaca.

Palabras clave
Aprendizaje Automático, Insuficiencia Cardíaca, Técnicas de Imagen Cardíaca, Inteligencia Artificial, Aprendizaje Profundo.

Introducción

Congestive heart failure (CHF) has become a significant public health problem, as delay in the implementation of timely treatment can lead to an increase in avoidable morbidity and mortality. This problem affects about 64 million people worldwide and is not limited to a specific geographic region.[i]

However, its impact is particularly serious in developed countries, where aging, the increase in cardiovascular risk factors, and improved survival from diseases such as myocardial infarction have increased the

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Aplicación del aprendizaje automático para la identificación de riesgo y diagnóstico de insuficiencia cardíaca

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prevalence of CHF. This increase in survival is due to therapeutic advances, such as percutaneous coronary intervention and the use of beta-blockers. In these countries, the incidence of CHF is estimated at 1-2 % in the general population.[ii]

A specific example is the United States, where according to Van Nuys, *et al.*, the prevalence of people aged 65-70 years with CHF will increase from 4. 3 % in 2012 to 8. 5 % in 20303. CHF carries a high economic cost due to the fact that 83. 7 % of emergency consultations end in hospital admissions4. In 2012, the estimated cost was 30. 7 billion US dollars. This will increase to 69. 8 billion US dollars by 2030.[v]

The reduction in the economic and social cost of this disease is limited by the progression of cardiac dysfunction for years before the diagnosis of CHF.[vi] This can be seen in the National Health Service of the United Kingdom, where 80 % of cases are diagnosed in hospitals, despite the fact that 40 % of patients have symptoms that should have been explored in an early evaluation.[vii]

Currently, methods for early detection of exacerbations and deterioration of cardiac function are based on diagnostic algorithms nd predictive models. These are used for ambulatory monitoring of clinical parameters, both continuously and intermittently. These algorithms are based on physiological parameters such as blood pressure, oxygen saturation, heart rate and weight. Among these, very few manage to achieve a sensitivity and specificity of more than 80 %.[viii] With this in mind, there are emerging technologies that seek to improve these statistics.

Artificial intelligence (AI) enables the analysis of large databases and improves the efficiency with which patterns are interpreted.[ix,x] Machine learning investigates how computers can learn from data. This is a sub-branch of artificial intelligence, which in turn is a branch of computer science.[xi,xii] These technologies are used in different methods of analysis. In the case of descriptive methods, unsupervised machine learning is used, while predictive methods are associated with the use of supervised machine learning.[xiii,xiv]

Algorithms for the diagnosis of congenital heart disease have been studied since 1960.[xv]v In this line of research, machine learning has been used to create cardiovascular risk calculators, to read imaging studies and to identify acute ischemic events.[xvi,xvii] In addition, it has facilitated the interpretation of multiple clinical findings.[xiii,xiv]

There is a wide variety of studies on the subject, especially in cardiology. Quer, *et al.*, show the growing interest in machine learning. More than 3000 combined articles have been published in PubMed, arXiv and bioRxiv (open access preprint servers) during 2015-2020. Furthermore, by 2020, one in every 1000 publications in PubMed was related to artificial intelligence and/or machine learning in cardiology.[xix]

Heart disease, particularly heart failure, has benefited greatly from these technologies. They can be applied at all levels of care and can identify alterations in cardiac output even earlier than conventional echocardiographic diagnosis.[xx]

A review of the literature on the use of machine learning in heart failure was carried out, including original studies and review articles whose publication date did not exceed 7 years. Artificial intelligence was not used in the preparation of this document. The search was performed in English and Spanish in the databases, PubMed, HINARI, Google Scholar and Elsevier with the MeSH terms: "Artificial intelligence", "Machine Learning", "Algorithm", "Cardiology", "Heart Failure", "Heart Failure/diagnosis", and "Heart Failure/prevention and control". The objective was to determine the application of machine learning for risk identification and diagnosis of heart failure.

Discussion

Overview of machine learning and its use in cardiology

Machine learning, a branch of artificial intelligence, seeks to mimic and even surpass the human cognitive ability to recognize patterns and trends in a data set. This is achieved by systems that learn autonomously through repeated exposure to data. Recently, the application of this technology in cardiology has shown potential in clinical applications such as early diagnosis of CHF, risk prediction, prognosis, accurate reading of electrophysiological studies and cardiology images, optimization of patient care, treatment and monitoring.[xxi]

Machine learning can be subdivided into supervised and unsupervised learning, depending on the presence or absence of labels in the data used to train the model, i.e. whether the predictor and outcome variables are known (supervised) or not (unsupervised). Unsupervised models, in turn, are classified into dimensionality reduction models such as Principal Component Analysis (PCA) and classification models, such as clustering.

Clustering consists of grouping data into categories or clusters, so that the elements within the same group are more similar to each other than to those of other groups, allowing the detection of subgroups of patients with common characteristics, genetic phenomena or similar epidemiological patterns. In contrast, supervised models are classified into regression and classification models. Regression models, such as linear regression, are used when the target variable is continuous, while classification models, such as logistic regression, decision trees (decision three) and random forests, are used when the target variable is categorical. Both types of models learn from labeled data to predict or classify events, establishing relationships between the predictor variables and the outcome variable.[xxi] The use of one model or the other will depend on the complexity of the problem to be solved or the need for greater precision.

Another branch of machine learning is deep learning, which uses multiple neural networks to find more complex patterns in larger data. It is inspired by human neurobiology and has the ability to learn through diverse experiences. Most studies that rely on the use of machine learning use these models to integrate information and create algorithms that are analyzed according to the objectives of the study.

The basic operation of a neural network is shown in Figure 1 and consists of an input layer that represents the variables to be studied, one or more hidden layers that analyze these variables, the number of layers and neurons to be used depending on the complexity of the analysis, and an output layer that produces the final result of the analysis.[xxiii]

There is crrently controversy about the use of tools powered by artificial intelligence due to the ethical-legal problems that the unregulated collection of personal information produces.[xxiv]

However, the reduction of cardiovascular disease mortality has been one of the main objectives in recent decades and the integration of these technologies has aroused much interest.

Among the uses of greatest interest is the ability to interpret highly complex cardiac imaging studies25. 25 For example, Narula, *et al.* used databases from a cohort study with 62 verified cases of hypertrophic heart disease (HCM) and 77 verified cases of physiologically hypertrophic heart in high-performance athletes (ATH). They describe a combined model of neural networks, random forest and unsupervised learning capable of differentiating ATH and HCM according to echocardiographic parameters with a sensitivity of 96 % and specificity of 77 %, superior or equal to the ratio between early and late diastolic transmitral velocity (sensitivity = 79 %, specificity = 77 %; $p<0.01$)26. Early and late diastolic transmitral velocity are key measures in echocardiography to assess the diastolic function of the heart, i.e., how the left ventricle relaxes and fills with blood between beats. Similarly, models have been compared to differentiate between constrictive pericarditis and restrictive cardiomyopathy where a positive learning curve was observed in all the supervised models used, with an average diagnostic accuracy of up to 93. 7 %.[xxvii]

In addition, machine learning has shown its usefulness in complex nuclear study readouts. Otaki, *et al.*, used a deep learning model investigating the prediction of obstructive coronary artery disease using myocardial perfusion single photon emission computed tomography (SPECT) in 3578 patients. The model was compared with total perfusion deficit (TDP) and expert opinion. The deep learning model had a higher area under the curve (AUC) (AUC 0. 83;

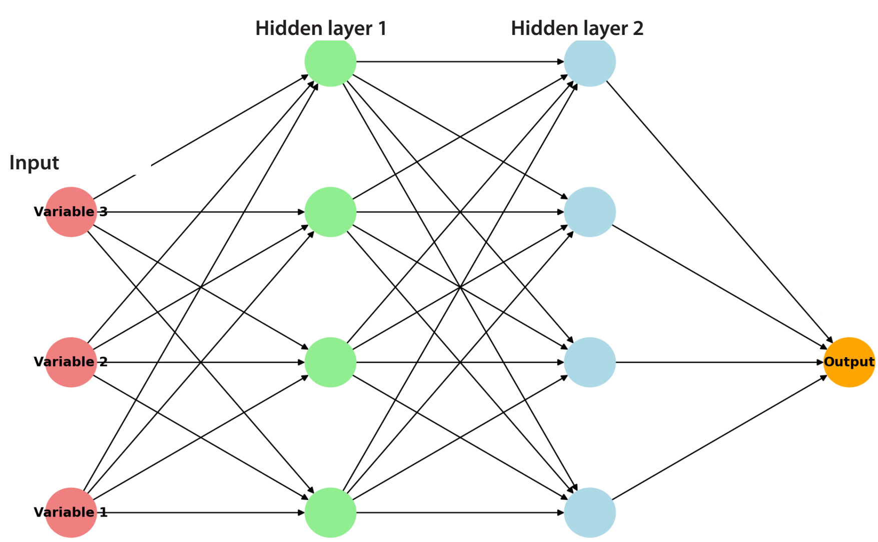

Figure 1: Basic operation of a neural network

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95 % CI 0. 82-0. 85) than either DPT (AUC 0. 78; 95 % CI 0. 77-0. 80) or expert reader (AUC 0. 71; 95 % CI 0. 69-0. 72; $p < 0.01$ for both) for the detection of obstructive coronary artery disease.[xxviii]

In addition, the use of these technologies in electrophysiology is noteworthy. It is currently possible to couple portable electrocardiogram (ECG) systems with automatic learning systems in smartphones for the ambulatory management of atrial fibrillations29. In addition, it can be used for the identification of left ventricular dysfunction on ECG. Attia, *et al.*, used deep learning methods and analyzed ECGs from 52 870 patients following model training. This model provided a high degree of discrimination between ejection fraction ≤ 35 % with an AUC of 0. 93, when examining the ECG alone.[xxx]

Machine learning allows diagnosis to be made, and facilitates the grouping of patients by phenotypes based on molecular biomarkers for the creation of intelligent calculators.[xxxi]

Machine learning and risk of heart failure.

Machine learning and artificial intelligence can be used to analyze data and, from that data, make predictions or inferences about characteristics, behaviors or trends in an entire population based on a sample of that data. Such systems can be highly useful in various fields of medicine. One field that has seen increasing development is cardiology, especially in pathologies such as heart failure, where such models are being used to determine risk and complications.[xxxiii]

Heart failure, being a multifactorial disease, can be studied from two perspectives. The clinical perspective, which encompasses databases of wearable devices, medical records, imaging and electrocardiography. And the genetic perspective, which focuses on transcriptome analysis, genomics and proteomics. Machine learning algorithms can be useful in both of these areas.[xxxiv,xxxv]

Due to the complexity of heart failure, clinicians are faced with the need for tools to facilitate decision making. Angraal, *et al.*, used data from the TOPCAT (treatment of preserved ejection cardiac function with an aldosterone antagonist) trial where four machine learning models and one logistic regression model were used. These models were trained to evaluate mortality and hospitalization in patients with heart failure with preserved ejection fraction. The best performing model for predicting hospitalization was the random forest model with an AUC of 0. 72 for mortality and 0. 76 for hospitalization. This shows high fidelity when stratifying data as probabilistic prediction models.[xxxvi]

Mortazavi, *et al.*, used similar models to analyze readmission of heart failure patients using telemedicine data. Readmission prediction using echocardiographic assessment of ejection fraction was compared with a machine learning data analysis model. It was found that, when using machine learning algorithms, there was a higher predictive value in the random forest model (AUC 0. 628 vs. 0. 533) and in the logistic regression model (AUC 0. 678 vs. 0. 543).[xxxvii]

In addition, Banerjee, *et al.*, conducted a study in which data were collected from the UK healthcare system. Five groups were formed for the predictive analysis of the development of heart failure and one-year mortality: early-onset, late-onset, atrial fibrillation-related, metabolic and cardiometabolic.

A supervised random forest model was used using continuous variables that overlap between clusters. This model showed a good predictive value for 1-year mortality for patients with early-onset heart failure (c-statistic 0. 68, 95 % CI 0. 65-0. 71), patients with metabolic pathologies (AUC 0. 71, 95 % CI 0. 70-0. 73) and patients with cardiometabolic pathologies (AUC 0. 68, 95 % CI 0. 65-0. 70).[xxxviii]

These data can be compared to the model created by Kwon, *et al.*, which consists of a deep learning algorithm. The objective of this was to predict mortality in patients with heart failure. During performance tests, the algorithm achieved an AUC of 0. 88 for predicting in-hospital mortality. In addition, it was able to predict high-risk patients in terms of post-discharge survival ($p < 0.001$).[xxxix]

Transcriptional and genomic analysis of heart failure is another field where machine learning has been applied. Venkat *et al.*, used RNA sequencing and an expectation maximization algorithm to identify de novo transcriptomes. From these data, regression analysis was performed using a random forest model. The gene expression data were then integrated into an algorithm with clinical diagnostic capabilities. Using this algorithm, a proportional relationship was established between the development of heart failure and age (R=0. 8), gender (R=0. 14) and race (R=0. 06). Based on these data, a genomic correlation was performed in which the NR3 °C2 gene was identified as having a high predictive value (0. 52).[xl]

On the other hand, Yang *et al.*, used genetic mapping tools to identify the single nucleotide polymorphisms (SNPs) that had the highest predictive value for the development of heart failure. In this study, three supervised algorithms were used to identify specific PNUs. Using machine learning, 20 frequently recurring PNUs were identified. Using three machine learning algorithms it was determined that the support vector machine algorithm had the best performance in determining whether a patient was in stage A or B heart failure (AUC 0. 931 and performance ratio of 0. 899).[xli]

Machine learning for heart failure diagnosis

One of the mainstays of heart failure diagnosis is the assessment of ejection fraction by echocardiography. However, determining ejection fraction by manual tracing is time-consuming and operator-dependent. Also, visual assessment of this is inherently subjective, so new initiatives have sought to use machine learning. Ouyang *et al.*, created EchoNet-Dynamic, a deep learning-based algorithm for calculating ejection fraction from echocardiogram videos. On a database to which it had not been exposed during its training the algorithm was able to classify heart failure with reduced ejection fraction (AUC of 0. 97).[xlii]

However, automated interpretation extends beyond routine echocardiographic parameters. Currently, the aim is to identify features linked to different heart diseases, which are subtle and difficult to identify. Zhang, *et al.*, created a deep learning-based black-box model to identify three diseases (hypertrophic cardiomyopathy, cardiac amyloidosis and arterial hypertension) through echocardiographic findings. A cohort of patients with hypertrophic cardiomyopathy and controls was used to evaluate this model. Artificial intelligence was able to identify patients with hypertrophic cardiomyopathy with an AUC of 0. 93 (95 % CI, 0. 91-0. 94).[xliii]Because in black-box models the process of derivation and variable selection is completely handled by the training algorithm, further analysis is necessary to understand how it works. In the case of hypertrophic cardiomyopathy two features were associated with the pathological process by artificial intelligence. These were greater left atrial mass (p=0. 01) and greater left ventricular mass (p= 0. 001).[xliv]

Another function of echocardiography is to determine diastolic function. With current algorithms, many patients are classified as having indeterminate diastolic function, that is, their cardiac function cannot be defined as normal or abnormal due to lack of information or conflicting measurements. This limits the clinical usefulness of the results for decision making.[xlv]

Pandey *et al.*, created an artificial intelligence to assess diastolic function through echocardiographic parameters. This was used in a cohort of patients undergoing both echocardiography and invasive left ventricular filling pressure measurements. The model was able to predict elevated left ventricular filling pressure better than the clinical guidelines of the American Association of Echocardiography (AUC0. 88 vs 0. 67). Furthermore, it separated these patients into two groups (high and low risk).[xlvi]

On the other hand, automated learning has been used to assess right ventricular function. Beecy *et al.*, created an artificial intelligence capable of measuring the circumference of the tricuspid annulus using 2D ultrasound. This model consistently identified right heart failure defined by cardiac magnetic resonance imaging through indices such as linear displacement of the tricuspid annulus (AUC 0. 69, 95 % CI 0. 63-0. 76). This performance is similar to that of conventional echographic indices of heart failure such as tricuspid annulus systolic displacement (TAPSE) (AUC 0. 80, 95 % CI 0. 73-0. 86) and S' (AUC 0. 78, 95 % CI 0. 71-0. 85).[xlvii]

This type of model has also been applied to 3D ultrasound. Genovese *et al.*, tested an artificial intelligence capable of assessing the function and size of the right ventricle. Its use was evaluated in 56 patients referred by clinical indication for cardiac magnetic resonance imaging. The model required post-processing endocardial contour editing in 68 % of the patients, which prolonged the analysis time from an average of 15 seconds to 114 seconds. With these adjustments, right ventricular volume and ejection fraction measurements were accurate compared to baseline cardiac MRI (right ventricular ejection fraction, bias-3. 3 % +/- 5. 2 %).[xlviii]

Another imaging modality that has benefited is cardiac magnetic resonance (CMR), which allows assessment of ventricular function and tissue characterization49. 49 Segmentation in CMR is a tedious process that attempts have been made to automate with artificial intelligence. Davis *et al.*, created a model trained in 1923 resonance imaging. It performed the segmentation process in 20 seconds compared to the 13 minutes it took the physicians. Errors were found in the automated segmentation of 72 images from a database of 34,486. These errors occurred in rare pathologies not found in artificial intelligence training.[l]
One of the advantages of CMR is tissue characterization. Currently, this is performed by

late gadolinium uptake. Zhang *et al.*, used artificial intelligence to create "Virtual native enhancement images" (VNE) from pre-contrast T1 mapping and cine images. Experienced operators evaluated the image quality, visuospatial agreement, and myocardial lesion quantification of images obtained with late gadolinium uptake and VNE. Operators felt that image quality was significantly better with VNE (n = 345 data sets; p < 0. 001 [Wilcoxon test]). Furthermore, the agreement between these two methods for the extent of myocardial fibrosis was high (r = 0. 77-0. 79 for hyperintense lesions, r = 0. 70-0. 76 for lesions of intermediate intensity).[li]

Conclusion

Machine learning represents a tool with great potential in the management of heart failure, particularly in risk identification and early diagnosis through advanced analysis of clinical and imaging data. The studies reviewed demonstrate its capacity to improve diagnostic accuracy and optimize predictive models, which can contribute to more efficient care and timely detection of complications.

However, their implementation in clinical practice faces important challenges, such as the availability of representative databases, adequate training of the models and the need for external validations to ensure their applicability in various contexts. In addition, ethical and regulatory issues must be addressed to ensure the responsible use of these technologies for the benefit of patients.

In summary, although the advances described are encouraging, further research and evaluation of machine learning in real clinical scenarios is needed to establish its definitive role as an adjunct in heart failure care.

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