The emerging roles of machine learning in cardiovascular diseases: a narrative review

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Background and Objective: With the wide application of electronic medical record systems in hospitals, massive medical data are available. This type of medical data has the characteristics of heterogeneity and multi-dimensionality. Traditional statistical methods cannot fully extract and use such data, but with their non-linear and cross-learning modes, machine-learning (ML) algorithms based on artificial intelligence can address these shortcomings. To explore the application of ML algorithms in the cardiovascular field, we retrieved and reviewed relevant articles published in the last 6 years and found that ML is practical and accurate in the auxiliary diagnosis of cardiovascular diseases. Thus, this article reviewed the research progress of ML in cardiovascular disease.

Methods: This study searched relevant literature published in National Center for Biotechnology Information (NCBI) PubMed from 2016 to 2022. The relevant literature was extracted from NCBI PubMed with the following keywords and their combinations: "machine learning", "artificial intelligence", "cardiology", "cardiovascular disease", "echocardiography", "electrocardiogram" and "prediction model". All articles included in the review are English.

Key Content and Findings: The review found that ML is practical and accurate in the diagnosis of cardiovascular diseases. Besides, ML can build clinical risk prediction models and help doctors evaluate the prognosis of patients.

Conclusions: The study summarized the progress of ML in cardiovascular diseases and confirmed its advantages in clinical application. In the future, models and software based on ML will be common auxiliary tools in clinical practice.

Keywords: Machine learning (ML); artificial intelligence (AI); cardiology

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Introduction

Cardiovascular disease (CVD) is one of the leading causes and is estimated to account for approximately 19 million deaths globally in 2021 (1). CVD can be divided into several types, including heart failure (HF), arrhythmia, coronary heart disease (CHD), hypertension, valvular heart disease and other diseases (2). Early diagnosis and assessment of CVD are crucial to reduce serious complications and deaths. With increasing attention to health and development of electronic medical record systems, more and more health data and clinical examination data are accessible. The use of these data to diagnose and treat CVD or to predict the prognosis of CVD depends on experienced clinicians. However, human beings cannot process the exponential growth of medical data. Thus, the rise of artificial intelligence (AI) brings new ideas for data processing and mining (3).

AI refers to technologies or systems that can simulate certain human thought processes and intelligent behaviors (4). With the development of computer technology, AI has been widely applied in many fields. Machine learning (ML) refers to the ability of machines to independently learn and make accurate predictions (5). As an important branch of AI, ML has been widely applied in various fields. In recent years, more and more researchers have focused on the application of ML in the medical field and found that ML plays an important role in the auxiliary diagnosis of CVDs (6,7).

ML is mainly divided into supervised and unsupervised learning (2). Supervised learning refers to the establishment of mathematical models that use known samples of specific characteristics as training sets, and then map new unknown samples with established models (2). Thus, supervised-learning models use input training sets that have labels and features (2). Commonly, supervised-learning models include logistic regression, decision tree, support vector machine (SVM), naive bayes, random forest (RF), and artificial neural network models (8,9). Unsupervised learning refers to the solving of various problems by pattern recognition according to training samples of unknown categories. Thus, unsupervised-learning models use training sets that have no labels and no features. Unsupervised-learning models mainly include K-means, and hierarchical clustering models (10).

Supervised ML has been widely used in clinical practice, including disease diagnosis and risk-prediction models. Unsupervised ML is mainly used to discover hidden structures in data and explore relationships between variables. For example, unsupervised learning can be used to discover new subtypes of diseases and break them down into more precise, individual subtypes (10,11). With the increasing application of ML in clinical practice, a large number of studies have shown that ML is accurate in auxiliary diagnosis. This article explores the value of ML in the auxiliary diagnosis of CVDs. We present the following article in accordance with the Narrative Review reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1853/rc).

Methods

The present study was conducted at the digital libraries of Nanjing Medical University, Jiangsu, China. There was no need for ethical approval or permission as no animal or human subjects were directly included. The associated literature about the definition, application, model construction of ML as well as its role in the diagnosis and prognosis of CVDs was collected. All the data were collected from National Center for Biotechnology Information (NCBI) PubMed. For data collection, we used some Medical Subject Headings (MeSH) terms and their combinations in [tittle/abstract]: "machine learning", "artificial intelligence", "cardiology", "cardiovascular disease", "echocardiography", "electrocardiogram" and "prediction model". Following table (*Table 1*) describes the study sequence and details:

Model building for ML

In ML, the input data set is divided into training set, test set, and verification set (12). The whole data used in the training set are large, and are used to develop the ML model. Test sets are used for model testing and parameter adjustment (12). Validation sets (unknown samples) are fed into the constructed ML model to evaluate the overall performance of the model (12). The modeling process of ML is as follows: (I) the data required for model construction are obtained from an electronic medical record system, laboratory indicators, and imaging, and the collected data are preprocessed to delete any invalid data; (II) traditional statistical methods (traditional linear regression analysis or ML algorithms) are used to screen the independent variables that are meaningful to the outcome variables, and appropriate eigenvalues are selected as predictors based on relevant guidelines or clinical experience; (III) a suitable ML

Table 1 The search strategy summary

Items	Specification
Date of search	2021-10-01 to 2022-01-30
Databases and other sources searched	NCBI PubMed
Search terms used (including MeSH and free text search terms)	"machine learning", "artificial intelligence", "cardiology", "cardiovascular disease", "echocardiography", "electrocardiogram", "prediction model"
Timeframe	2016-01-01 to 2022-01-30
Inclusion and exclusion criteria	The study collected the relevant literature published in English from 2016-01-01 to 2022-01-30. The literatures mainly cover the field of medicine, especially cardiovascular diseases
Selection process	Liang Chen, Zhijun Han and Junhong Wang jointly collected and assembled the data. Then Liang Chen conducted the classification and analysis of the information. Finally, all authors reached an agreement on the manuscript
Any additional considerations	None

MeSH, Medical Subject Headings; NCBI, National Center for Biotechnology Information.

algorithm is selected according to the characteristics of the data and the corresponding ML model is constructed; and (IV) the ML model is verified and the sensitivity, specificity, and area under the curve (AUC) of the corresponding model are obtained to evaluate the performance of the model (13).

Application of ML in the diagnosis of CVDs

Currently, ML has gradually become a novel research hotspot among auxiliary diagnosis and have subsequently captured the attention of the cardiovascular research field. An increasing number of studies have demonstrated that ML can help distinguish imaging pictures and electrocardiograms, suggesting the application of ML in the auxiliary diagnosis of CVD (2,3). Thus, we discuss the diagnostic values of ML in CVD.

Application of ML in image acquisition and classification

Echocardiography of the heart is a non-invasive test used to diagnose heart disease. It quantitatively measures a patient's cardiac function. Muse *et al.* used ML algorithms to help doctors collect high-quality ultrasound images (14). Their model guides doctors to move the ultrasonic probe after insetting the patient's height, weight, gender, and other data. Once a high-quality image has been obtained, the image can be locked automatically. The accuracy of the model is up to 90% even among nurses who have no experience in using echocardiography (14). In addition to obtaining high-definition ultrasound images, accurate image recognition and classification are the most important parts of an echocardiography diagnosis. Østvik *et al.* used more than 7,000 ultrasonic images to train a convolutional neural dimension network model, and the model constructed was able to accurately identify and classify the images (15). The recognition accuracy of a single frame and 2 images was 98.3% and the time spent on recognition and classification was satisfied (15). Besides, Azarmehr *et al.* developed a new neural architecture search algorithm to improve image classification speed and performance (16). Overall, ML can assist doctors to collect, recognize, classify and distinguish echocardiogram data.

Application of ML in the diagnosis of HF

HF is one the most common CVDs with the characteristics of impaired ventricular filling or ejection (17). Cardiac output cannot meet the requirement of tissue metabolism due to structural or functional impairment of the heart, leading to pulmonary circulation congestion or systemic circulation congestion (17). In the clinic, HF patients mainly have the symptoms of respiratory difficult, decreased physical strength and fluid retention (17). In recent years, several models of ML have been built to help diagnose HF. For example, Asch *et al.* collected more than 50,000 images from the echocardiographic database and built a deep learning model to assess left ventricular systolic function (18). The constructed model was tested among 99 patients to automatically obtain the data of left ventricular ejection fraction (LVEF), and the results were compared with the average value of LVEF measured by three experts using traditional volume-based techniques. The results showed little difference between the model and traditional volume-based techniques, suggesting that LVEF obtained by the model was the same reliable as those obtained by the experts (18). Additionally, some scientists attempted to use electrocardiogram to diagnose HF instead of echocardiography. For instance, Attia *et al.* collected electrocardiography (ECG) and echocardiogram data of 44,959 patients and defined LVEF <35% as cardiac insufficiency (19). A convolutional neural network was used to train the data, and the model was independently verified using the data of 52,870 external patients. The area under the receiver operating characteristic (ROC) curve, sensitivity, specificity, and accuracy of the model were 0.93, 86.3%, 85.7%, and 85.7%, respectively (19). It is proved that the diagnosis of HF by ECG based on ML is highly consistent with that by echocardiography (19). Besides, the studies of Adedinsewo *et al.* and Potter *et al.* also proved that AI algorithms can diagnose patients with left cardiac insufficiency relying only on ECG, which is an independent, non-invasive, and inexpensive examination (20,21). In conclusion, these studies show that ML is a promising instrument in the auxiliary diagnosis and may therefore reforms diagnosis of HF.

Application of ML in the diagnosis of CHD

CHD refers to coronary artery stenosis and is caused by atherosclerosis in the coronary arteries, thus leading to myocardial ischemia and hypoxia (22). Recently, increasing models of ML have been built to detect coronary artery stenosis. Take an example, Zreik *et al.* developed a ML model based on coronary computed tomography angiography (CTA) to detect the type of coronary artery plaque, as well as the stenosis degree and anatomical significance (23). In their study, the central lines of coronary arteries were extracted, and multiplanar reconstruction images of coronary arteries were reconstructed (23). Convolutional neural networks were used to extract features along the coronary arteries, and the extracted features were then aggregated by recursive neural networks with multiple classification tasks. The accuracy of the model for the detection of coronary artery stenosis was 77%, and the accuracy for the detection of coronary artery stenosis degree was 80%. The results showed that the automatic detection and classification of coronary plaque based on coronary computed tomography (CT) is feasible (23). Besides, Larroza *et al.* extracted texture features from cardiac magnetic resonance imaging (MRI) to differentiate acute myocardial infarction (AMI) from chronic myocardial infarction (CMI) (24). The study extracted 279 texture features from predefined regions of interest (ROIs) including the infarcted area on late gadolinium enhancement (LGE) MRI and the entire myocardium on cine MRI. The results showed that texture selection technique combined with polynomial SVM could achieve good classification accuracy, demonstrating that texture analysis can distinguish AMI and CMI, both in LGE and cine MRI (24). Additionally, another study manifested that texture analysis based of ML can detect myocardial infarction (MI) using non-contrast-enhanced low radiation dose cardiac computed tomography (CCT) images, which experienced radiologists cannot diagnose (25).

Application of ML in the diagnosis of cardiac arrhythmia

Cardiac arrhythmia is one of the leading causes of cardiac death, including abnormal frequency of heart impulses, abnormal cardiac rhythm, abnormal origin of heart beat and abnormal conduction velocity of heart (26). Clinically, ECG is often used to diagnose cardiac arrhythmias. However, ECG waveform interpretation requires electrophysiological experts with specialized knowledge of ECG, and is highly dependent on personal experience. Further, different doctors often interpret electrocardiograms differently. However, ML can assist doctors to diagnose arrhythmia-related diseases by reading, processing, segmenting, extracting features, training, and learning ECG graphics. Early ML algorithms had high sensitivity and specificity for sinus rhythm, but their diagnostic ability for arrhythmia was far inferior to that of professional electrophysiology experts (27). In recent years, with updates in ML algorithms, development of ECG noise reduction technology, progress in ECG feature extraction, and optimization of the addition and deletion methods, the accuracy of ML models in the diagnosis of arrhythmia has greatly improved, and the accuracy of some models have even achieved up to 95% (28). At present, most models of ECG diagnosis are single-diagnostic model, thus increasing multi-label ECG diagnostic models are being developed (29-31). For example, Chinese experts Zhu *et al.* developed an automatic multi-label diagnosis model based on deep learning for heart rhythm and conduction abnormalities (32). The study collected 180,112 electrocardiograms from 70,692 patients, which included

21 different diagnoses of arrhythmias or conduction abnormalities, and used convolutional neural networks to train, learn, build, and test a ML model (32). The independent external data of 828 new patients were used to validate the model (32). Then, the study compared the model's interpretations with those of electrophysiologists with various seniority. The results showed that the ML model was perfectly matched in 658 (79%) cases of the 828 ECG diagnoses at the multi-label level, and surpassed doctors with 0–6 years' experience of reading images (552 cases, 67%), doctors with 7–12 years' experience of reading images (571 cases, 69%), and doctors with more than 12 years' experience of reading images (621 cases, 75%) (32).

Application of ML in other CVDs

CVD also contains other types of CVDs including valvular heart disease, myocardiopathy and so on. ECG based on ML can help in the screening and early diagnosis of mitral regurgitation. Kwon *et al.* collected 5,667 electrocardiograms for training and internal validation and used the data of 10,865 patients for the external validation (33). The areas under the ROC curve of the diagnostic model for mitral regurgitation in training and internal sets were 0.758 and the areas under the ROC curve in external sets were 0.850 (33). Besides, Sawano *et al.* also used a convolutional neural network to develop a ML model for aortic valve regurgitation. Their study suggested that AI ECG can be used to diagnose significant aortic regurgitation (34). Simultaneously, Jin *et al.* developed an anatomically intelligence in ultrasound model to locate mitral valve prolapses, and Narula *et al.* developed a ML model using a variety of ML algorithms for the differential diagnosis of cardiomyopathy, and both have shown benefit in their respective fields (35,36). Additionally, some scholars even developed a ML model for hyperglycemia evaluation using AI ECG, whose area under the ROC curve was 0.95, sensitivity was 87.57%, and specificity was 85.04% (37). Consequently, the application of ML in diagnosis of CVDs remains to be explored.

Risk-prediction model based on ML

ML algorithm is different from traditional statistical linear analysis methods, which has a powerful data processing ability. It adopts a non-linear learning mode and can extract more characteristic values for training to construct risk-prediction models of various diseases more effectively and reliably than traditional methods (38). In the field of CVD, ML algorithms can be used to predict the risk of CVD, the incidence of adverse events, the mortality rate of hospitalized patients, and the expected rate of out-of-hospital readmission. Zhao *et al.* collected the physical examination data of 29,700 patients, identified the main risk factors of hypertension through a single-factor analysis, and then trained and tested the data using multiple ML algorithms and optimized the model through methods of cross-validation (39). The results showed that body mass index, age, heredity, and waist circumference were the main risk factors for hypertension (39). Additionally, external data verification showed that compared to other ML models, the RF model had the best performance in predicting hypertension risk (AUC 0.92, accuracy 82%, sensitivity 83%, and specificity 81%) (39). Motwani *et al.* collected 25 clinical parameters and 44 coronary CTA image parameters from 10,030 patients with suspected CHD, and developed a boosting algorithm that predicted the 5-year all-cause mortality of patients (40). The AUC of the ML model was 0.79, which is better than that of the previous Framingham Risk Score (40). Rajkomar collected 46,864,534,945 data nodes of 216,221 patients, including their clinical records, based on the electronic health records of adult patients hospitalized for at least 24 hours, and developed a deep-learning model that could relatively accurately predict in-hospital mortality, 30-day unplanned re-hospitalization, and extended stays (41). The model had an area under the ROC curve of 0.93–0.94 (in-hospital mortality), 0.75–0.76 (30-day unplanned re-hospitalization), and 0.85–0.86 (extended stays), respectively (41). Additionally, Chu *et al.* developed a risk-prediction model for the incidence of adverse events in pregnant women with congenital heart disease and their fetuses through different ML algorithms (42). The AUC of the ML models developed by Chu *et al.* for maternal adverse event risks was 0.70 and the AUC for neonatal adverse event risks was 0.80 (42). The model is helpful for clinicians to manage and diagnose congenital heart disease in pregnant women and their fetuses during pregnancy (42).

With its unique inherent advantages, ML can collect and integrate a large amount of clinical data and produce better performance prediction models through specific algorithms, which is conducive to doctors' clinical decision and can improve the prognosis of patients.

Summary

ML is being applied more and more commonly in the medical field, and has great practicability and high effectiveness. ML, combined with imaging examination technology and ECGs, has played an important role in the auxiliary diagnosis of CVDs, and ML can help clinicians make more optimized clinical decisions by constructing prediction models using specific algorithms. However, the popularization of ML still faces some problems. First, in terms of data quality, the electronic and standardized process for electronic medical records in foreign countries is relatively optimized, as is the data quality; thus, the convenience of collection and feature extraction of relevant data makes it easy to construct ML models. However, our country still needs some improvements in this respect. Second, in terms of data sharing, data from different electronic medical record systems are often incompatible and cannot be shared, which makes multi-center clinical research difficult. Additionally, ML itself faces some challenges, including (I) that ML models use data collected and classified by human beings, and thus the data itself may have selection biases due to human factors; (II) ML models do not consider humanistic ethics and other factors when making certain decisions or risk predictions, but these have to be considered in real clinical applications; (III) ML models are subject to the "black-box" effect; that is, ML models are similar to "black boxes" in their calculation processes, and their working principles cannot be expressed in a way that can be understood by human beings, and are thus unexplainable and uncertain. In summary, the reasonable and effective use of ML algorithms can help clinicians make a more comprehensive and accurate diagnosis, predict the prognosis of patient-related diseases, and remind clinicians to implement intervention measures as soon as possible. In the future, models and software based on ML algorithms will become common auxiliary tools in clinical practice.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1853/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1853/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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