Integration of Machine Learning in Imaging Analysis for Clinical Diagnosis of Cardiovascular Diseases

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ABSTRACT

In recent years, artificial intelligence (AI) has emerged as an important technology revolutionizing the diagnosis and prognosis of cardiovascular diseases. In cardiology, machine learning models can reduce the cost and time-to-diagnosis, as well as increase diagnostic precision, consequently improving the quality of care for patients. Therefore, this review provided an overview of innovative models in cardiology-based image analysis for disease diagnosis. Recent reports on studies evaluating the performance of these models were reviewed. Common approaches to training AI models include supervised learning, semi-supervised learning, unsupervised learning, and various other approaches. Logistic regression, support vector machines, random forests, cluster analysis, and neural networks are examples of machine learning architectures used in modern times. AI is used in cardiac magnetic resonance imaging to detect artifacts and assess image quality, as well as to quantify blood flow faster and more accurately. Convoluted neural networks are utilized in echocardiography and electrocardiography to enhance the precision of visualizing cardiac structures and assessing cardiac functions, respectively. AI models in X-ray imaging are employed to identify structural anomalies in the heart and assess their severity. In response to the need for high-quality data while safeguarding patient privacy and confidentiality, specialized databases with comprehensive datasets have been established, such as the UK Biobank and the MIT-BIH Malignant Ventricular Arrhythmia Database. Prospects in machine learning-based screening in cardiology include digital heart winners in precision medicine, explainable AI, and radionics.

Keywords: Machine learning, Cardiovascular imaging, Convolutional neural networks, Cardiac MRI, Digital heart twin

Highlights

- Convolutional neural networks are the most employed AI algorithm in diagnostic models for cardiovascular diseases.
- Combinations of machine learning prediction and human expertise typically perform better than human expertise alone.
- Drawbacks of the machine learning model include limited data, computer bias, and lack of transparency in machine learning decisions.

Background

Cardiovascular disorders, such as cardiomyopathies, coronary artery disease, myocardial infarction, valvular heart diseases, and heart failure, are recognized as predominant global causes of mortality, resulting in approximately 17.9 million deaths annually.[1] This mortality rate is expected to rise to 20.5 million in 2025 and 35.6 million in 2050.[2] To address this pressing issue, previous studies have emphasized the need for early diagnosis, as this will ensure that preventive and management strategies commence early, thereby limiting disease progression and reducing the incidence of complications and deaths.[2,3]

The advent of precision medicine, particularly the application of artificial intelligence (AI) innovations, has led to numerous advancements in the management of cardiovascular disorders. Artificial intelligence is the simulation of human intellectual capabilities in computer-based technologies.[4] This is exemplified in robot-assisted surgery, which enables focused access to various anatomical locations and structures in the body without damaging proximal critical organs. In addition to robotics, another important branch of AI is machine learning, which involves training computers on extensive datasets to enable them to recognize patterns, perform predictive analysis, and complete related tasks.[5] Machine learning applications are used in other branches of AI, such as natural language processing, computer vision, expert systems, and deep learning.[6] The innovations have led to the development of systems that aid evidence-based risk stratification and diagnosis. Furthermore, some machine learning models offer recommendations that may be used by clinicians in decision-making and treatment planning for patients.[4]

Medical imaging plays a crucial role in the accurate diagnosis of cardiovascular disorders, and significant developments and advancements have been made in this field in recent years. This study aimed to provide cohesive evidence by reviewing reports on machine learning innovations and their integration in the analysis of medical image data to aid in the diagnosis of cardiovascular disorders. The findings from this review are expected to provide a comprehensive overview of reports from recent studies that designed and/or assessed machine learning frameworks for clinical diagnosis in cardiology. In addition to serving as a point of reference for clinicians, this review highlighted current gaps in machine learning in the field of cardiovascular health, thereby potentially informing future research endeavors in this field.

Machine Learning

Machine learning refers to the ability of machines to independently learn and make accurate predictions. Considerable evidence has demonstrated their capacity to perform deep quantification of imaging phenotypes.[3] Machine learning approaches to image-based diagnosis rely on models that are trained to uncover hidden

and complex imaging features by identifying patterns in clinical data.[7] In machine learning, datasets are divided into training, test, and validation sets. Large datasets are used in the training set to develop models through either supervised, unsupervised, or semi-supervised learning (Figure 1). A combination of these approaches or other variations may also be used.[8]

Machine Learning Approaches
Supervised Learning
Supervised learning refers to the development of mathematical models that utilize a training dataset with specific characteristics annotated with clearly defined outcomes or output labels, enabling the algorithm to learn.[9] For imaging analysis in cardiology, algorithms are trained to recognize patterns and features in medical images that are indicative of specific cardiovascular conditions. This process begins with the accumulation of data from various imaging modalities, including echocardiography, magnetic resonance imaging (MRI), computed tomography (CT), and other imaging techniques, to construct the model. Data may then be cleaned and pre-processed using traditional statistical methods, such as logistic regression, naive Bayes, or artificial neural network (ANN) models, to identify variables that are meaningful to the required outcome. Using these data characteristics, a suitable machine-learning algorithm is selected, and the corresponding machine-learning model is constructed.[3] The breakthroughs in supervised learning machine learning algorithms for cardiovascular disease diagnosis are evident in the use of ultrasonic probes to obtain high-definition ultrasound images and the application of neural architecture to improve image classification and enhance performance, as described by Muse et al.[10] as well as Azarmehr et al.,[11] respectively.

Unsupervised Learning
Unlike supervised learning, machine learning training models using unsupervised learning approaches operate independently and identify data relationships with minimal guidance and without predefined data labels.[9] It involves addressing issues through pattern recognition using training samples of unknown categories or training sets devoid of features. This may involve collecting a large dataset of medical images that do not indicate a specific condition and using algorithms, such as K-means and hierarchical clustering algorithms, to categorize the images based on similarities in their features.[12] This can help identify different subtypes of cardiovascular diseases or distinguish between healthy and diseased tissues. Given the advantage of unsupervised machine learning in discovering hidden structures in data and exploring relationships between variables, its use has been adopted in several settings, combining imaging data and clinical parameters to phenotype patients with heart morbidities.[12]

Semi-supervised Learning
Semi-supervised learning is a combination of supervised and unsupervised learning, utilizing both labeled and unlabeled datasets to train models.[13] The labeled data helps the model learn to recognize patterns and features associated with specific cardiovascular conditions, whereas the unlabeled data facilitates the generalization of the model to improve its performance. With the rise of deep learning in recent years, semi-supervised learning has emerged as a crucial approach to harness the strengths of deep neural networks in capturing complex image features while also benefiting from unlabeled data parameters for patient phenotyping.[14] In real-world settings where the challenge of limited labeled data persists,
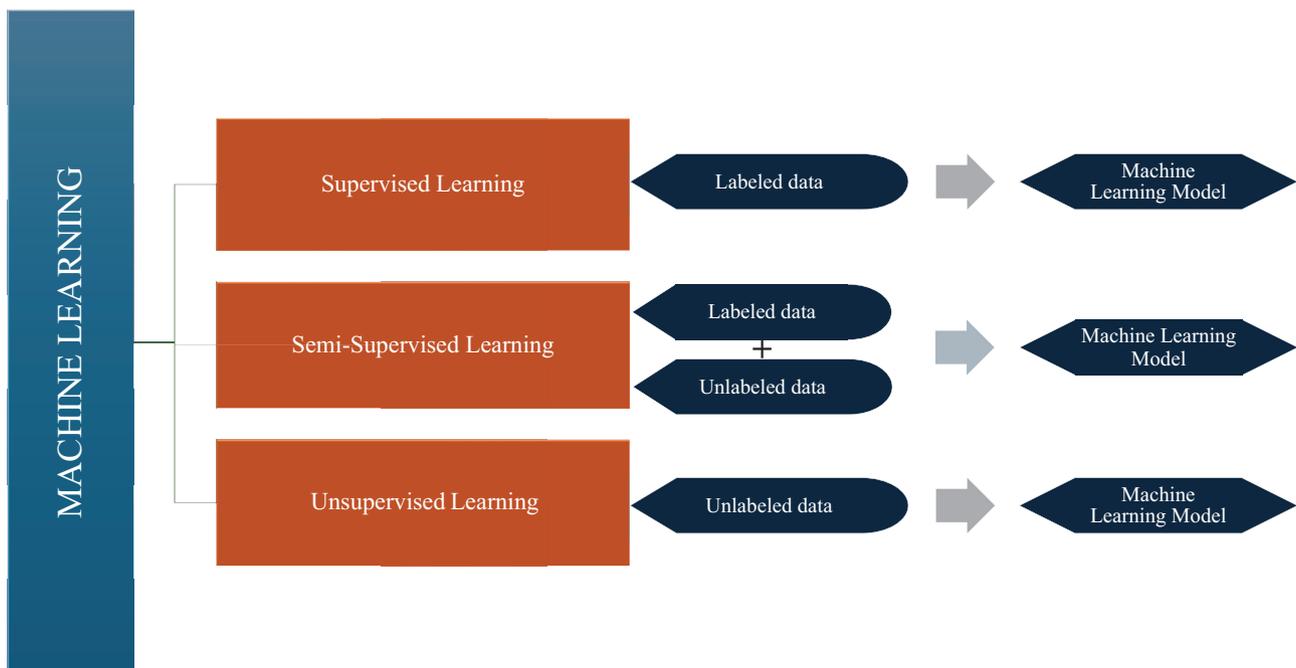

Fig 1 | Common machine learning techniques

semi-structured learning proffers a solution to address this prevailing gap with promising implications for improving the accuracy and efficiency of cardiovascular imaging analysis.

Other types of learning, including reinforcement, multi-task, transfer, few-shot, and active learning, are sometimes combined to create powerful models.[3,12,15] However, these models are less commonly used and have yet to gain a significant foothold in cardiovascular imaging.

Machine Learning Architectures

In cardiac imaging, specific machine learning algorithms are commonly adopted in various ways to improve the accuracy and efficiency of cardiovascular disease diagnosis and treatment. These include logistic regression, decision trees, support vector machines, naive Bayes, random forests, and ANN (Figure 2). The different algorithms are designed to handle specific types of data and problems.

Logistic Regression

A Logistic regression model estimates the probability of an event occurring by fitting data into a logistic curve. The model analyzes the effect of a group of independent variables and delivers a binary or dichotomous outcome (e.g., yes or no, present or absent), assuming that no missing variables are present.[16] In logistic regression, the core of the model is the sigmoid function, which maps real-valued numbers into a value between 0 and 1. The learning data consists of pairs (x_i, y_i) of a vector of covariates and a dependent variable. These input features are then combined linearly using weights (coefficients) and a bias term before being passed through the sigmoid function.[17] A stepwise forward or backward selection procedure is used to remove variables based on the Akaike information criterion and to select variables that are eventually included in the model. However, this stepwise cycle stops if neither adding nor removing variables yields an improvement. The logistic regression aims to find an optimal equation that maximizes the likelihood estimator or minimizes the loss function of the model. The model can thereafter be validated, assessing its discrimination ability by calculating the area under the curve (AUC) as well as its accuracy, sensitivity, specificity, and precision.[18]

The logistic regression model is widely used in medicine, particularly for predicting patients' risk of various cardiovascular conditions, and is a valuable model for low-complexity tasks that require integrating different data sources into a binary classification.[7] However, this model is limited when the relationships between the outcome and predictors are nonlinear and when the number of candidate predictors is high relative to the sample size.

Support Vector Machines

Support vector machines represent one of the most frequently used supervised machine learning techniques for classifying tasks and achieving optimal performance in discriminating imaging patterns.[19] Compared with logistic regression, support vector machines have a good generalization performance, and its classifier shows special advantages in overcoming the challenges with non-linearity, high dimensionality, local minima, and pattern recognition problems of small samples. This algorithm requires a relatively small number of samples, and due to the wide choice of kernels they can be applied with, a wide variety of data, including texts, handwritten digits, images, and bioinformatics, can be analyzed using these tools.[20]

Mathematically, support vector machines operate by identifying the optimal linear hyperplane that separates data points of different classes, thereby maximizing the margins between points to achieve improved generalization and prediction.[21] This involves solving the optimization problem using techniques such as Sequential Minimal Optimization and evaluating the trained model on the test set using metrics like accuracy, precision, recall, and F1 Score.[22] However, in many real-world scenarios, especially in cardiovascular events, data is not always linearly separable; hence, a kernel trick is used to transform the data into a higher-dimensional space where a linear hyperplane can be found. This is a crucial part of support vector machines as the kernel function $K(x_i, x_j)$ computes the dot product of the mapped features in the higher-dimensional space, allowing them to handle non-linear classification problems. By using kernel functions, regularization parameters, and approaches that permit the rejection of weak data, the discrimination capacity of the support vector machine model is facilitated, indirectly affecting feature selection and optimization.[23]

Random Forest

The random forest technique is a supervised machine learning algorithm used for both classification and regression tasks. It is a regression tree technique that utilizes bootstrap aggregation and randomization of predictors to achieve high degrees of predictive
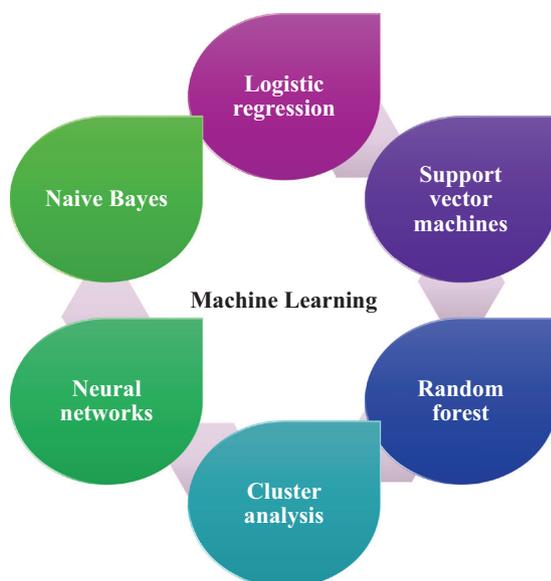

Fig 2 | Examples of machine learning algorithms

accuracy, even with large datasets.[24] The random forests model uses "parallel ensembling," which fits several decision tree classifiers trained on different random samples of a training set to transform a problem into a set of hierarchical queries (i.e., a tree-like structure with subsets of decisions).[25] This approach involves recursively partitioning the data into two groups based on predefined conditions, starting with the bottom of the decision tree, which are referred to as decision nodes. The dataset is then sampled with replacement (bootstrap sampling) and aggregated (bootstrap aggregation). A second randomization is thereafter conducted at the decision nodes, with each node having a certain number of predictors based on the different classified data.[26] The algorithm then tests all possible thresholds for all selected variables and selects the variable-threshold combination that yields the best split. This process is reiterated until either "pure" nodes are reached (containing only cases or controls). This is the decision tree. The tree-growing process is repeated (commonly 100–1000 times) to grow the random forest, which can then be used to discover meaningful interactions and non-linear effects of the predictors.[27] For instance, a random forest algorithm may be used to evaluate stroke risk based on images recursively classified on the decision tree until the pure node is reached. However, using the random forest model can often lead to the loss of generalization due to its discriminatory power on training datasets.

Cluster Analysis

The cluster analysis algorithm is an unsupervised machine learning technique in which unlabeled data are aggregated as data points based on similarity or proximity in a given parameter space.[28] Without the need for prior data labeling, they identify groups of objects or clusters that are more similar to each other than to other clusters; as such, they are used in models to provide intuitive explanations about relevant aspects of a dataset.[29] Owing to the large amount of noisy, incomplete, and sampled data used in clustering, the performance of this algorithm can vary substantially for different applications and types, thus necessitating different cluster approaches, including the hierarchical, k-means, and density-based clustering methods.[30] The hierarchical clustering creates a hierarchy of clusters using a tree-like structure called a dendrogram, which may be agglomerative (bottom-up) or divisive (top-down). The k-defines a prototype centroid (typically the mean of a group of points) and is usually applied to objects in a continuous n-dimensional space. Points are attached to centroids as clusters continuously until no point changes in the cluster are observed (i.e., the centroid remains the same).[28] Achieving such clustering saturation is useful for patient stratification to inform the understanding of cardiovascular disease pathophysiology and the effectiveness of targeted therapies.[31]

Neural Networks

Neural networks consist of interconnected nodes organized into input, hidden, and output layers, which utilize receiver operating characteristic curves and AUC to evaluate the accuracy of the generated model.[32] Neural networks are classified as ANNs, convolutional neural networks (CNNs), or recurrent neural networks with each exhibiting different architectures and suited for different types of tasks.[33] ANNs are designed based on the structure and interactions of biological neural networks and are used for pattern recognition. Analogous to cell bodies and neuronal communications, they contain nodes interlinked via connections, which are weighted based on their ability to provide a desired outcome. ANN is a feedforward neural network, and its activation functions transform a node's input into a desired output.[34] CNNs are an extension of ANNs used for image recognition tasks where spatial information for nodes is essential for final prediction. It overcomes limitations in ANN and functions by feeding patches of images to specific nodes, thereby preserving the spatial context from which the feature was extracted. Using this algorithm, a model can be trained to extract specific features from images, such as cardiac abnormalities, and mark their locations on a feature map, thereby enhancing its usefulness for disease prediction and effectively handling complex tasks and unstructured data.[35] However, recurrent neural networks, in contrast with ANNs, can be employed for sequential data, such as predicting future cardiovascular events based on time-series data of patient health records.

Integration of Machine Learning in Cardiovascular Imaging Modalities

Cardiac MRI

Cardiac MRI is a common imaging modality that uses radio waves and magnets to generate images of the heart, which is then used to assess cardiovascular function, blood flow, and tissue characteristics.[36] This technique is used in the diagnosis of cardiovascular conditions, as well as in monitoring the efficacy of therapy or disease progression. Image quality is sometimes a concern, as artifacts resulting from breathing or other motions may reduce the quality of the image produced, consequently negatively impacting clinical assessments (Figure 3).[37]

Radiologists typically manually examine images to identify artifacts and determine the usability of the images, as well as the need for additional imaging. To address this, Oksuz et al.[32] designed neural network algorithms, including 3D-spatio-temporal CNN and long-term recurrent convolutional network, for detecting artifacts and determining image quality. The study utilized data from the UK Biobank. Given that most images from the biobank were of high quality, as they were obtained from healthy volunteers, the authors designed a data augmentation technique using k-space to generate synthetic images that contain artifacts. The synthetic images were then used to assess the performances of the algorithms in terms of artifact detection. Overall, using 10-fold cross-validation, the algorithms, particularly the long-term recurrent convolutional network, outperformed other quality assessment methods, including random forests,

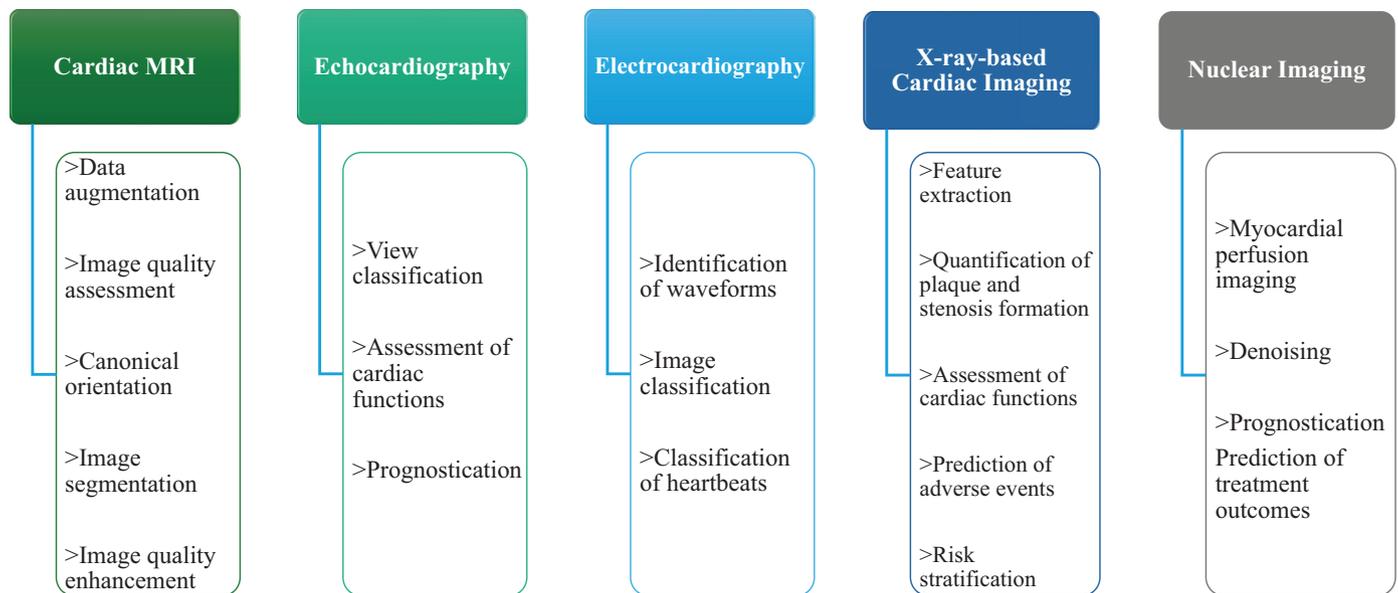| Cardiac MRI	Echocardiography	Electrocardiography	X-ray-based Cardiac Imaging	Nuclear Imaging
>Data augmentation >Image quality assessment >Canonical orientation >Image segmentation >Image quality enhancement	>View classification >Assessment of cardiac functions >Prognostication	>Identification of waveforms >Image classification >Classification of heartbeats	>Feature extraction >Quantification of plaque and stenosis formation >Assessment of cardiac functions >Prediction of adverse events >Risk stratification	>Myocardial perfusion imaging >Denoising >Prognostication Prediction of treatment outcomes

Fig 3 | Summary of machine learning applications in specific imaging modalities. MRI: magnetic resonance imaging

decision trees, support vector machines, Naturalness Image Quality Evaluator, and Adaboost. The metrics, scaled by a factor of 1000 for improved comparison, indicated that the 3D spatio-temporal CNN achieved an accuracy of 961, a precision of 957, a recall of 959, and a balanced accuracy of 958. Conversely, the long-term recurrent convolutional network recorded an accuracy of 963, a precision of 963, a recall of 965, and a balanced accuracy of 964. Among the other quality assessment methods, the Naturalness Image Quality Evaluator demonstrated the highest performance (accuracy: 922, precision: 919, recall: 925, and balanced accuracy: 923); however, these results were lower than those of the 3D-spatio-temporal CNN and long-term recurrent convolutional network.

Another example of automated processing in cardiac MRI is a study on segmentation in phase contrast cardiac MRI, an imaging modality used to quantify blood flow in the heart.[36] The study involved patients with coronary artery disease undergoing imaging examinations, and the AI-based processing model utilized a modified U-Net, a deep learning architecture. In terms of speed, the model required approximately 0.01 minutes per case, compared to manual segmentation by human specialists, which took nearly 4 minutes per case. Furthermore, the model demonstrated minimal differences from human specialists in terms of accuracy, with discrepancies of less than 5 mL in nearly all cases.

Other machine learning models, predominantly using neural networks, have been developed specifically to enhance diagnoses based on cardiac MRI. The algorithms include Omega-Net for canonical orientation and automated segmentation,[33] 3D residual U-Net for image-quality enhancement,[38] and a combination of deep CNNs and Bayesian filtering for image classification and image segmentation, resulting in the accurate depiction of the left atrium.[39]

Echocardiography

Echocardiography, also known as cardiac ultrasound, is the most common cardiovascular imaging modality, utilizing sound waves to produce images of the heart called echocardiograms. View classification is a typical preliminary step in echocardiogram examination, ensuring that the required anatomic structures are captured. This premise informed the development of a deep learning-based view classifier by Naser et al.[41] The models utilized 2D and 3D ResNet-18 CNNs and were trained, validated, and tested using images from transthoracic echocardiographic studies. The models were further tested using point-of-care videos from multiple ultrasonography machines. In the testing sets using images from transthoracic echocardiographic studies, the 2D and 3D CNNs achieved overall accuracies of 96.8% and 96.3%, respectively, and AUCs of 0.997 and 0.998, respectively. Likewise, in the point-of-care datasets, the 2D and 3D CNNs achieved accuracies of 98.4% and 95%, respectively, and AUCs of 0.998 and 0.996. Although the models demonstrated similar and high-performance metrics, the 2D CNN mostly had higher values. This was attributed to the higher input data in the 2D CNN model, which recognized consecutive frames of the same cine loop as independent images rather than as an example, unlike the 3D CNN model.

CNNs, such as the EchoNet framework, have also been used for the identification of cardiac structures after view classification.[42] In this study, echocardiographic videos and still images from the Stanford Echocardiography Database, which contains clinical data from different patients with diverse cardiovascular conditions, were utilized. With high precision, the model identified structures such as the presence of pacemakers (AUC: 0.89, F1 score: 0.73) and cellular changes in the left atrium (AUC: 0.85, F1 score: 0.68) and left ventricles (AUC: 0.75, F1 score: 0.57).

Furthermore, the model assessed cardiac function by estimating end systolic and diastolic volumes in the left ventricle as well as ejection fraction. Furthermore, the model predicted phenotypes that modify cardiovascular risk, which may not be readily detectable by human experts when examining medical images visually. These models streamline the process of image analysis and guide clinical assessments by radiologists.

For differential diagnosis based on echocardiographic findings, Liu et al.[43] used an end-to-end deep learning framework (AIEchoDx) to distinguish between multiple cardiovascular conditions, including atrial septal defect, hypertrophic cardiomyopathy, dilated cardiomyopathy, and the characteristic morphologic features of a previous myocardial infarction compared to healthy controls. The framework demonstrated good performance, comparable between the testing dataset (AUC: 98.53−99.93%) and a real-world dataset (AUC: 96.90−99.83%). Deep learning models, such as ResNet and CatBoost models, are also used to predict prognosis in heart failure by estimating 1-, 3-, and 5-year mortality rates.[40] The area under the receiver operating characteristic curves for predicting 1-, 3-, and 5-year mortality were 82%, 82%, and 78%, respectively, for ResNet and 78%, 73%, and 75%, respectively, for CatBoost. The models' performance showed a high correlation with standard risk assessment scores, such as the MAGGIC risk score and the Kansas City Cardiomyopathy Questionnaire.

Electrocardiography

The contraction and relaxation of the heart are coordinated by electrical signals that are generated by the sinoatrial node.[44] These signals are measured with electrocardiography to assess heart functions and detect arrhythmias. The progression of these signals is represented by the P, QRS, and T waveforms on the electrocardiogram. Aziz et al.[45] applied machine learning algorithms to identify these waveforms and their features (peaks, intervals between peaks, etc.) for classifying heartbeats into normal, premature ventricular contraction, atrial premature contraction, left and right bundle branch blocks, and paced heartbeats. The model combined two event-related moving averages and fractional Fourier-transform algorithms to enhance peak detection. Then, support vector machine and multi-layer perceptron classifiers were used to classify the electrocardiograms, with the latter showing predominantly higher performance metrics for various heart diseases across multiple databases. For instance, in the Shaoxing People's Hospital database, support vector machine and multi-layer perceptron classifiers yielded precision values of 0.666 and 0.883, recall values of 0.580 and 0.782, and F1-scores of 0.620 and 0.830, respectively. A similar approach was employed in another study, which aimed to optimize the performance of conventional machine learning classification frameworks, including support vector machines, k-nearest neighbors, gradient-boosted decision trees, and random forests, using a metaheuristic optimization algorithm—a highly adaptive and versatile framework for optimizing complex issues.[46] This resulted in an average accuracy of 99.92% and a sensitivity of 99.81%.

Similar to other imaging modalities, such as echocardiography, innovations in electrocardiography also employ deep learning models for image classification and disease diagnosis.[44] Attia et al.[47] trained a CNN on electrocardiographic data and echocardiograms from patients at the Mayo Clinic to identify patients with left ventricular dysfunction who were not exhibiting symptoms as well as other patients at risk of the condition, yielding an accuracy of 0.93. A major limitation of the study is that electrocardiography and echocardiography are seldom performed simultaneously for the same patient, as the two modalities assess different heart parameters.

X-ray-based Cardiac Imaging
Cardiac CT
Given the increasing morbidity and mortality associated with coronary artery disease, swift diagnosis is highly essential. AlOthman et al.[48] introduced deep learning into the analysis of CT scans to enhance the accuracy of diagnosis and assessment of coronary artery disease severity. To overcome a previously established challenge in applying machine learning for feature extraction, the authors utilized the Features from the Accelerated Segment Test (FAST) algorithm to extract features from the CT images. The features were used as input for DenseNet, a CNN that establishes connections between each layer and all other layers. The approach yielded accuracies of 99.2% and 98.73% for the two datasets used in the study. This highlights the efficiency of both the extraction method and the deep learning model. In a similar vein, another study on the clinical evaluation of coronary artery disease employed a deep learning CNN (hierarchical convolutional long short-term memory network) to quantify plaque and stenosis formation.[49] This network had two branches, which are further bifurcated into data extraction and segmentation heads. The study reported good agreement between the measurements of plaque volume and arterial diameter (intraclass correlation coefficients of 0.964 and 0.879, respectively) obtained using the model and those obtained by human experts.

Chest X-ray
Given that chest X-rays are most commonly used to assess pulmonary disorders, a retrospective study[50] utilized chest radiograph data and echocardiographic data to train and validate a deep learning model (EfficientNet) for identifying valvular diseases and assessing cardiac function. The model was used to determine left ventricular ejection fraction, tricuspid regurgitant velocity, mitral regurgitation, aortic stenosis, aortic regurgitation, and mitral stenosis, among other parameters. The study showed good performance in terms of AUC, accuracy, sensitivity, and specificity for classifying the conditions, yielding 0.92, 86%, 82%, and 86%, respectively, for predicting left ventricular ejection fraction. Similar models trained on chest

radiograph data have been employed for predicting adverse events in patients with heart failure,[51] assessing cardiomegaly,[52] and risk stratification for atherosclerotic cardiovascular disease.[53] Machine learning models have been shown to exhibit superior performance as clinical diagnostic tools to assist radiologists compared to the traditional process of diagnosis by radiologists alone.[54]

Nuclear Imaging

Nuclear imaging involves the introduction of safe doses of radiotracer substances, including technetium-99m, fluorodeoxyglucose, and thallium-201, through injection into the body to visualize and assess the metabolic functions of tissues and organs.[55] Common nuclear imaging modalities in cardiology include positron emission tomography (PET) and Single-photon emission computed tomography (SPECT). PET produces medical images through the detection of energy released when electrons annihilate positrons from the radiotracer from surrounding tissues, while SPECT directly measures gamma rays that are released from radiotracers when they concentrate in the target tissues.[56]

SPECT

Coronary artery disease is a common etiology in cardiology requiring accurate diagnosis and treatment. Myocardial perfusion imaging with SPECT is crucial for evaluating blood flow and viability of heart muscle for clinical diagnoses of cardiovascular disorders. However, the presence of noise and artifacts in medical images often poses a critical challenge to cardiologists, increasing the risk of misdiagnosis. Therefore, to minimize this risk, machine learning models have been introduced in the interpretation of SPECT images. Kusumoto et al.[57] integrated a newly developed three-dimensional convolutional neural network (CNN) into the classification of myocardial perfusion imaging SPECT data. The performance, in terms of accuracy and speed, of AI-guided diagnoses by cardiologists was compared with that of cardiologists who did not use the AI model. The AI-guided diagnosis by cardiologists demonstrated better performance (80% vs. 65%) and resulted in shorter diagnosis times (12 min vs. 31 min). In another study,[58] the integration of deep learning frameworks in the analysis of myocardial perfusion imaging SPECT datasets was examined, assessing the performance of three CNN models: RGB-CNN, VGG-16, and DenseNet-121. RGB-CNN demonstrated the highest accuracy (91.86%), followed by VGG-16 (88.54%) and DenseNet-121 (86.11%).

PET

To assess the prognostic value of PET myocardial perfusion imaging in patients suspected of having coronary artery disease, Lehtonen et al.[59] developed two XGBoost-based models trained on separate datasets. One model was trained on clinical and coronary CT angiography data, whereas the second was trained on the combination of clinical data, coronary CT angiography data, and PET imaging variables. The authors reported that the model trained on datasets that included PET scan data predicted patient clinical outcomes with an AUC of 0.82, which was significantly higher than that of the model trained on data that excluded PET data. These findings highlight the advantages of integrating machine learning innovations into the interpretation of PET images for prognosticating coronary artery disease and predicting treatment outcomes. Likewise, Singh et al.[60] investigated the utility of deep learning models for predicting mortality risk using data from PET myocardial perfusion imaging. Similar to the study by Lehtonen et al.,[59] this study also reported an AUC of 0.82. In comparison with calcium score and expert prediction of risks of myocardial infarction occurrence and mortality, machine learning-based model prediction has been shown to exhibit superior concordance index and AUC.[55]

Real-World Examples of AI-based Diagnostic Innovations in Cardiology

After scientific evaluation for safety and efficacy, many AI-based innovations have been approved for real-world applications. An example of this is DeepRhythmAI, a CNN-based algorithm that denoises electrocardiograms, thereby facilitating the precise interpretation of the heart's electrical activity.[61] The model was approved by the Food and Drug Administration (FDA) in 2022. In a recent assessment of the tool, it yielded a 98.6% sensitivity for identifying critical arrhythmias.

Another software-based FDA-approved AI tool is the EchoGo Heart Failure. This tool, which also utilizes CNNs in its model, detects heart failure with preserved ejection fraction using transthoracic echocardiography scans, achieving a sensitivity of 87.8% and a specificity of 81.9%.[62] Furthermore, the Eko Low Ejection Fraction Tool is a medical device that diagnoses low ejection fraction and prompts clinical interventions.[63] The tool was developed in collaboration with the Mayo Clinic and, in a validation study, demonstrated an area under the receiver operating characteristic curve of 0.85 for detecting ejection fractions ≤40%. The tool is currently used in multiple National Health Service clinics in the UK.

To circumvent the need for ingesting radiotracer substances and related processes for diagnosing coronary artery disease, the CorVista Capture Device was designed to simultaneously capture photoplethysmogram and orthogonal voltage gradient signals, which are then analyzed using machine learning to predict the likelihood of coronary artery disease.[64] The tool was validated through the IDENTIFY trial, demonstrating an AUC of 0.80.[65] This point-of-care device has been enhanced with another feature to predict the presence of pulmonary hypertension and is currently marketed in the US.[66]

Endoscopic procedures, such as transcatheter aortic valve replacement, percutaneous ventricular assist device implantation, and percutaneous coronary intervention, are associated with a considerable risk of endovascular bleeding. This risk increases with the invasiveness and complexity of the procedure and may

result in life-threatening outcomes such as hematoma, anemia, and even death. The Saranas Early Bird Bleed Monitoring System was designed using a machine learning algorithm to facilitate early detection and prompt clinical management.[67] The system, through a vascular access sheath, measures and analyzes bio-impedance, which reflects changes in intravascular structural changes and the distribution of blood between the intravascular and extravascular spaces. The system was validated and approved for use in humans, showing a high level of agreement (Cohen's kappa = 0.84) with bleeding diagnosis using CT.[68]

Furthermore, to expedite and improve the accuracy of coronary CT angiography for diagnosing coronary artery disease, CNNs were applied in Cleerly ISCH-EMIA, an FDA-approved AI-aided software used to analyze imaging data from the test.[69] In addition to excellent performance metrics, the software exhibited close agreement with expert readers both on a per-vessel and per-patient basis, with intraclass coefficients of 0.73 and 0.73, respectively.[70]

Limitations of Machine Learning in Cardiac Image Analysis

The performance and accuracy of the machine learning model depend on the quantity and quality of the available datasets.[71] Notable databases comprising extensive health data have been developed, especially in high-income countries. Examples of these are the UK Biobank[72] and the Cardiovascular Disease Knowledge Portal.[73] However, such databases are not widely available in resource-constrained settings, which limits the availability of population-specific data in many regions. Aside from resource limitations, a common reason for the lack of data in some regions is apprehension regarding data security and safety, given the ethical considerations surrounding patient health data.[5] This challenge is circumvented by the de-identification and anonymization of data, ensuring that patients are not identifiable through such data. Sometimes, the available database may contain limited datasets. Data augmentation and boosting techniques, including artificial data generation, interpolation, and imputation, offer an innovative approach to addressing this challenge.[32] Furthermore, transfer learning, a technique in machine learning that involves applying knowledge gained by models from one task to another, may also be used.[15]

Computed bias has been highlighted as a notable shortcoming of machine learning models, which may result in perpetuating discriminatory practices or making erroneous diagnoses because of patients' backgrounds or peculiarities.[71] Moreover, underfitting, in which machine learning models are too basic to identify patterns in data, and overfitting, in which a model focuses too much on patterns in a specific dataset and is unable to identify patterns in others, could also impair performance and accuracy.[74] These pose risks to patients and could negatively impact diagnoses and treatment planning. Hence, given the widespread application of machine learning in cardiology, among other areas of healthcare, there is a need for regulatory oversight of machine learning products.[75] Before

applying machine-learning models in clinical settings or commercialization of machine-learning-based medical devices, it is essential that these models are vetted by a regulatory body to minimize risks to patients or end-users.

Machine Learning Prospects in Cardiology
Digital Heart Twin

Cardiovascular morbidities are physiologically complex, and treatment outcomes are not always predictable, particularly when an investigational treatment is being used. A digital heart twin has been proposed to enhance diagnosis and prognostication, as well as to mitigate the inherent risks associated with treatment modalities.[76] A digital heart twin is a virtual replica of the heart developed using modern computational modeling combined with patients' health data.[77] The digital twin is utilized to enhance understanding of pathogenesis and disease progression, thereby facilitating accurate diagnosis and prediction of clinical outcomes. Furthermore, investigational treatments whose side effects and complication risk have not been completely mapped could be applied to the digital heart replica to determine their effects on the heart, thereby protecting the physical heart from harmful treatment and enhancing the personalization of treatment guidelines. For instance, Lai et al.[78] designed virtual heart replicas using ECG data from patients and investigated different implantable cardioverter defibrillator parameter settings on the virtual heart to determine which settings would provide the best benefits to patients. The study employed a reinforcement learning algorithm to investigate different parameter settings and reported better outcomes with determined settings compared to the default settings of the implantable cardioverter defibrillator. Likewise, Scotto et al.[76] employed a similar model to improve health outcomes in a patient with heart failure. Efforts are underway to design comprehensive virtual heart replicas that incorporate various physiological and pathological heart parameters to enhance the diagnosis and screening of experimental treatments.

Explainable AI

Several significant developments have been documented with the integration of machine learning in various areas of healthcare management. However, machine learning models, particularly those utilizing CNN frameworks, are complex, and it is challenging to determine or explain how they arrive at their predictions.[71] This raises concerns about the accuracy, bias, and trustworthiness of outputs from machine learning models. Therefore, explainable AI, an emerging field, aims to enhance the transparency and trustworthiness of AI model decision-making processes and predictions.[79] SHAP, LIME, and H_2O Driverless AI, etc., are tools used in this field. SHAP or SHapley Additive exPlanations was applied to visualize the predictions of a random forest regarding the impact of physical activity parameters on LV structure in older patients.[80] The addition of the SHAP framework to the model also

enabled the identification of parameters that contributed to the prediction of changes in the LV and those that did not. Future studies should focus on combining these interpretation tools with machine learning frameworks to enhance transparency and, consequently, the reliability of predictions from machine learning models.

Radiomics

Another aspect of medical imaging that has garnered increased interest in recent years is the field of radiomics, which involves extracting quantitative features from medical images. The analysis of these features is used to characterize biological structures and obtain information regarding disease diagnosis or treatment outcomes.[81] Statistical algorithms are used in the extraction of the features; these features are then used to develop machine-learning models that may be used for prediction.[81] Radiomics features extracted from native T1 mapping, a cardiac MRI approach, were investigated for risk stratification in patients with dilated cardiomyopathy. The final model performed significantly better than models created using conventional data. This approach has also been applied to coronary CT angiography to predict cardiovascular events.[82] However, the application of radiomics is currently limited in clinical settings due to a lack of standardization of radiomic features, highly variable reports from existing studies, and data limitations, necessitating further research.

Conclusions

With the increasing prevalence of cardiovascular disease incidence and mortality, addressing the limitation of human expertise for processing the exponential growth of medical data remains crucial. Hence, the integration of machine learning in processing cardiovascular imaging data holds significant value in aiding the diagnosis, treatment, and prognosis of cardiovascular diseases. This review focused on the integration of machine learning models in image analysis for diagnostic purposes. Approaches to machine learning, including supervised, semi-supervised, and unsupervised learning, were explained alongside common machine learning frameworks such as logistic regression, support vector machines, random forests, and neural networks.

In cardiac MRI, machine learning models are utilized to denoise, classify, and segment images, as well as quantify blood flow, particularly in patients with coronary artery disease. Furthermore, while echocardiography-based machine learning focused on improving the depiction of cardiac structures for diagnosis, electrocardiography-based machine learning models aimed to assess heart function with high precision. These two categories mostly employed deep learning frameworks, especially CNNs. Moreover, in X-ray-based cardiac imaging, AI models are utilized for feature extraction and the identification of heart diseases, including valvular diseases, cardiomegaly, and heart failure.

Many studies assessing the applications of machine learning models evaluated performance indices such as AUC, F1-score, receiver operating characteristic curves, sensitivity, and specificity. These indices were compared with those of human expertise or between different models, with the experimental models commonly demonstrating superior performance. Conversely, this review also highlighted the challenges of machine learning models, including limited data and ethics of health data. Furthermore, computer bias, overfitting, and underfitting were identified as shortcomings of AI, and the need for dedicated databases containing extensive, de-identified datasets, as well as regulatory oversight, was emphasized.

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