

Artificial Intelligence and Machine Learning-Based Models for Prediction and Treatment of Cardiovascular Diseases: A Review

Sreedevi Gandham, Balaji Meriga



Abstract: *Advances in Machine Learning (ML) algorithms, computing and Artificial Intelligence (AI)-based systems have been gradually finding applications in several domains including medical and health care systems. By using big data analytics and machine learning methodologies, AI has become a promising tool in the diagnosis and treatment of cardiovascular diseases. AI-ML based applications enhance our understanding of different parameters and phenotypes of heart diseases and lead to newer therapeutic strategies to tackle different types of cardiovascular ailments, a newer approach to cardiovascular drug therapy and a post-marketing survey of prescription drugs. Although AI has wide range of applications, it is in infant stage and has certain limitations in the clinical use of results and their interpretations such as data privacy, selection bias etc, which may result in wrong conclusions. Thus, AI-ML is a transformative technology and has immense potential in health care systems. This review covers various aspects of cardiovascular diseases (CVDs) and illustrate AI and ML based methods including supervised, unsupervised and deep learning and their applications in cardiovascular imaging, cardiovascular risk prediction and newer drug targets.*

Keywords: Artificial Intelligence, Machine Learning, Big Data, Supervised Learning, Reinforced Learning.

I. INTRODUCTION

Cardiovascular diseases (CVDs) incur enormous health care costs and remain the major cause of illness and mortality worldwide. The prevalence of CVDs has been rapidly escalating from the last decade and about 17.6 million deaths were recorded in 2016 due to CVDs [1]. Research studies reveal that high rate of CVD-related mortality (70%) occurs in underdeveloped countries owing to poor economic status and non-affordability for required medicare. On the other hand, in many developing countries, there has been a sea change in lifestyles due to rapid economic transformation and increased purchasing power parity in the past two decades, that lead to decreased physical activity coupled with consumption of high-calorie diets resulting in overweight-obesity and diabetes which are strong risk factors to develop CVDs [2]. However, CVDs are largely preventable or could be delayed if they are detected early and

appropriate medication is followed up. The common risk factors for CVDs include family history, blood pressure, physical inactivity, lipid profile, age, smoking, energy foods, alcoholism, obesity, diabetes, some biochemical alterations, etc. However, a high percent of CVD events occurs in people without established risk factors, or with low-to-moderate overall risk. Currently available risk prediction models are based on a limited number of parameters and fall much short of optimal performance. Therefore, the development of novel strategies for improving accuracy in the diagnosis and treatment of CVDs is necessary to save mankind from premature deaths. Data-driven techniques based on Artificial intelligence (AI) and Machine learning (ML) have already found significant applications in different domains of science, technology and medicine and might enhance risk prediction performance to aid clinicians for accurate diagnosis and treatment of CVDs [3, 4]. Various methods involving different algorithms and predictor variables have been developed to calculate the severity and risk assessment of CVD patients. Extrapolation model is one of the commonly used methods to forecast mortality because it strongly correlates the future state to the past and presumes [5]. In the medical and scientific literature, a lot of information and big data like historical electronic health records (EHRs) are available and much useful to develop artificial intelligence (AI) models that can foster better prediction of the health outcomes of patients. The Information obtained from EHR such as patient's demographic profile, health indices, biomedical images, clinical and medical reports serve as inputs for AI model, while structured medical claims data are rarely used [6].

II. ARTIFICIAL INTELLIGENCE (AI)

Artificial Intelligence was first proposed by Alan Mathison Turing more than sixty years ago but its definition is still not clear. It is more popular as a computer science involving multidisciplinary theory and practice. AI, also known as machine intelligence, can be defined as a branch of computer science that mimics the human mind process in analyzing the data/task and taking a decision [3]. With the advancement of Machine learning, AI has been gradually put into practice instead of just remaining as theory. The potential applications of AI have found a place in internet search engines, email spam and malware filtering, to identify fraudulent transactions of credit cards and to meet individual and business requirements such as marketing, gaming, robotics and entertainment domains apart from research and development (R & D) wings, military warfare and many more [6].

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* Correspondence Author

Dr. Sreedevi Gandham*, Associate Professor, Department of Electronics & Communication Engineering, Siddhartha Educational Academy Group of Institutions, C. Gollapalli, Tirupati (A.P), India. E-mail: sreedevi.gd@gmail.com

Dr. Balaji Meriga, Associate Professor, Department of Biochemistry, Sri Venkateswara University, Tirupati (A.P), India. E-mail: balaji.meriga@gmail.com

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AI has started revolutionizing the activities of not only industrial and service sectors but also the health care systems across the world by utilizing high throughput machines, robotics and big data analysis for disease diagnosis, treatment and drug development [7]. The contemporary medical and health systems have many shortcomings such as shortage of senior clinicians, shortage of paramedical staff, long training periods, high medical expenses, misdiagnosis etc. At this juncture, the multiple applications of AI have been realized and appreciated in clinical and therapeutic domains also. The Food and Drug Administration (FDA) of US has approved several AI-based devices and instruments [8]. Artificial intelligence technology encompasses a noteworthy role ahead in changing the face of the medical industry and medical services. Figure 3 depicts the central role of AI in health systems research and management.

A. Big Data Analytics

The expression Big data is used to denote very huge datasets which take a very long time and efforts to identify and store data or/and to search, perform analysis and interpretation by means of traditional data processing methods. Big data is a store house of data collected from various platforms such as socio-demographics, mobile phone applications, wearable technology, lifestyle-related factors, "omics" data banks (e.g., genomics, metabolomics, proteomics, and lipidomics), data from standard hospitals and electronic health records (EHRs) [9-11]. As such big data by themselves are not much useful, however, processing of such data using AI and Machine learning (ML) has the potential to transform the data in to meaningful results, interpretations, making predictions that could greatly improve the current understanding of clinical medicine and practice and to arrive at suitable clinical decision in health care. Figure 1 depicts the sources of big data, integration of big data analytics and AI towards precision medicine.

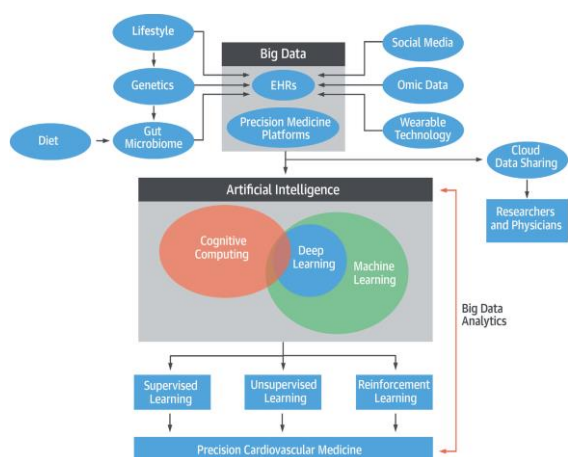


Figure-1: Big data sources and integration to AI for precision medicine.

The field of Big data analytics has immense scope and potential to identify cardiac risk factors such as primary hypertension (PH), dyslipidemia, obesity, anti-platelet/thrombolytic agents in addition to standard biochemical diagnostic parameters. It also enables to identify the unknown risk factors for cardiac ailments including acute coronary syndrome (ACS), myocardial infarction (MI), cardiac arrhythmias and even the ill effects of controversial

issue of statins or other drugs administration[10]. Although big data utilization has made considerable inroads in the field pharmaceuticals and drug development of health system, it is still in amateur stage in cardiovascular medicine but . sure to find prominent place soon.

Machine Learning

The term machine learning was used by LA Samuel of USA in 1950s in the field of computer gaming and artificial intelligence. Machine learning is a subset of AI which enables computers to learn from a given set of data and improve problem-solving efficiency by making use of big data. It means, ML identifies interaction patterns among variables, without human assistance. Unlike traditional statistics, machine learning works to build automated diagnosis/treatment systems and gives scores such as risk score, readmission or surgery or recovery scores and enables physicians/surgeons towards accurate diagnosis and treatment, rather than simple estimated score systems [12, 13]. Moreover, ML focuses to find the regular pattern behind observed data and build a model based on that data. Thus, the machine can use the model to predict and determine future data. While c-statistics are considered important in the selection of options for traditional data-processing methods, Learning curves and Area under the curve (AUC) are important choices in the selection of a machine-learning algorithm [13].

A. Supervised Learning(SL)

In recent times supervised learning algorithms have found their application in cardiovascular image analysis for the diagnosis and treatment of CVDs [16]. In SL, algorithms are presented with input data/images with the aim to map an input to output. For instance, interpretation of automated chest x-ray, electrocardiogram (ECG), computed tomographic (CT) scan or identification of an image or handwriting recognition etc.

In supervised learning, one can use a database for a set of observations and their outcomes and based on this a predictive model is framed to classify outcomes. For this purpose, some algorithms and statistical methods such as linear regression, logistic regression, survival analysis, and decision trees are used [12, 13]. Various algorithms can be trained using supervised learning method. For example, one could train a machine for 20 or 30 key variables (such as atherogenic index, C-reactive protein, LDH levels, ESR, homocysteine, QTc interval, E/A ratio, and SYNTAX score [an angiographic tool]). Then, the algorithms could generate a forecast model using key variables of the training dataset. Later, one could apply the algorithms to a new testing dataset to predict the risk of cardiovascular diseases(CVDs); the machine then could calculate the CVDs risk from the given set of 20 or 30 potential variables in the new dataset. The prediction efficiency is dependent on the type of algorithm(s) applied, dataset used , and the proposed hypothesis. A thorough understanding of the proposed algorithms is necessary because suitable algorithms are required for different hypotheses so as to apply them in an optimal manner to effectively test the hypotheses.

Fixing the objectives and using the appropriate methodology/techniques to test the hypotheses is critical to carry out ML effectively and accurately. Some of the algorithms employed in supervised learning include fuzzy logic, artificial neural network (ANN), support vector machine (SVM), decision tree, random forests, naive Bayes classifier, and K-nearest neighbor (KNN) [18]. Each of the said algorithms has its advantages and deficiencies. The difficulties encountered in Supervised learning method are generally grouped into (a) classification-related that predict categories, (b) regression-based that predict values, and (c) related to anomaly detection which predict unusual patterns. While choosing suitable algorithms, due consideration needs to be given to such factors as number of relevant parameters, training time, data features, learning curves and features. Among different supervising algorithms, ANN and SVM are said to be more popular because of their compatibility to process large and complex data (like genomics/proteomics data) with higher accuracy. ANNs, which work on the lines of human neuron concept, do well for processing of electrocardiographic (ECG) images and echo-cardiographic data [19]. ANNs are applied where traditional statistical analyses fail or in nonlinear relations. ANNs have greater predictive accuracy and efficiency than linear or logistic regression models and are found to be flexible in various data types. They are quite often used with deep-learning algorithms. The major drawbacks associated with ANN are, it takes lengthy times for computation of data, overfitting of data, and have more parameters when compared to most of the supervised learning algorithms. When compared to ANNs, SVMs are less inclined to data over fitting and require less memory.

Indeed, SVMs give better performance for text classification in electronic health records and pattern recognition in echo-cardiographic imaging to categorize cardiovascular risk and guide clinicians to take better decisions [20]. Moreover, an SVM can be used for nonlinear data or large complex data, because kernel functions, as a means to accelerate the learning process to augment their accuracy and decrease processing time [20, 21]. However, the choosing of kernel functions is crucial because selection of wrong choice may result in increased error percentage. When compared to ANN and SVM, other algorithms such as naive Bayes classifier, random forest and decision tree have lower accuracy, however, they are user friendly and could be applied to small datasets also [22, 23].

The advantage with decision tree algorithm is its easy understandability and it is less prone to data over fitting owing to its comparatively small dataset. In this, very simple questions like yes/no are used in a series to classify data into different categories and it finds its applications in clinical risk prediction also [24]. An extension of decision tree algorithm is random forest algorithm. In this model, decision trees are combined, however, each decision tree is independently trained [25]. Random forest algorithms are widely used in analyzing clinical data including HF risk, coronary computed tomography angiography, survival prediction models and readmission of patients [26]. Moreover, by using random forest model it is easy to make predictions in sensitivity meta-analysis and this is comparatively less prone to selection bias. A simple probabilistic classifier method

originated from Bayes' theorem is the naive Bayes classifier. It suits well for small training datasets and is often used in text classification problems, for example in identification of CVD risk factors [27].

Fuzzy logic model works on the similar lines as that of human reasoning and decision-making where in logic returns values, not like true or false. For instance 10% or 30 % possibility of myocardial infarction (MI) or pericarditis etc, instead of just yes/no answers. Fuzzy logic is well used in health care systems including diagnosis of early-stage CVDs, cardiac arrhythmias and risk assessment after a cardiac surgery [28, 29]. K-nearest neighbor is a simple and easy to perform nonparametric method employed for quick execution on small training datasets and for interpretation of ECG issues [30].

(a) Limitations of supervised learning

In supervised learning, using small training datasets may result in inaccurate decisions during validation, if the training datasets are biased, hence, large datasets are needed to train the model and testing by other datasets. Moreover, in SL, training datasets need to be manually labelled to predict only known output results like mortality or/and readmission rate etc. In SL although multiple functions can fit a given training dataset, there is scope for bias and it may lead the learning algorithm to prefer one hypothesis or function over another.

B. Unsupervised Learning(USL)

In this method, using unlabeled/unclassified data the unknown results are predicted and the algorithm has to find out the hidden patterns or models in the dataset. USL is employed in deep learning, for example, it is implemented in robots, driverless vehicles, in speech-and pattern recognition applications of electronic devices or others [31].

In case of CVDs, by using 2-dimensional (2D) or 3-dimensional (3D)-STE data, unsupervised learning could enable recognition of new disease patterns or phenotypes contributing to precision medicine programs. The algorithms used in USL are broadly classified into two types (1) clustering algorithms; and (2) association rule learning algorithms. The former can be used to group unlabeled data into different groups.

In clustering, data items that are similar or have common features are grouped into 1 cluster and this group is "dissimilar" to other clusters and this will be helpful when there are no clear natural groupings to differentiate. Association rule-learning algorithms assist to find out relationships between outwardly unrelated data items. For instance, a common effect or side effect observed due to drug-drug interactions.

(a) Limitations of unsupervised learning

One major limitation of USL is difficulty in identifying the initial cluster pattern, because the final cluster pattern and the result is dependent on the initial cluster pattern, hence, it might lead to errors or biases, resulting in inaccurate decisions and therefore needs validation through several cohorts.

In addition, to deal with some complex problems, instead of USL, supervised training has to be followed by manually labelling data to recognize the optimal algorithm. For example, manual denoising and pre-processing are required for noisy data of 3D-STE images to get accurate predictions. Therefore, it indicates USL may require manual coding in some parts, if not for all parts, and further validation to get the best results.

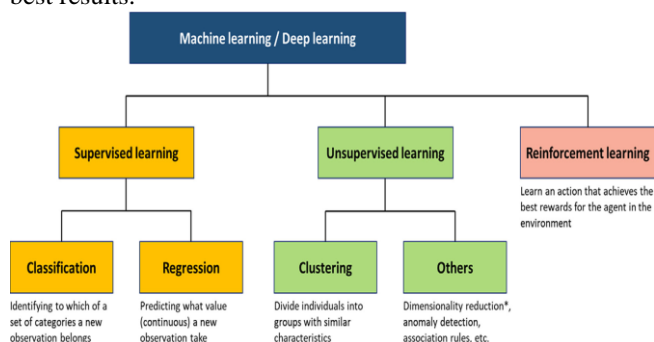


Figure-2: Machine learning and its types

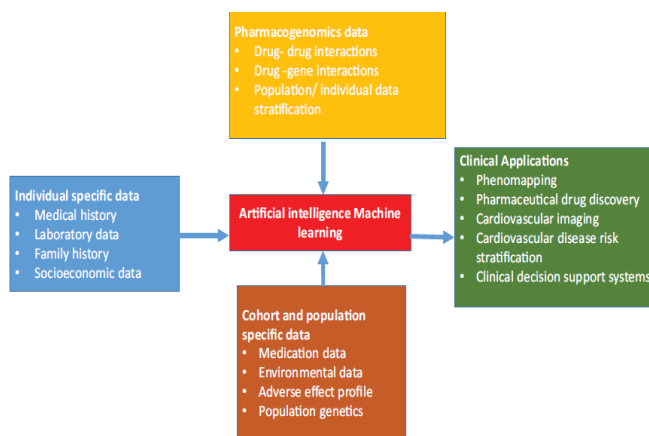


Figure-3: Key role of artificial intelligence in cardiovascular medicine and research

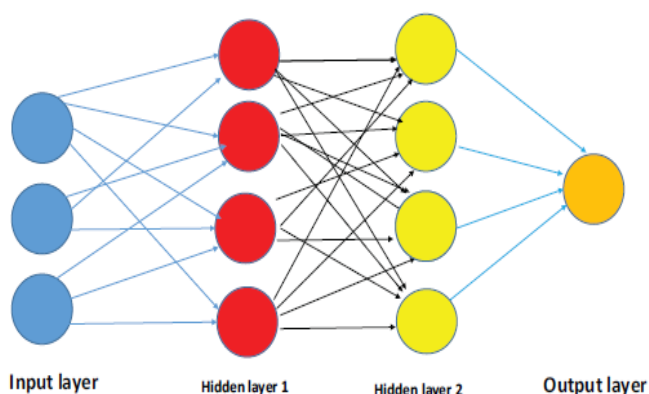


Figure-4: Deep learning network showing multiple layers. Hidden layers can be from one to several layers

C. Deep Learning (DL)

Deep learning is a subset of ML which mimics and functions similar to human brain using multiple layers of artificial neuronal networks that can produce automated predictions from the input data. DL has gained considerable significance in obtaining promising results. Deep learning can be very powerful in novel drug-drug interaction, image recognition such as CV imaging (angiography, cardiac magnetic

resonance, 2D-STE, 3D-STE) and facial recognition in social media [32]. In addition, DL algorithms also work well with noisy data, enable using of artificial real-time cardiovascular imaging with better spatial and temporal resolution and there is no limitation on working memory. Thus, there is scope for a great improvement in the quality of health care and costs.

Deep learning with neuronal network algorithms are of three types (1) Recurrent neural networks (RNN), (2) Convolutional Neural Networks (CNN) (3) Deep neural networks (DNN) [32]. The first two models are dominant in image captioning, language translation and speech recognition. For instance, end-systolic and end-diastolic volumes in cardiac magnetic resonance were reported by Uno et al, [33] by using a supervised CNN model. Choiet al., [34] forecasted heart failure 9 months before the diagnosis was made by physicians by using RNN model and reported that RNN (AUC: 0.777) was superior to supervised machine learning algorithms. Similarly, by using a DL network model, Kannathal et al., [19] classified the ECG signals of cardiac patients into normal, risky, and life-danger categories, and confirmed the classification to be correct in about 99% of test cases. Another example is in games where Google developed a deep neural network known as Google Deep Mind Alpha Go that defeated human champions in the Go game in 2016. Deep learning (with multiple layers and transformations) has proven to be promising and superior to other machine-learning techniques, such as SVM, because SVM used 2 layers.

(a) Limitations of deep learning

Deep learning is usually a nonlinear analysis and over fitting may be a major challenge to get the best predictive performance because DL involves many parameters and multiple layers. However, the issue of over fitting could be overcome by enhancing the size of the training dataset or decreasing the number of hidden layers. Deep learning needs a large training dataset, which could be obtained through collaboration amongst various institutions and EHR linkages such as American Heart Association or European Medical Association, MIT-BIH or ICMR etc. In addition, DL requires high-end computing machines, such as graphics processing unit-accelerated computing, for example, MLHPC'17, NVIDIA DIGITS Dev Box and Amazon EC2. Also, setting up a neural network using DL algorithms is also laborious process. Figure 4 shows deep layers and networking.

(b) Clinical implications of deep learning

Deep learning is found to perform well without human assistance in industrial and service sectors such as self-driving, playing some games, machine vision software in cameras, in math textbooks, reading scientific literature or answering phone calls/ questionnaire and robots. Implementation of DL in cardiovascular medicine involves some basic steps. First, unsupervised deep learning could augment in assessing the novel factors in score systems or may add hidden risk factors to the existing models.

Second, DL facilitates to classify different phenotypes and genotypes from heterogeneous groups of CVDs, for example pulmonary hypertension (HTN), cardiomyopathy and heart failure with preserved ejection fraction (HFpEF) [35]. Third, automated deep-learning prediction models facilitate to assess the risk of bleeding, stroke or other by weighing and comparing different parameters like congestive heart failure, stroke or transient ischemic attack, hypertension, vascular disease, abnormal renal or liver functions, drug therapy, alcohol intake etc, and thus facilitate suitable doses and duration of anticoagulant therapy. Fourth, DL may also be helpful to identify additional CV risk factors for example left atrial strain on echocardiography and real-time risks from wearables and include such factors into new models for anticoagulant therapy [36].

III. CONCLUSION

AI and ML have several applications in the field of medical and health care systems. Primarily, by making use of big data analytics and advanced computing methods, AI can guide clinicians to accurately diagnose disease and optimize treatment processes. In combination with traditional medical procedures, AI can significantly improve diagnostic and treatment efficiencies. Thus, the profound impact of AI-ML based methods in cardiovascular imaging will have a tremendous role on clinical care. ML algorithms would connect information from multiple sources in a seamless transition and automate several tasks which will provide more time for patient interactions with cardiologists. It greatly enhances the workflow and ultimately improves the health management system. Finally, AI and ML-driven algorithms are currently being considered as very important means in the field of CVDs for efficient diagnosis and treatment.

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AUTHORS PROFILE



Dr. Sreedevi Gandham, received Ph.D. in Electronics and Communication Engineering from Sri Venkateswara University, Tirupati. She is an Associate Professor in Dept. of ECE at Siddhartha Educational Academy Group of Institutions, Tirupati, Andhra Pradesh, India. Her research specialization is Biomedical Engineering. She has published 11 research papers in various International journals and she is a life member of Indian Science Congress.



Dr. Balaji Meriga, is currently working as an Associate Professor in the Department of Biochemistry at Sri Venkateswara University, Tirupati, Andhra Pradesh, India. He has published 64 research papers in various International journals and he is a life member of Indian Science Congress and Society of Biological Chemists.