REVIEW

Machine learning in heart failure: ready for prime time

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Purpose of review
The aim of this review is to present an up-to-date overview of the application of machine learning methods in heart failure including diagnosis, classification, readmissions and medication adherence.

Recent findings
Recent studies have shown that the application of machine learning techniques may have the potential to improve heart failure outcomes and management, including cost savings by improving existing diagnostic and treatment support systems. Recently developed deep learning methods are expected to yield even better performance than traditional machine learning techniques in performing complex tasks by learning the intricate patterns hidden in big medical data.

Summary
The review summarizes the recent developments in the application of machine and deep learning methods in heart failure management.

Keywords
artificial intelligence, deep learning, diagnosis, heart failure, machine learning, medication adherence

INTRODUCTION

Heart failure is a common condition and a major public health problem in approximately 1–2% of the adult population in developed countries, which rises to at least 10% in people aged more than 70 years [1,2]. Over the last three decades, improvements in heart failure management have improved survival, but the most recent data indicate that 12-month all-cause mortality for hospitalized and stable/ambulatory heart failure patients are still quite significant at 17 and 7%, respectively [3]. The economic costs of heart failure is estimated to be in the billions of dollars per year, necessitating clinicians, researchers and health policy makers to look at innovative ways of addressing this problem. The past decade has seen the rapid development of machine learning and deep learning techniques in the management of diverse medical conditions such as diabetes, liver diseases, infections, such as dengue and heart diseases [4]. Machine learning techniques use existing medical data (including demographic, test results or imaging) to gain insights into the management of conditions such as heart failure. The abundance of medical data related to heart failure and the availability of highly powerful computing hardware and software provide researchers with the perfect opportunity to apply more complex and computationally intensive machine learning algorithms to critically analyze this disease. In this article, we have reviewed the literature for the application of machine learning and deep learning methods in heart failure including aiding in diagnosis, classification, readmissions and medication adherence. Lastly, we have also aimed to provide future perspectives in this rapidly burgeoning field.

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KEY POINTS

- Recent studies have shown that the application of machine learning techniques may have the potential to improve heart failure outcomes and management including cost savings by improving existing diagnostic and treatment support systems.
- Machine learning techniques use existing medical data (including demographic, test results or imaging) to gain insights into the management of heart failure.
- The abundance of medical data related to heart failure and the availability of highly powerful computing hardware and software provide researchers with the perfect opportunity to apply more complex and computationally intensive machine learning algorithms to critically analyze this disease.
- Deep learning methods are expected to yield even better performance than traditional machine learning techniques in performing complex tasks by learning the intricate patterns hidden in big medical data.
- Deep learning methods are ideally suited for future research in this rapidly developing field

MACHINE LEARNING AND DEEP LEARNING IN MEDICINE INCLUDING HEART FAILURE

Machine learning is a field of computer science that utilizes artificial intelligence to learn relationships or patterns from the data without the need to define them a priori [5]. Deep learning is a particular kind of machine learning, which performs better than the traditional machine learning approaches by virtue of its ability to learn meaningful abstractions from the input data using neural networks with a large number of hidden layers. Deep learning is different from traditional machine learning in how representations are learned from the raw data [6].

A growing body of literature has accumulated showing the usefulness of machine learning methods in medical image analysis for the detection of anatomical structures, segmentation, computer aided detection and computer aided diagnosis [7]. Previous work by Shen *et al.* [8] and Miotto *et al.* [9▪] have reviewed the use of deep learning techniques in various medical domains such as translational bioinformatics, medical informatics including electronic health records, genomics, public health and mobile data from sensor-equipped smart phones and wearable devices . Together, these studies have simultaneously highlighted the role of deep learning algorithms in achieving diverse medical insights in diagnosis of diseases like cancers, drug design, 3D brain reconstruction, tissue classification, organ segmentation, human behavior monitoring and infectious disease epidemics, but also the need for the improvement of the current deep learning models [8,9▪]. Tripoliti *et al.* [10] recently reviewed machine learning methods for diagnosis, severity estimation and adverse event prediction in heart failure patients based on studies from 2005 to 2016. Although this review provides a good foundation, the focus was limited to the traditional machine learning algorithms that are related to heart failure and not more contemporary deep learning methods thereby limiting its impact.

DATASETS USED FOR HEART FAILURE ANALYSIS

A very detailed and meticulous amount of data related to heart failure patients is maintained in countries with state-of-the-art medical facilities. These data include hospital visits, procedures, laboratory tests, imaging and pharmacy records. These are collected mostly by the healthcare professionals at hospitals and healthcare facilities or at times by digital devices. The data can be in textual form (clinical notes) or images (ultrasound, tomography) or signals (ECG). A variety of data related to heart failure have been used in previous studies, and a brief description of a few important ones is provided in Table 1. The datasets include patient demographics, medical history, patient examinations, laboratory results, and diagnosis and procedure codes. Of note, PhysioNet and Holter datasets contain data in the form of ECG signals, whereas the other datasets carry text data [11▪▪,12,13▪,14–16].

MACHINE LEARNING FOR THE DETECTION OF HEART FAILURE

Different kinds of data sets have been used for heart failure diagnosis (Fig. 1). These include clinical findings, characteristics of heart and electronic hospital records. Yang *et al.* [17] developed a system for the detection of heart failure based on clinical features that include blood test results, heart rate variability, echocardiography, ECG, chest radiography, 6-minute walk test and a physical test. In their study, the participating individuals were divided into three classes, namely, healthy (no cardiac dysfunction), heart failure-prone (asymptomatic stages of cardiac dysfunction) and heart failure (symptomatic stages of cardiac dysfunction). They used a machine learning method, the support vector machine (SVM) for the classification into three classes and achieved an overall accuracy of 74.44%. In a deep learning model, built on a dataset of

Table 1. International datasets for heart failure research

Name	Type	Number of patients	Data details
Sutter-PAMF [11••]	Clinical codes	4178 (heart failure); 29 139 (controls)	EHR dataset contains demographics, tobacco and alcohol consumption, clinical and laboratory values, ICD-9 codes for encounters, orders, and referrals, procedure information in CPT codes, and medication prescription information
PhysioNet [12]	ECG	15 (heart failure); 18 (normal)	3-lead ECG recordings
Holter ECG data [13•]	ECG	18 (systolic heart failure); 12 (diastolic heart failure)	Contains systolic and diastolic heart failure data
EFFECT [14]	Clinical data	3697 (EFFECT-1); 4515 (EFFECT-2)	Clinical data obtained by chart review, demographics, vital signs and physical examination, medical history, and laboratory tests' results
OASIS-C [15]	Patient information including telehomecare	552	Carries patient's health status, living situation, severe pain experiences, frequency of activity-limiting pain, skin issues, ability to dress lower body and number of therapy visits
New Zealand National Minimum Dataset [16]	Clinical codes and Patient information	1.3M (total patients)	Carries procedure codes, diagnosis codes, diagnosis related groups, age, sex and hospital information

CPT, Current Procedural Terminology; ECG, Electrocardiography; EFFECT, Enhanced Feedback for Cardiac Treatment; EHR, Electronic Health Record; ICD, International Classification of Diseases; OASIS, Outcome and ASsessment Information Set; PAMF, Palo Alto Medical Foundation.

40 patients, Gharehchopogh *et al.*[18] used age, sex, blood pressure and smoking habits as variables and achieved an area under the receiver operating characteristic (AUC) curve of 0.95 for heart failure classification. Furthermore, their model, which was based on neural networks achieved a precision of 95% with the false positive proportion of 9%. Wu *et al.* [19] evaluated heart failure prediction based on electronic health record data of 6 months. The health data used in this study constituted of demographic, health behavior, use of healthcare, clinical diagnosis, clinical measures, laboratory data and prescriptions. In their study, heart failure could be predicted more than 6 months before the clinical diagnosis, with an AUC of 0.76, using logistic regression and boosting [19].

The use of too many variables in machine learning increases the complexity of the system and creates problems such as over-fitting. To overcome this, investigators have used other methods such as rough sets and linear regression to reduce the number of attributes within the dataset. Son *et al.* [20]

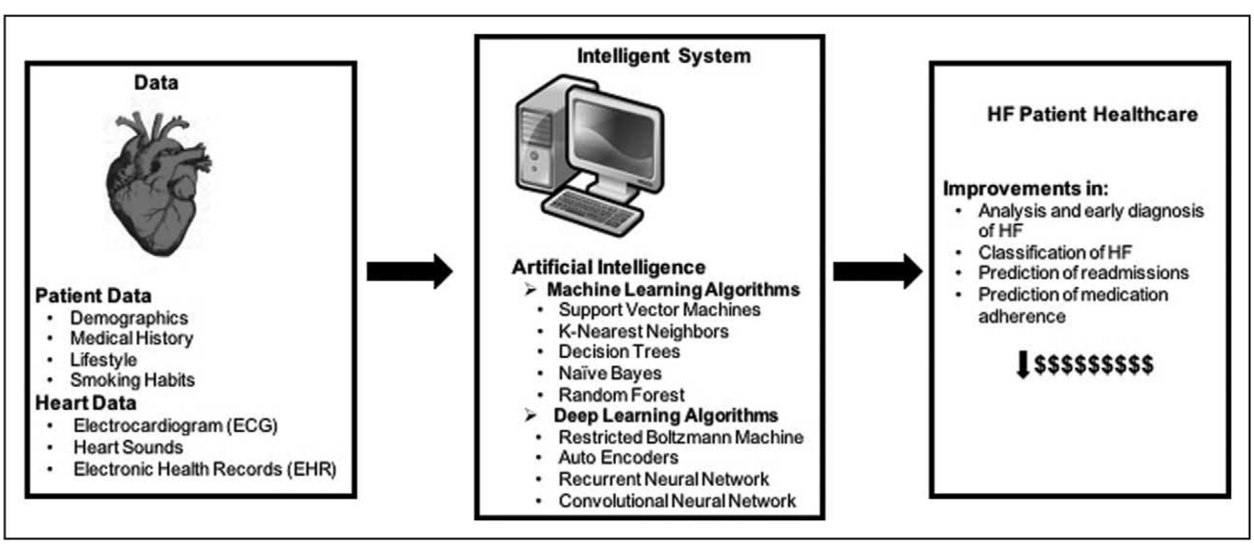

FIGURE 1. Patient datasets and machine learning techniques used in heart failure for diagnosis, classification, predicting readmissions and medication adherence to improve heart failure patient healthcare. HF, heart failure. Computer icon available at: http://www.iconshock.com/img_vista/STROKE/computer_gadgets/jpg/desktop_computer_icon.jpg.

used a machine learning method of decision trees that utilizes rough sets and linear regression models by conducting 10-fold cross validation in a dataset that contained 72 laboratory findings. The rough set method (accuracy 97.5%, sensitivity 97.2% and specificity 97.7%) outperformed the regression method (accuracy 88.7%, sensitivity 90.1% and specificity 87.5%) in discriminating heart failure patients from those with dyspnea. Although previous studies have used a binary output variable, in which the prediction would be either the presence or absence of heart failure, Aljaaf *et al.* [21] proposed a multilevel risk assessment method for heart failure based on a dataset composed of clinical features that included chest pain type, chest pain location, blood pressure, cholesterol level, smoking habits, family history of coronary artery disease and exercise features. The authors added obesity and physical activity as additional features to improve the performance. Their study used C4.5 decision tree classifier (a machine learning algorithm used for classification) with a 10-fold cross validation to classify every test instance into one of the following classes: 1, no risk; 2, low risk; 3, moderate risk; 4, high risk; 5, extremely high risk for heart failure. Their system outperformed the previous best machine learning systems and yielded an accuracy of 86.5%, sensitivity of 86.5% and specificity of 95.5% [21].

An innovative diagnostic system was developed by Zheng *et al.* [22] who built a model for heart failure diagnosis based on heart sound characteristics and cardiac reserve features. The authors applied various algorithms such as least square SVM, artificial neural network and hidden Markov models on the data consisting of 152 patients. The least square SVM classifier gave the best performance as depicted by 95.39% accuracy, 96.59% sensitivity and 93.75% specificity for the detection of heart failure. However, as heart sound characteristics are influenced by many confounders, the labeling of heart sound data was a limitation, which affected the overall performance of their diagnostic system.

Other datasets such as ECG have also been used to detect heart failure. Cornforth *et al.* [12] used a three-lead ECG data (heart rate variability analysis) in a study constituting 33 individuals (18 normal and 15 heart failure). They used the 'Renyi Entropy' along with 'Standard Deviation of all RR intervals' and 'Root Mean Square Successive Difference' as input features. They reported a sensitivity and specificity of 80.0 and 94.4%, respectively, for diagnosis of heart failure. Masetic *et al.* [23] used a random forest approach on ECG data to detect heart failure. This approach implemented the Burg method to extract features out of the ECG databases. Their study yielded 100% accuracy and an *F*-measure value of 1 over a very small number of heart failure patients in the dataset.

Lastly, Choi *et al.* [11▪▪] investigated the use of temporal relations among events in electronic health records to predict heart failure. This is the only study, to our knowledge, which has used the state-of-the-art recurrent neural networks for heart failure diagnosis. The dataset used for their study had 3884 incident heart failure cases and 28 903 controls. The recurrent neural networks outperformed the classical machine learning algorithms for detection of incident heart failure, and achieved an AUC of 0.78 and 0.88 for 12-month and 18-month observational window, respectively.

MACHINE LEARNING FOR CLASSIFICATION OF HEART FAILURE

The treatment of heart failure is dependent on the subtype of heart failure. The two main types of heart failure are – heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF). Previous investigators working in the machine learning field have targeted not only the basic classification of heart failure but also the other issues related to classification such as the gray area ambiguity and the New York Heart Association (NYHA) class change in heart failure patients.

Classification of heart failure

Austin *et al.* [14] utilized 34 variables including demographic characteristics, presenting signs and symptoms, vital signs and symptoms, laboratory data and previous medical history of patients to develop machine learning models based on classification trees, bagged classification trees, random forests, boosted classification trees and SVM methods for predicting and classifying the heart failure subtype. In their study, they used the Enhanced Feedback for Cardiac Treatment (EFFECT) study data for the model development and validation. They showed that modern flexible tree-based methods offer improvement in prediction over conventional classification and regression trees. Isler [13▪] used modeling techniques of short-term heart rate variability as a discriminating factor between subtypes of heart failure. Shah *et al.* [24▪] were the first to use unsupervised machine learning algorithms, which do not require labeled data to subclassify HFpEF patients into distinct categories. The authors used clustering algorithms on clinical, laboratory and ECG for phenotyping of patients on a dataset of

397 patients, which had 67 continuous variables. These variables were grouped by an unbiased hierarchical cluster analysis and penalized model-based clustering algorithm and generated three distinct phenotypes that differed in hemodynamic outcomes, clinical characteristics and cardiac structure/function. Such a classification of this heterogeneous clinical disease may lead to identification of therapeutically homogenous patient subclass allowing more focused treatment.

Gray zone ambiguity during classification

The gray zone ambiguity arises whenever left ventricular ejection fraction is between 40 and 50%. This ambiguity hinders the classification of heart failure as HFpEF or HFrEF. Alonso-Betanzos *et al.* [25▪▪] proposed a solution for gray zone ambiguity by using machine learning models to classify heart failure subtypes within the ventricular volume domain rather than by the single use of left ventricular ejection fraction. The authors used end-systolic volume index as a discriminating feature for HFpEF and HFrEF in a dataset of 48 real and 63 simulated patients. Both supervised and unsupervised machine learning algorithms were used and demonstrated that selected machine learning models offer promise for classifying heart failure patients (including the gray zone) whenever driven by ventricular volume data.

MACHINE LEARNING TO PREDICT MEDICATION ADHERENCE IN HEART FAILURE

Poor medication adherence leads to an increased risk of adverse cardiac events, including hospital readmission and mortality. Machine learning approaches have been used to study the prediction of medication adherence. Son *et al.* [26] applied an SVM approach to predict medication adherence in heart failure patients. The authors evaluated 11 variables consisting of demographics and clinical characteristics in 76 patients and reported the highest detection accuracy for medication adherence as 77.63%. More recently, Karanasiou *et al.* [27▪] aimed to classify a patient using machine learning techniques as medication adherent or not, and also globally adherent (i.e. medication, nutrition and physical activity) or not. In their study, which had 90 patients, the authors used around 100 variables, which included allergies, medical condition, drugs, biological data related to heart failure and clinical examinations. The highest achieved detection accuracy was 82 and 91% for the global and medication adherence, respectively. Together, these studies demonstrate that machine learning-based models help classify patients and can be useful in predicting medical adherence.

MACHINE LEARNING TO PREDICT HOSPITAL READMISSIONS

Hospital care has the largest expenditure (about two-thirds) among the total cost of heart failure treatment [28]. Therefore, unsurprisingly previous studies have evaluated different machine learning methods for the prediction of hospital readmissions. Telemonitoring data obtained from heart failure patients is an easy and obvious target for researchers. Koulaouzidis *et al.* [29] built a system to predict hospital readmissions for heart failure patients using telemonitored physiological data. Their dataset contained information for left ventricular ejection fraction, NYHA class, comorbidities, blood pressure and medications. The authors used an analysis of vectors and signals to predict a score of readmission in their study. The best predictive performance gave an AUC of 0.82 with 8-day telemonitoring data. Kang *et al.* [15] used a J48 decision tree to build a prediction model for heart failure readmissions using the 'Outcome and Assessment Information Set-C' dataset of 552 telemonitored patients. From the decision tree technique, the presence of skin tissues, patient's living situation, patient's overall health status, severe pain experiences, frequency of activity limited pain and total number of anticipated therapy visits were identified as the risk predictors for rehospitalization. Mortazavi *et al.* [30] demonstrated the effectiveness of advanced machine learning algorithms over the traditional linear regression methods in a set of 472 telemonitoring variables to predict heart failure readmissions. Other authors have used a metaheuristic approach to machine learning modeling. Zheng *et al.* [31] developed models for hospital readmissions using metaheuristics, which included age, sex, length of stay, admission acuity, comorbidity index score and readmission risk. However, the dataset they used in their study had a class imbalance problem as the total number of positive classes of data was far less than the total number of negative classes of data. To overcome this problem, they applied random oversampling and obtained the best accuracy of 78.4 with 97.3% sensitivity. Bayati *et al.* [32] constructed a predictive model for readmission for heart failure and studied how its predictions can be used to perform patient-specific interventions. Such analyses are expected to be of immense value in situations wherever it is not economically feasible to provide all program to all patients. More recently, Baechle *et al.* [33] proposed Latent Topic Ensemble Learning, which uses an ensemble of topic-specific models to leverage data from different hospitals. This innovative method is in contrast to historical approaches that use local data to build the model, and the latter performs poorly whenever supplied with test data from different hospitals. Compared with baseline methods, Latent Topic Ensemble Learning significantly outperformed the best performing baseline methods for cost reduction because of hospital readmission [33].

CONCLUSION

A variety of machine learning techniques have been successfully used in heart failure patients for diagnosis, classification, predicting readmissions and medication adherence (Fig. 1). Deep learning methods, which perform better than the traditional machine learning and have the potential of visualizing complex patterns hidden in high dimensional data are ideally suited for future research in this rapidly burgeoning field.

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Conflicts of interest

There are no conflicts of interest.

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