

Review Article



Application and Potential of Artificial Intelligence in Heart Failure: Past, Present, and Future

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ABSTRACT

The prevalence of heart failure (HF) is increasing, necessitating accurate diagnosis and tailored treatment. The accumulation of clinical information from patients with HF generates big data, which poses challenges for traditional analytical methods. To address this, big data approaches and artificial intelligence (AI) have been developed that can effectively predict future observations and outcomes, enabling precise diagnoses and personalized treatments of patients with HF. Machine learning (ML) is a subfield of AI that allows computers to analyze data, find patterns, and make predictions without explicit instructions. ML can be supervised, unsupervised, or semi-supervised. Deep learning is a branch of ML that uses artificial neural networks with multiple layers to find complex patterns. These AI technologies have shown significant potential in various aspects of HF research, including diagnosis, outcome prediction, classification of HF phenotypes, and optimization of treatment strategies. In addition, integrating multiple data sources, such as electrocardiography, electronic health records, and imaging data, can enhance the diagnostic accuracy of AI algorithms. Currently, wearable devices and remote monitoring aided by AI enable the earlier detection of HF and improved patient care. This review focuses on the rationale behind utilizing AI in HF and explores its various applications.

Keywords: Heart failure; Artificial intelligence; Machine learning; Deep learning; Big data

INTRODUCTION

The prevalence of heart failure (HF) is increasing,^{1,2)} along with the complexity of its treatment and diagnosis. The accurate diagnosis of HF relies on various invasive and noninvasive tests, and tailored treatment is based on the characteristics and type of HF.³⁻⁶⁾ The diagnosis and management of patients with HF require a substantial amount of clinical information, leading to the accumulation of big data. However, traditional analytical methods are insufficient for handling large datasets.^{7,8)}

Consequently, the significance of big data approaches and artificial intelligence (AI) in medicine has grown.⁹⁾ This review discusses the role of AI in HF. We focused on traditional risk factors, electrocardiography (ECG), electronic health records (EHRs), and telemonitoring,

and excluded each detailed imaging modality (cardiac magnetic resonance image, echocardiography, nuclear imaging, etc.).

IMPORTANCE OF BIG DATA APPROACHES IN HF

The era of big data is upon us, a term that refers to the explosion of available information. Enormous amounts of extremely high-dimensional or unstructured data are being produced and stored at a much lower cost than ever before, driving the big data movement. The main goal of analyzing such high-dimensional data is to develop effective methods for accurately predicting future observations and results.¹⁰⁾ However, the large sample size and high dimensionality of big data introduce unique computational and statistical challenges, necessitating the development of new paradigms and analysis techniques.¹¹⁾ These innovations aim to address issues such as data noise, erroneous correlations, and computational power constraints.¹¹⁾ One common objective of computational methods is feature or dimension reduction.¹²⁾ Statistical learning and modeling are frequently employed to estimate populations (inference) or predict future experiments after preprocessing and performing possible dimension reduction. These analyses frequently rely on AI and machine learning (ML), which are algorithms that can perform computational tasks without specific user instructions.¹³⁾

HF is an important target for big data research because of its complex etiology, numerous comorbidities, and the prolonged and progressive course of the disease.^{7,14)} The 2 most popular big data types used in HF research are clinical data and omics. Clinical data are collected using various means such as imaging methods, echocardiography, ECG, wearables, and EHRs. In contrast, the omics technologies, including genomics, transcriptomics, proteomics, and metabolomics, are primarily used for analyzing heart tissue or blood samples.^{7,15)} However, the accuracy, structure, and volume of omics and clinical data present challenges for data analysis.¹⁶⁾ To advance biological comprehension and clinical care of patients with HF, both conventional statistical methods and ML approaches are employed to gather critical insights from big data sources.

APPLICATION OF AI IN HF

Concept of AI, ML, and deep learning (DL)

AI is defined as the intelligence of a computer or machine that enables it to imitate or mimic human capabilities.^{17,18)} This technology can make decisions without requiring human intervention.

ML is a subfield of AI that empowers computers to analyze data beyond programmatic procedures, identify patterns within the data, apply learned patterns to new data, and perform computational tasks more effectively than humans.¹⁹⁾

Traditional statistical methods and ML have several distinct and overlapping characteristics.²⁰⁾ High-dimensional datasets with numerous variables present a challenge for traditional statistical techniques, such as regression, whereas ML methods are well suited to handle such complex data. Moreover, ML can evaluate intricate connections between predictors and handle correlated or collinear data. To accommodate temporal changes in data, ML can generate dynamic models that are continuously updated using new training data. For instance, “baseline” features, such as vital signs, laboratory results, and comorbidities, may change over time. Although the evolution of these traits may be crucial for outcome prediction, conventional statistical tools are frequently ill-equipped to handle them.²⁰⁾ ML algorithms offer the ability to calculate nonlinear relationships more effectively and precisely; however, their higher accuracy comes at the expense of interpretability.²¹⁾

There are 3 primary/representative methods in ML: supervised, unsupervised, and semi-supervised learning (**Figure 1**).^{20,22)} Supervised ML is characterized by the use of human-labeled datasets that are intended to “supervise” or “train” algorithms to correctly classify data or predict outcomes. In contrast, unsupervised ML is used to analyze and group unlabeled datasets, uncovering hidden patterns in the data without human intervention. Semi-supervised is a method that combines both supervised and unsupervised methods with limited labeled datasets and unlabeled datasets, where the unlabeled datasets are grouped with labeled datasets based on their traits. In the field of cardiovascular medicine, ML can uncover disease mechanisms and increase the precision of diagnosis, management, and risk prediction by identifying clinically relevant patterns or phenotypes that may not be apparent to clinicians.²³⁾ In fact, algorithms such as regression, decision trees, random forest, support vector machine, naïve Bayes, K-Nearest neighbors, and extreme gradient boosting are commonly used to analyze medical data.

DL is a subset of ML that uses multiple layers of artificial neural networks to discover or predict patterns.²⁴⁾ It mimics the operation of the human brain and was originally developed by Dr. Warren McCulloch (neuroscientist) and Walter Pitts (computer scientist) in 1943 as the “McCulloch-Pitts (MP) neuron.”²⁵⁾ MP neurons are structured similarly to brain neurons. Similar to the dendrites of neurons, they receive external data, perform calculations in the nucleus, and output the results as binary signals (1 or 0) that are

transmitted through the axons. When these neurons are connected, they create a neural network structure that resembles that of the human brain. Recently, the computational power of MP neurons has advanced, and they are referred to as “Perceptron.” With significant advancements in computing power, brain neural networks have also become more complex, evolving into widely used DL models, such as deep neural networks and CNN (Figure 2).

DL is especially helpful when handling big data sources, such as EHRs, because it is less dependent on feature engineering or variable selection. Overall, DL is compelling in image recognition²⁶⁾ and modeling disease onset²⁷⁾ using temporal relations among events. DL models can predict incident HF by analyzing the temporal relationships among a large number of evolving variables such as comorbidities, physiological measurements, laboratory indices, medication prescriptions, and invasive procedures.²⁸⁾

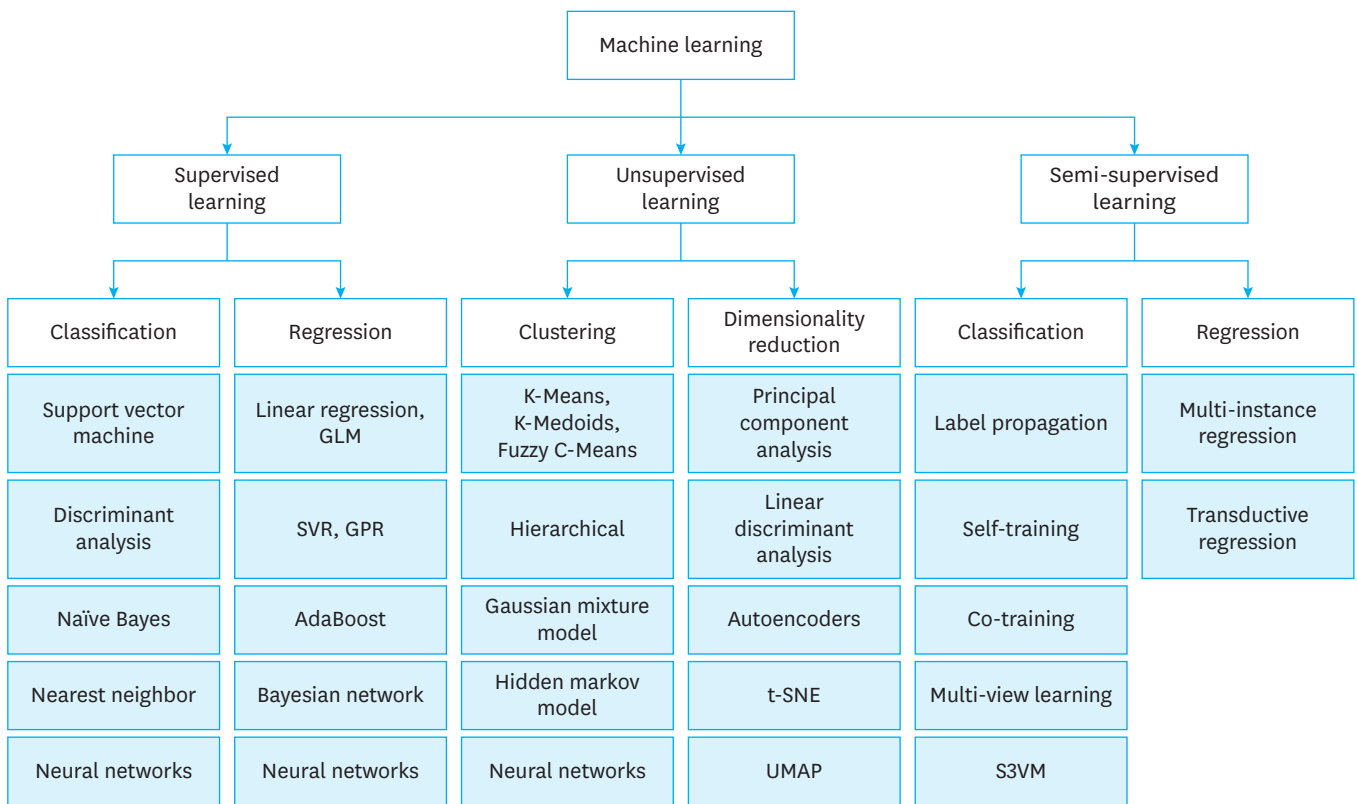


Figure 1. Classification of machine learning. GLM = generalized linear model; SVR = support vector regression; GPR = ground penetrating radar; t-SNE = t-Distributed Stochastic Neighbor Embedding; UMAP = Uniform Manifold Approximation and Projection; S3VM = Semi-Supervised Support Vector Machines.

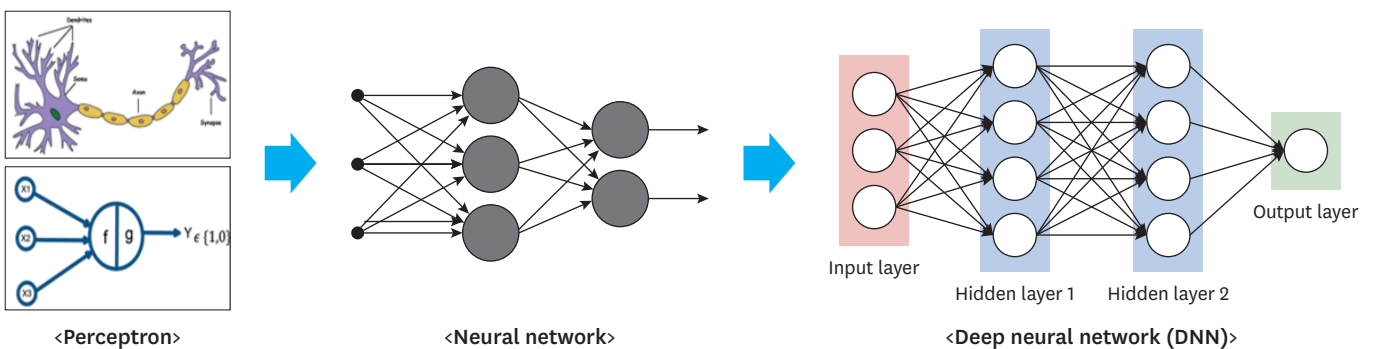


Figure 2. Evolution of deep learning.

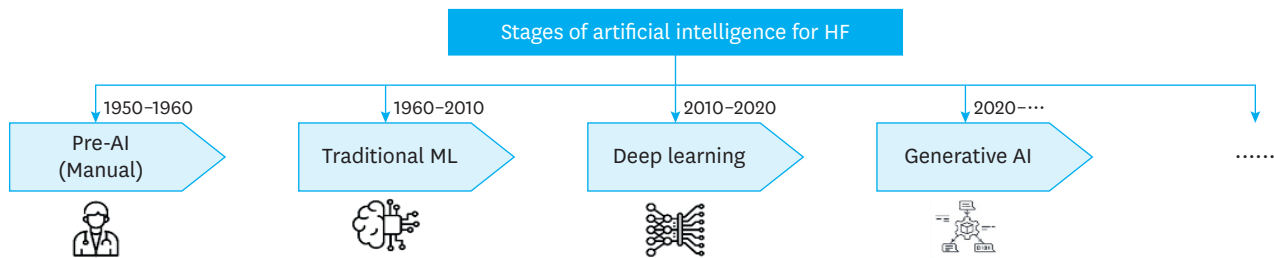


Figure 3. Stages of AI for HF.

AI = artificial intelligence; HF = heart failure; ML = machine learning.

Recently, generative AI has emerged as a great innovation in the domain of digital health (**Figure 3**). Generative AI is an AI that can generate novel content, such as creating unique and high-quality images or original writing, rather than solving traditional regression or classification problems.²⁹⁾ For example, ChatGPT, which was released to the general public about a year ago, can efficiently understand queries from humans and responds to complex questions, and even create a script or a source code. Its versatile applications have far-reaching implications for improving patient care and advancing medical research. One of the key applications of generative AI is in the medical imaging. Utilizing advanced algorithms such as Generative Adversarial Networks (GANs) and Variational Autoencoders, these models excel in generating synthetic medical images, including X-ray, computed tomography, and magnetic resonance images. As a result, they facilitate the development of more accurate and robust medical imaging systems.³⁰⁾ Research was conducted to find if an ML model could correctly capture the characteristics of congestive heart failure (CHF).³¹⁾ Unlike other diseases, such as lung cancer, where the characteristics can be found in the local area, CHF characteristics are widespread, making them difficult to detect. The authors have created a synthesized image utilizing the Wasserstein GAN model, by subtracting the features from the healthy image with the diseased image, and adding them to the original image. Verified by both ML model and radiologist, the model has well reflected the features of CHF in the synthesized image, proving both the performance of the model and the usability of generative AI model. Additionally, the digitization of EHRs benefits from generative AI, particularly in the context of natural language processing. These models proficiently generate and summarize patient notes, extract structured information from unstructured clinical text, and automate data entry into EHR systems, ultimately saving valuable time for healthcare professionals.³²⁾

Diagnosis of HF

Even for HF specialists, correctly diagnosing HF can be challenging because it is a complex syndrome caused by both structural and functional cardiac disorders rather than a single disease

entity. A classic example is leg edema, a common symptom of right-sided heart congestion. However, it can also develop in numerous alternative conditions, such as chronic venous insufficiency, chronic kidney disease, and drug side effects. Consequently, in clinical practice, many patients are misdiagnosed with HF and vice versa. In addition, contemporary physicians face difficulties in keeping up with the rapidly evolving scientific evidence, new medications, time constraints, and complexity of HF management guidelines, particularly in outpatient clinics. AI algorithms could help physicians identify HF in at-risk patients early and develop an AI-Clinical Decision Support System (AI-CDSS) (**Figure 4**).^{23,33-35)} AI-CDSS is a scalable and flexible medical assistant platform for different types of diseases. AI-CDSS consists of a total of 5 layers: Data Acquisition and Persistence Layer, Context Recognition and Monitoring Layer, Knowledge Acquisition and Inferencing Layer, Engineering Support Layer, and User Interface Management Layer. The third layer, Knowledge Acquisition and Inferencing Layer, creates hybrid knowledge models by combining rule generated from data such as images and text, and with rules created by experts and automatically evolve knowledge over time. Choi et al.³⁵⁾ developed and evaluated the diagnostic accuracy of the AI-CDSS for HF. It demonstrated a remarkable diagnostic accuracy of 98% for HF diagnosis, which was higher than that of non-HF specialists (76%). This suggests that the AI-CDSS could prove particularly useful for diagnosing HF, especially in situations where access to HF specialists is limited.

ECG is a non-invasive and simple diagnostic tool that is widely used in health checkups. Previous studies have shown a significant association between HF and ECG.³⁶⁻⁴⁰⁾ Attia et al.³⁸⁾ showed that the application of AI to ECG can be a powerful screening tool to identify left ventricular dysfunction in asymptomatic individuals. To achieve high accuracy, Kwon et al.⁴¹⁾ analyzed 55,163 ECGs of 22,765 patients and developed a deep-learning algorithm for ECG-based HF identification. Compared to logistic regression and random forest ML algorithms, the DL algorithm showed superior effectiveness in identifying HF with a reduced ejection fraction (area under the curve, 0.843; 95% confidence interval,

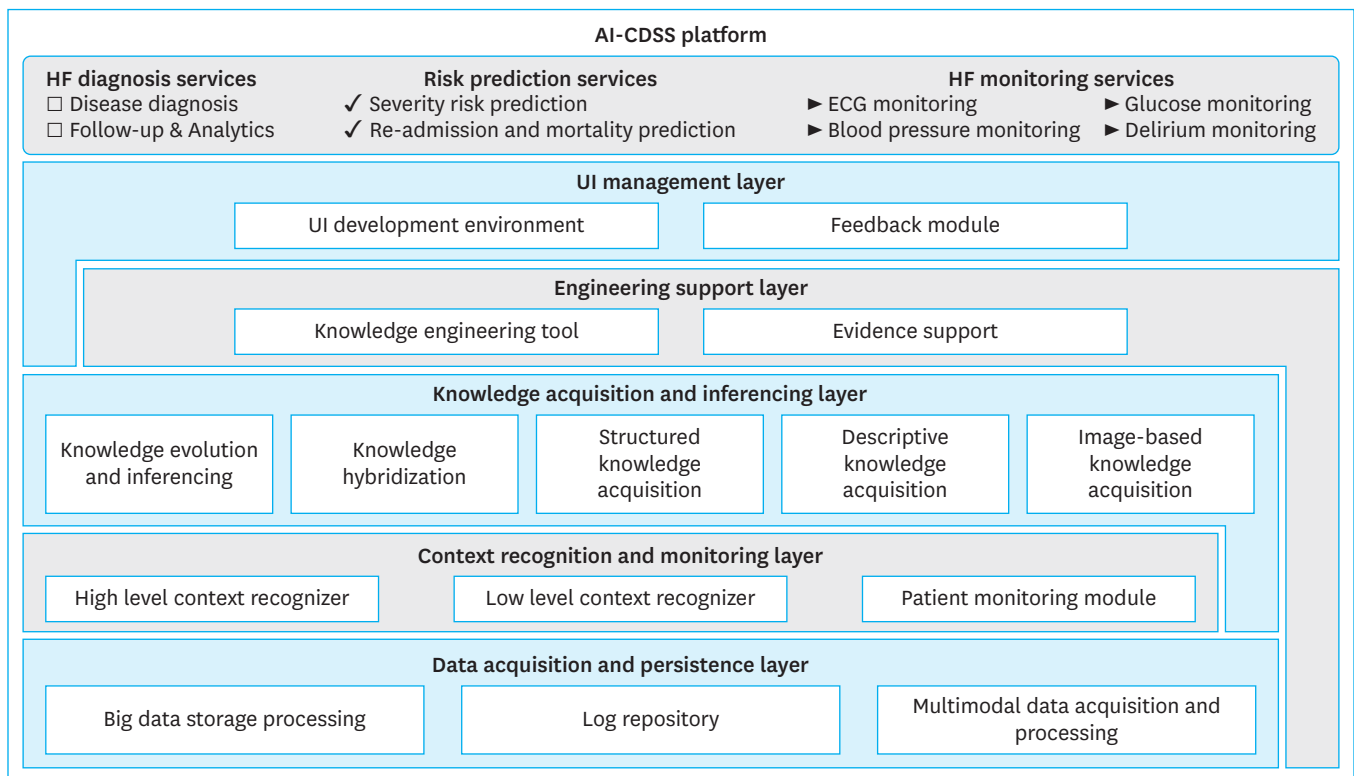


Figure 4. Hybrid AI-CDSS (expert system and machine learning) for diagnosis of heart failure. AI-CDSS = Artificial Intelligence-Clinical Decision Support System; HF = heart failure; ECG = electrocardiography; UI = user interface.

0.840–0.845). In addition, the DL model applied to ECG was shown to have a high performance in the detection of HF with preserved ejection fraction (HFpEF).^{39,42)}

Prediction of HF outcomes

HF is the leading cause of hospitalization in people aged 65 years and older.⁴³⁾ Moreover, patients with HF have a high risk of re-admission, especially immediately after discharge.⁴⁴⁾ Therefore, risk stratification is important for HF, and ML can be particularly valuable in predicting readmission for these patients. Golas et al.⁴⁵⁾ showed that DL techniques outperformed traditional techniques in predicting 30-day readmission in patients with HF. Furthermore, Kwon et al.⁴⁶⁾ showed that a DL-based algorithm predicted in-hospital mortality and long-term mortality more accurately than the existing scores, including the Get with the Guidelines-Heart Failure Score (GWTG) and Meta-Analysis Global Group for Heart Failure (MAGGIC) score. This might be because DL algorithms do not restrict the number of input or features without limiting to those with established associations or biologically plausible rationales.

Cardiac monitoring data can be used to develop risk prediction algorithms. In a cohort study of 900 patients, data from implanted

cardiac resynchronization therapy (CRT) were collected.⁴⁷⁾ The alert algorithm used heart sounds, respiratory rate, tidal volume, heart rate, and patient activity to provide a sensitive and timely predictor of impending HF decompensation.

Classification of HF phenotypes and treatment

The present HF classification may be enhanced using ML. Phenotype mapping was performed in a prospective trial with 397 ambulatory patients with HFpEF using ML algorithms and data from EHRs.⁴⁸⁾ A novel classification method for HFpEF was created using this technique, which grouped study participants into phenotypes based on their clinical traits, echocardiographic parameters, ECG, invasive hemodynamics, and outcomes. Another unsupervised ML analysis of 1,693 hospitalized patients with HF across the left ventricular ejection fraction (LVEF) spectrum identified 6 distinct phenogroups based on the common comorbidities: coronary artery disease, valvular heart disease, atrial fibrillation, chronic obstructive pulmonary disease, obstructive sleep apnea, or a few comorbidities.⁴⁹⁾ This grouping stratified the cardiovascular risk more effectively than LVEF.

ML algorithms can be used to improve HF treatment by assessing the heterogeneity of the response to HF therapies. Ahmad et al.⁵⁰⁾

studied 44,886 patients with HF in the Swedish HF registry, and utilized ML to classify patients into 4 subgroups based on their response to therapeutics and 1-year survival rates. This stratification allowed the identification of those most likely to benefit from guideline-directed medical therapy.⁵¹ ML can be used to prioritize patients who are most likely to benefit from interventions to optimize evidence-based therapies.⁵² Moreover, ML algorithms can assist clinicians in determining optimal sequencing and dosing of evidence-based therapies.⁵³

Furthermore, ML has a potential role in optimizing patient selection for HF device therapy. In general, one-third of patients with HF are non-responders to CRT.⁵⁴ A post-hoc analysis of the Multicenter Automatic Defibrillator Implantation Trial with CRT demonstrated that ML algorithms, by integrating clinical parameters and cardiac cycle imaging data, could classify a phenotypically heterogeneous HF cohort into 4 distinct phenotypes, thus potentially optimizing the response rate to CRT.⁵⁵ Implantable cardioverter defibrillators (ICDs) reduce the risk of sudden cardiac death in patients with HF. One study showed that unsupervised ML-based phenomapping could identify distinct phenotype subgroups in patients with clinically heterogeneous HF receiving secondary prophylactic ICD therapy, thus aiding the implementation of personalized medicine for these patients.⁵⁶ Shakibfar et al.⁵⁷ revealed that ML using daily summaries of ICD measurements in the absence of clinical information could predict the short-term risk of electrical storms. In addition, a DL model can assist in selecting patients with HF that are eligible for subcutaneous ICD.^{58,59}

Multiple data sources, remote monitoring, and wearable devices

AI serves as an essential tool to help physicians improve their clinical judgment and achieve precise diagnoses of diseases such as HF.⁶⁰ To detect and diagnose HF, multiple data sources (e.g., ECG, EHRs, and imaging data [echocardiography and cardiac magnetic resonance imaging]) are integrated, and further AI algorithms are developed to improve the diagnostic accuracy. Ongoing research is focused on areas such as ECG analysis, natural language processing for EHR data mining, and echocardiography image analysis. Cho et al.⁶¹ showed that HF with a reduced ejection fraction could be screened not only with a 12-lead ECG, but also with a single-lead ECG performed by a wearable device using an AI algorithm. By incorporating such algorithms, AI can be of great assistance in analyzing raw imaging data from cardiac imaging techniques.⁶⁰

With the increasing amount of data from remote monitoring and wearable devices, the role of AI is expanding.⁶² Kwon et al.⁶³ showed that an AI-enabled smartwatch with a 2-lead ECG detected HF with reduced ejection fraction with acceptable performance.

The LINK-HF (Multisensor Non-invasive Remote Monitoring for Prediction of Heart Failure Exacerbation) study evaluated the performance of a personalized analysis platform using continuous data streams to predict rehospitalization after HF admission.⁶⁴ This study showed that physiological telemetry from a wearable sensor could provide accurate early detection of impending rehospitalization. In the future, the use of wearable devices or remote monitoring is expected to enable the earlier detection of HF.

LIMITATIONS OF AI IN HF

However, there are several limitations in the widespread use of AI in cardiovascular medicine. Dichotomy and improper calibration are recognized issues in ML techniques based on AI.²³ The performance of ML models can be compromised by inaccurate or missing training data.⁶⁵ This is especially true when ML algorithms rely on continuous data inputs, such as EHRs. For accurate predictions, data must be cleansed and validated by detecting out-of-range values and skewness.⁶⁵ Missing data can be filled in using ML algorithms and techniques while maintaining the algorithm performance.⁶⁶

In addition, an obvious situation in visual-based diagnosis and predictive tasks (e.g., segmentation of the left ventricle endocardium, epicardium, and left atrium regions in echocardiography for providing fine-grained cardiac information) is the limited availability of well-annotated imaging data owing to expensive labor costs and time consumption. Furthermore, ML and DL algorithms are vulnerable to domain shift issues, wherein diagnostic or predictive outcomes may be adversely affected by inherent differences in distribution between the trained and applied datasets (e.g., those collected and combined from various hospitals with different configurations of data-capturing machines). Thus, external validation is crucial in medical AI.

Another drawback is the opaque reasoning and lack of explainability that underlie an ML model's output of a specific prediction, especially when using DL algorithms because many physicians are skeptical of recommendations generated by a "black box" algorithm. False prediction due to wrong data based training rises a critical problem in the medical field. In an image-based prediction, a slight manipulation of an image or noise leads to a different conclusion,⁶⁷⁻⁶⁹ and in text-based prediction, hallucination problem arises that the DL algorithm believes the prediction is correct, which is misled by wrong input data.^{70,71} In addition, the failure to evaluate the clinical impact of ML algorithms in prospective studies, which makes the benefits of ML approaches hypothetical, is one of the biggest obstacles to their

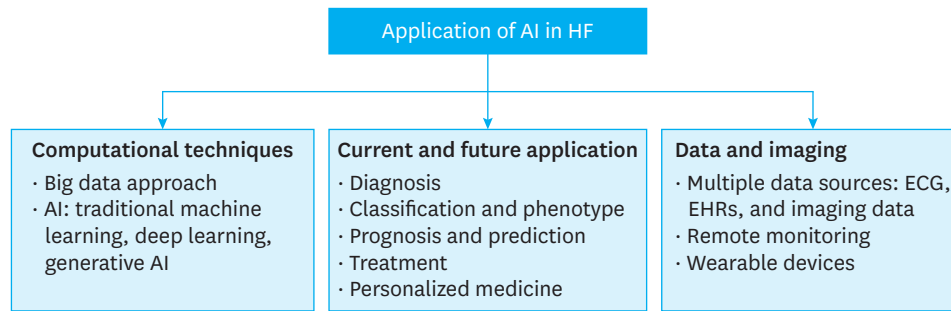


Figure 5. Application of AI in HF.





AI = artificial intelligence; HF = heart failure; ECG = electrocardiography; EHR = electronic health record.

adoption.⁹⁾ There is an increasing need for prospective AI validation studies to address these limitations. Lastly, there have been recent issues with the use of patient data, particularly protected health information.

CONCLUSION

Nowadays, big data approaches, AI, ML, and DL are widely used in the field of HF. AI algorithms can help in the diagnosis and classification of HF and predict the prognosis and therapeutic response. Various data, including ECG, echocardiography, and EHRs, are used in AI. In addition, the integration of data from remote monitoring and wearable devices has expanded the potential applications of AI in HF. The incorporation of AI tools is expected to revolutionize HF management and significantly impact patient outcomes, thereby enabling more precise and personalized care of patients with HF (Figure 5).

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Conflict of Interest

Jin Joo Park, serves as an associate editor of the *International Journal of Heart Failure*, but has no role in the decision to publish this article. Except for that, no potential conflict of interest relevant to this article was reported.

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Conceptualization: Yoon M, Park JJ, Hur T, Hua CH, Hussain M, Lee S, Choi DJ; Data curation: Yoon M, Park JJ, Hur T, Hua CH, Hussain M, Lee S, Choi DJ; Funding acquisition: Choi DJ; Investigation: Yoon M, Park JJ, Hur T, Hua CH, Hussain M, Lee S, Choi DJ; Methodology: Yoon M, Park JJ, Hur T, Hua CH, Hussain M, Lee S, Choi DJ; Project administration: Yoon M, Park JJ, Lee S, Choi DJ; Supervision: Lee S, Choi DJ; Visualization: Yoon M, Park JJ, Hur T, Hua CH, Hussain M, Choi DJ; Writing - original draft: Yoon M; Writing - review & editing: Yoon M, Park JJ, Hur T, Hua CH, Hussain M, Lee S, Choi DJ.

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