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Emergence of Artificial Intelligence in Cardiology - The Future

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Abstract

Artificial intelligence (AI) is a nontechnical, popular term that refers to machine learning (ML) of various types, but most commonly deep neural networks. The field of cardiology is at the forefront of AI in medicine. Using search terms related to AI and cardiology, we searched PubMed and MEDLINE databases without date restriction. Relevance was considered when selecting articles. In this article, we highlight the major advances in cardiology in recent years and demonstrate how AI is poised to take center stage in the future. To identify the most relevant problems to solve with AI, computer scientists, clinical investigators, clinicians, and other users must collaborate closely. When generating and implementing AI, best practices include selecting ideal data sources, taking into account common challenges during interpretation, validation, and generalizability, and addressing safety and ethical concerns before final implementation. As investigators and clinicians continue to collaborate, AI in cardiology and in medicine in general will have a bright future.

Keywords: Acute coronary syndrome, Artificial intelligence, Coronary artery disease, Clinical decision support, Cardiac resynchronization therapy, Deep learning, Electrocardiogram

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Introduction

We live in a world where AI is pervasive. Besides auto-completing sentences as we type, it also populates Google searches before we finish our thoughts, enables cars to drive themselves, enables us to speak to our phones, and supports language translation. It has been used in medicine to identify pathologic specimens, identify mammogram lesions, and identify retinal pathology with a level of skill exceeding that of trained ophthalmologists [1, 2].

Despite being vilified as a tool that will result in mass unemployment and economic disruption, it has also been lauded as a potential savior that will liberate humanity from tedious tasks and enable people to engage, interact, and exist on a higher level, while at the same time vilified as a tool that will lead to massive unemployment and economic disruption [3].

ML of various types, but most often deep neural networks, is called AI [4]. Although there are many types of neural networks, broadly speaking, deep neural networks permit sophisticated recognition of subtle patterns in a nonlinear manner using models that contain many layers of data abstraction and synthesis, which leads to an uncanny ability to "read" mammograms and electrocardiograms (ECGs) or recognize faces. The term "artificial intelligence" refers to ML of various types, such as deep neural networks [5, 6]. By using models containing many layers of abstraction and synthesis of data, deep neural networks can recognize subtle patterns in a nonlinear manner. In this way, mammograms, ECGs, and faces can be read uncannily. In spite of the fact that deep neural networks provide deep intelligence, they are currently limited in their ability to provide spontaneous adaptability or general intelligence, as they provide only a narrow type of intelligence with very focused skills [7-10]. This narrative review used search terms related to AI and medicine and cardiology subspecialties to search PubMed and MEDLINE databases without date restrictions. Relevance was considered when selecting articles for inclusion.

Mounting evidence reveals that ML will power the new tools that drive cardiovascular medicine in the near future. The article highlights the rapidly emerging role of ML in cardiovascular medicine [8]. The use of AI has included interpreting echocardiograms, automatically identifying heart rhythms from ECGs, uniquely identifying individuals from ECGs as biometric signals, and detecting left ventricular dysfunction from the surface ECG as a sign of heart disease. Cardiovascular specialists are unlikely to be replaced by AI, however [9-11]. It may instead serve as a tool for skilled practitioners to expand their clinical capabilities, make more accurate and timely diagnoses, and improve care delivery [12].

AI is unlikely to replace cardiovascular specialists, however. AI has the potential to expand the clinical abilities of skilled practitioners, to increase the accuracy and speed of diagnoses, and to improve care delivery as a whole [13].

It is essential that we understand AI's strengths, limitations, opportunities, and risks, just as we do with any statistical method or tool. We explore the nature of ML, how it is developed, the types of problems it poses, and its limitations, as well as some of its current and promising applications in cardiovascular medicine. Meanwhile, we will emphasize potential risks, such as a potential bias when AI is applied to populations outside those represented in a training set, data security threats, and data ownership concerns. We must embrace the powerful emerging tools enabled by AI to ensure that they are properly applied for the benefit of humanity as we care for patients and practice cardiovascular medicine. In this review, we aim to provide a foundation for understanding benefits.

Principles for Responsible Use of AI in Health Care

We should ask ourselves first and foremost what human purpose AI serves, as with any technological innovation. AI shouldn't be advanced just for the sake of advancing AI - it should be developed to improve people's lives and well-being [14].

In order to help alleviate overstretched healthcare systems, AI is clearly needed to help meet the growing global demand for healthcare. Several articles have already explored how AI can assist healthcare providers in diagnosis and treatment - improving health outcomes at lower cost, while improving staff and patient satisfaction (known as the Quadruple Aim) (Figure 1).

General AI Principles for Clinicians

ML

Human experts develop algorithms by deriving rules based on their experience based on prior data. To create the relationship between inputs and outputs, programmers will implement these hard-coded rules [15]. As a result, an expert system relies on static knowledge of the entire process and works only within the parameters programmed into the computer. On the other hand, in supervised learning, we use a general algorithm, such as a neural network, to approximate a complex mathematical relationship between input data and expected outputs [16]. The input and output of some models, such as convolutional neural networks, can be optimized without specific knowledge of their content or structure. The algorithm finds insights in the data using its inner structure and statistics when we use unsupervised learning as clustering [17]. An AI model can discover new relationships in data that have eluded humans because the rules are created without human intervention. As part of the training algorithm, these discoveries are quantified as coefficients or weights of the function being approximated.

There are many AI architectures and algorithms that we can use for a specific task—some are better suited to images or data with spatial correlation, some are better suited to structured data or language processing, and some are better suited to deciding which action to take in several stages [18]. As soon as we select the preferred algorithm, we must train it by showing it examples of inputs with or without the expected outputs and adjusting the weights and parameters of the model until we find the minimum error [19]. Gradient descent methods are used for optimizing, and the loss function that represents the error we want to minimize is optimized for. A linear regression model, one of the simplest ML models, optimizes the "mean squared error," which penalizes the difference between the expected value and the observed value. We use "cross-entropy" in "logistic regression," where we have to classify a sample into one of two or more categories by assuming a binomial distribution for the data [20]. Weights are usually created randomly and adjusted after each batch of training samples is evaluated using the loss function.

Figure 1: 5 principles for responsible use of AI in health care.

The weights and how well the model performs the task will be influenced by a variety of factors during the training stage. An iterative process is inherent to machine learning-start with a guess, evaluate the data based on that guess, and then refine the guess [21]. To ensure computational resources can process the data, large data sets are often randomly partitioned into smaller units called batches. As part of training, we adjust the weights after each step (learning rate), as well as how many epochs the model was shown the entire training size (number of epochs), which are called hyperparameters. The key to the success of the training stage is optimizing these hyperparameters [22] (Table 1).

In training and testing an ML model, the data set used for training and testing is more important than selecting the right algorithm and hyperparameters. A model will perform poorly in real life if it is not based on a clean and versatile data set since all the rules are created based on the data. For an algorithm to be useful, a set of rules must be created that can generalize well and perform poorly on any other data set in exchange for performing well on the given data set [23, 24].

The bias-variance trade-off is known within the ML and statistical communities. This term refers to the model's ability to fit the observed data well. When presented with new, subtle data, the variance shows how well the model performs [25, 26]. When low bias and high variance are combined, it is called overfitting, and while it can also happen with traditional algorithms, the risk is much higher when the rules are derived automatically by an algorithm designed to recognize patterns [27]. A bias-variance trade-off curve with an optimal balance should be monitored carefully to avoid overfitting. It is also essential to hide some of the data during the training stage and use it to test the algorithm after it has been trained.

Natural language processing (NLP)

In electronic health records (EHRs), clinical narratives make up more than 80% of the data. Health care professionals are required to review and abstract this free-text information manually in busy clinical practices [28]. To enable automatic identification and extraction of information, these narratives must be converted into a computer-managed representation because they are unstructured, free-text documents [29]. By converting unstructured text into a structured form, NLP has enabled automated information extraction from narrative texts.

Clinical notes, radiology reports, and pathology reports have all been analyzed using NLP [30-32]. Using NLP, for instance, lung cancer staging has been extracted from pathology reports, breast cancer diagnosis from mammography reports, brain tumor status from magnetic resonance imaging reports, and peripheral artery disease and critical limb ischemia diagnoses from clinical notes.

Table 1: Types of ML.

Type of ML	Examples
Supervised learning	Logistic regression and random forests
Unsupervised learning	Hierarchical clustering, tensor factorization
Reinforcement learning	Robotics and control systems
Deep learning	Image recognition (echocardiography, chest x-ray, and computed tomography)

Current and Future Applications of AI in Specific Areas

Echocardiography

In order to evaluate cardiac structure and function in a timely and cost-effective manner, echocardiography remains the predominant imaging modality. The accessibility, quality, and diagnostic utility of echocardiography vary considerably despite its increasing availability for diagnostic and point-of-care applications. A high level of operator experience is needed for the acquisition and interpretation of echocardiograms, which makes it an area that can be enhanced and standardized with AI [33]. A selection of recent echocardiography AI research indicates that the interest in this topic has increased considerably as convolutional neural networks have matured for image classification in ML. Echocardiography AI platforms can be developed to take advantage of the enormous amount of clinical echocardiography data. By automating quantification, identifying pathologic features (valve disease, regional wall motion abnormalities, cardiomyopathies), and applying outcome data to the point of care, innovations in this area may improve interpretation, standardization, and workflow. Detecting subtle or unrecognized imaging features that can indicate subclinical diseases or patient outcomes is the strength and prospect of echocardiography AI research [34, 35].

Despite the continuing improvement of AI models, it is imperative to acknowledge that AI must overcome several important challenges before it can be safely applied in clinical practice. It is essential to consider the clinical characteristics and quality of development data when developing a model. In order to develop a robust echocardiography AI platform, it will be necessary to train and validate it using a large number of studies that include a wide range of clinical characteristics, pathologic characteristics, ultrasound machine vendors, and image quality. Currently, most echocardiography AI studies are limited by institutional, geographic, or even echocardiography machine brand boundaries, resulting in limited sample sizes that risk overfitting and limit generalizability [36]. Despite the inherent variability in interpretation and measurement, echocardiography AI research has largely relied on human interpretation as the ground truth.

Echocardiography is poised to be revolutionized by AI. With AI-based models of echocardiography, patient outcomes can be improved, point-of-care decisions can be made more accurately, and diagnostic tools will be made more widely available. Echocardiography AI is expected to impact patient care, and we look forward to clinical studies that document improved clinical outcomes and cost effectiveness [37-39].

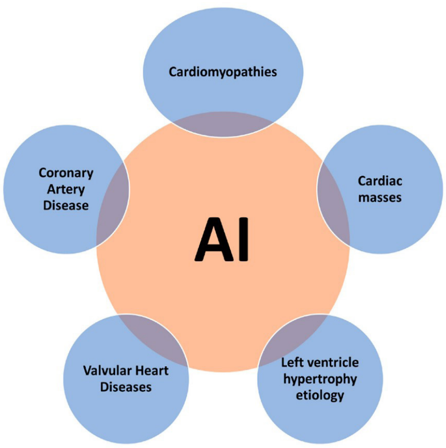

Figure 2: Clinical applications of AI in echocardiography [22].

Nuclear cardiology

A number of routines in nuclear cardiology have already incorporated AI techniques. As a result of artificial intelligence algorithms, single-photon emission computed tomography (SPECT) and myocardial perfusion imaging (MPI) can be performed completely automatically, including motion correction, reconstruction, oblique reorientation on tomography, quantification, and high-level analysis [40, 41].

Computer-aided adjunctive diagnostic tools have been developed to aid expert readers in identifying hypoperfused myocardium using commercialized and Food and Drug Administration (FDA) approved image viewing software programs that compare myocardial perfusion distributions to databases of normal myocardial perfusion distributions [42]. Through automation and the availability of digital image data for ML, AI algorithms have been applied to SPECT MPI data, alone or in combination with clinical characteristics, to improve the prediction of angiographic coronary artery disease (CAD), prognosis, and/or revascularization, and to facilitate structured reporting and provide clinical decision support (CDS) in recent studies.

Enhanced diagnosis

An ML algorithm that incorporates only imaging variables (perfusion deficits, ischemic changes, and ejection fraction [EF] changes between stress and rest SPECT MPI by quantitative software) outperformed individual quantitative imaging parameters in overall diagnostic accuracy (86% vs 81%; $p < 0.01$) per patient [3, 43].

Comparing the ML algorithm to both visual readers, the area under the curve (AUC) for detecting obstructive CAD was also significantly higher for the ML algorithm [44]. In another study, the same group incorporated both clinical and imaging variables (total perfusion deficit (TPD) calculated by an automated program) into an AI algorithm.

The investigators documented higher accuracy with ML (87.3% ± 2.1%) than with 1 of 2 expert readers (82.1% ± 2.2%) or automated TPD (82.8% ± 2.2%; $p < 0.01$) and higher AUC (0.94 ± 0.01) than TPD (0.88 ± 0.01) or 2 visual readers (0.89 ± 0.01 and 0.85 ± 0.01; $p < 0.0001$) for the detection of obstructive CAD. Using a solid-state SPECT scanner and 1638 patients without known CAD, deep learning was found to have higher AUC both per-patient (0.80 vs 0.78; $p < 0.01$) and per-vessel (0.76 vs 0.73; $p < 0.01$) basis.

With the DL threshold set to the same specificity as TPD, per-patient sensitivity improved from 79.8% (TPD) to 82.3% (DL) ($p < 0.05$), and per-vessel sensitivity improved from 64.4% (TPD) to 69.8%

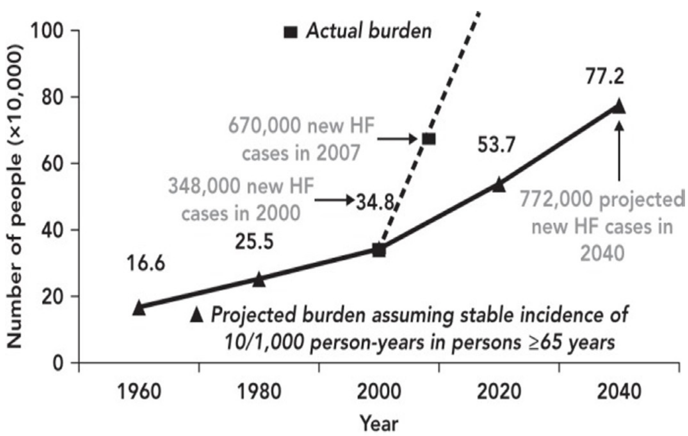

Figure 3: The annual incidence of heart failure reported in US [76].

(DL) ($p < 0.01$). For SPECT MPI, AI algorithms improved the prediction of obstructive CAD by approximately 2.5% and approximately 5% over current clinical methods, respectively. A number of other studies have also shown that trained neural networks can successfully identify coronary arteries with stenotic lesions compared with expert physician visual analysis [45].

Prediction of treatment and prognosis

In 713 SPECT MPI studies with corresponding invasive angiography within 90 days after the initial MPI scan, AI was also tested for its ability to predict early revascularization in patients with suspected CAD. In order to predict revascularization events, an ML algorithm integrated several automatically derived imaging variables as well as clinical parameters such as sex, diabetes mellitus and hypertension history, ST-segment depression on baseline ECG, ECG and clinical response during stress, and post-ECG probability (33 variables in total) [46]. The AUC for revascularization prediction by ML (0.81 ± 0.02) was similar to that of one reader (0.81 ± 0.02) and superior to another reader (0.72 ± 0.02; $p < 0.01$). Thus, ML was found to be comparable to or better than the experienced reader in the prediction of early revascularization after MPI in this study. Developed an AI algorithm to predict major cardiac events (MACEs) based on 28 clinical, 17 stress test, and 25 imaging variables (including TPD) [47-49]. The authors compared AUCs for outcome prediction between ML combined with all available data (ML-combined), ML combined with only imaging data (ML-imaging), and ML combined with all available data (ML-imaging), as well as visual diagnosis (physician diagnosis) and quantitative imaging analysis (stress TPD and ischemic TPD). They found that MACE prediction was significantly higher for ML-combined than ML-imaging (AUC, 0.81 vs 0.78; $p < 0.01$) [50]. The ML-combined model also had higher predictive accuracy compared with physician diagnosis, automated stress TPD, and automated ischemic TPD (AUC, 0.81 vs 0.65, 0.73, and 0.71, respectively; $p < 0.01$ for all). As a result of ML-combined diagnosis compared with visual physician diagnosis, 26% of risks were reclassified ($p < 0.001$). Using AI, the authors proposed that MACE risk computations could be personalized in patients who underwent SPECT MPI based on their study results [51].

AI-driven structured reporting and CDS

AI-driven algorithms have also been incorporated into the first and only FDA-approved nuclear imaging software to use a CDS tool and natural language for automated report generation [52]. Over 230 rules of perfusion, reversibility, function, and patient demographic characteristics are integrated into the system, along with additional information (if available) on prone versus supine images, attenuation-corrected images versus nonattenuation-corrected images, as well as quality control information [53]. Using a subset of 1000 patients, a study validating this AI-driven system for CAD detection found no significant differences between the AI-driven structured report and 9 experts' impressions [54].

Despite the widespread use of quantitative tools in nuclear cardiology, higher-level tools combining multiple features and clinical data are still rare. Recent research studies describe applications in clinical practice with high potential. Additionally, upcoming AI focus in nuclear cardiology should include refining and building upon studies that enhance diagnosis and prognosis, as well as developing AI-driven algorithms to assist clinicians in determining the appropriateness of tests, test selection, scheduling, workflow prioritization, protocoling, reporting, and managing patients [55]. Physicians and other health care professionals will not be replaced by these developments. Rather, they will be provided with highly accurate tools to detect disease, stratify risk, and optimize patient care.

Electrophysiology

Among the opportunities for integrating AI into electrophysiology are data management (i.e., how to manage large amounts of patient data), data interpretation (democratizing access to expert-level interpretation of often complex data), and real-time data integration across multiple methods [56]. Additionally, evolving findings suggest that the ability to screen for disorders not typically associated with the ECG may provide scalable opportunities to improve population health by using AI-enhanced, cost-effectively acquired electrophysiologic data (e.g., ECGs).

The integration of ambulatory-obtained ECGs into clinical practice is one of the major current debates in electrophysiology. In many cases, cost-effective screening tools can be used to screen a population before they have become established as patients with a known cardiovascular disorder, such as implantable loop recorders and smartphone- or smartwatch-enabled ECG devices. An individual may purchase an ECG device over the internet, record their own ECGs, and then need to interpret the results accurately [57-59]. The accuracy and automatic interpretation of these ECGs has improved in recent years, but there is still a substantial risk of false-positives and false-negatives.

As ECGs become more affordable at a population level, human-based review may not be scalable as health care settings become more adept at reading them. Research is underway to assess the effectiveness of AI techniques for interpreting these strips, as well as referring patients to physicians, such as electrophysiologists or cardiologists [60]. Computational needs and effectiveness cannot be evaluated at the population level at the present time.

The interpretation of electrophysiologic data is another current issue in electrophysiology. QT interval measurement, for example, is highly variable and has poor accuracy even among cardiologists and some electrophysiologists, which is important for identifying those at risk for sudden death or antiarrhythmic drug toxicity [61]. DL AI techniques may help recognize risk imposed by specific QT intervals based on the ECG alone, according to initial findings.

Additionally, by using expert-level QT interpretation to train neural networks, non-QT experts, non-electrophysiologists, and non-cardiologists may be able to improve interpretation accuracy. In addition to intracardiac mapping of arrhythmias, these principles also apply to other electrophysiologic data [3, 62, 63]. A major opportunity in electrophysiology today is how to properly interpret and optimize therapy for a given patient by integrating often multiple complementary but separately obtained data streams. When patients with arrhythmias undergo invasive evaluation for cardiac ablation, preoperative imaging (e.g., magnetic resonance imaging to evaluate scar distribution, electrocardiogram to determine the source of the arrhythmia) and intraoperative imaging (e.g., intracardiac echocardiography, fluoroscopy, and electroanatomic mapping) are used to optimize treatment. Due to the fact that these data were obtained at different points in time using different techniques, it is difficult to integrate them [64, 65]. Data suggests that AI techniques might facilitate data integration across modalities, which could, in turn, help the physician identify and target relevant sites responsible for the patient's condition more efficiently or effectively.

Additionally, AI applied to electrophysiological data has the ability not only to democratize, scale, and facilitate accurate interpretation and synthesis of data, but also to improve population health through nonhuman-interpretable insights. The reason for this principle lies in the fact that ECGs often contain subtleties that are not readily interpreted by humans. ECG alone can, for example, be used to identify conditions such as low EF with a high degree of accuracy, as we recently described. A scalable, low-cost method of improving risk stratification at a population level may be possible based on the ECG for several other conditions. Therefore, recognizing underdiagnosed, potentially treatable conditions from an ECG in a cost-effective manner could improve population health.

CAD detection and prognosis

According to ECG and biomarkers, acute coronary syndrome (ACS) is classified as ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina (UA). It is imperative to diagnose STEMI as soon as possible to facilitate timely management, and an ECG evaluation is required to facilitate this. Using a smartphone platform with a single-lead diagnosis is now documented to be feasible. As a result of this technology being widely disseminated and paired with ML interpretation, STEMI patients may be rapidly triaged. Having an institution that offers percutaneous coronary intervention could facilitate an expedited transfer in a timely manner, potentially improving outcomes [3, 66]. Out-of-hospital cardiac arrests, most of which are caused by ACS, are also being explored. Using smart home speakers and phones, machine learning algorithms have been used to analyze home recordings to identify agonal breathing, a typical sign of cardiac arrest.

In the vast majority of arrests that occur unwitnessed at home, accurate detection of such recordings could enable the activation of emergency response. It can be more challenging to manage ACS outside STEMI (for example, NSTEMI and UA). ML has been used to interpret 12-lead ECGs in this area in a preliminary manner. According to recent studies, ML improves upon existing validated risk scores such as TIMI's (Thrombolysis in Myocardial Infarction) or GRACE's (Global Registry of Acute Coronary Events) in the management of UA/NSTEMI. In the same way, a longer-term prognosis about mortality or treatment complications can be improved. By refining the method for identifying high- and low-risk patients, resources will be better utilized, and care will be more individualized. Multimodality noncardiac data are being synthesized to further refine ACS diagnosis, treatment, and prognosis. The use of AI will likely improve the care of patients with stable CAD as well, for example, identifying those who will benefit from revascularization or balancing the antithrombotic benefit with the risk of bleeding. In the work described, AI has the potential to prevent and treat CAD in a wide range of ways. Randomized controlled trials remain crucial for clinical validation in many cases. Even in this early stage of ML's influence on CAD, it is promising that it can provide better prognosis and uncover new risk factors which will further improve the care of patients [67].

Coronary angiography and interventional cardiology

Cardiovascular innovation has traditionally been led by interventional cardiology. The past decade has seen an increase in the use of minimally invasive (as well as invasive) cardiovascular surgical procedures, invasive intravascular imaging, exercise hemodynamics, and robotics. AI is expected to make rapid progress in predicting diagnostic outcomes, designing therapeutic strategies, selecting devices, optimizing procedures, and avoiding complications [68]. Research into the use of AI for coronary artery assessment has begun with the recent CEREBRIA-1 study, which demonstrated that ML and AI are comparable when determining the physiologic importance of coronary lesions and the recommendation for revascularization.

Even though a good emergency response system is currently available across the country, diagnostic and management decisions are subject to considerable variation during critical early-stage interactions. A series of predictive questions could be used by intelligent algorithms in the future to establish a diagnosis before transportation services arrive based on the patient's medical history and risk factors. The humble ECG is likely to be replaced by technology that will provide definitive diagnostic information within 5 to 10 minutes of arriving in the emergency department with devices that can scan the skin and place an intravenous line without human intervention and high-resolution computed tomography scanners that provide both anatomical and physiologic assessment of coronary arteries [69]. Invasive coronary angiography may soon be obsolete due to the above steps, which may not even require human intervention. As of now, artificial intelligence-based diagnostics have been used to analyze coronary artery lesions with mixed results. Angiographic analysis accuracy may approach that of fractional flow reserve at 82%.

Inefficient interfaces and high start-up costs have limited magnetic navigation systems and robotics for coronary intervention over the past decade. Through the use of multimodal technologies that blend real-time thermal, ultrasound, and flow data with robotics and previously acquired diagnostic computed tomographic images, AI-guided vascular access and interventional device navigation to the lesion site will be possible. AI-directed coronary revascularization is also possible, and the interventional cardiology team can monitor and control the equipment without exposing themselves to radiation [70]. The development of nanoparticles that can self-navigate to atherosclerotic tissues and deliver targeted therapies is already underway, and ligand-linked aggregation and magnetic guidance further concentrate the beneficial effects while minimizing adverse effects on other organs.

AI could also be applied to valvular disease, congenital anomalies, and life support technologies. The future of coronary angiography and interventional cardiology may be determined by the ability to assess anatomic structures in real time, and to integrate this information with 3-dimensional bioplotters that can generate custom devices incorporating autologous living cells as well as polymer and rigid metallic composites on demand in cardiac catheterization laboratories.

Heart failure (HF)

Current HF care models are insufficient because delays in diagnosis are common, rates of HF risk factor recognition, treatment, and control are relatively low, and most patients with HF and reduced EF (HFrEF) are not receiving therapies or doses of therapies proven to reduce mortality and morbidity [71]. Further, the pathophysiologic characterization of HF phenotypes remains rudimentary. These gaps can be addressed by AI-enabled strategies.

HF prevention

HF preventive interventions have been shown to reduce HF incidence dramatically in clinical trials. The prevention of HF requires a method to identify patients at risk for HF as well as the prevention of HF itself. It is possible to target more intensive and expensive interventions to a subset of patients at highest risk, thereby enhancing feasibility and reducing overall costs. Overall benefit will be determined by the efficacy of the intervention component [72].

There are a number of accurate HF risk scores available, but they are not used clinically. A supervised machine learning algorithm was developed by Ng et al. [24] using EHR data to predict incident HF. As a result of the ML algorithms, AUC for predicting future HF was approximately equal to 0.79, however predicting imminent HF (this is happening within six months) was much more accurate, limiting the possibility of modifying risks in advance [73]. ML algorithms embedded in the EHR may not have better predictions than traditional models, but they could provide physicians (and patients) with instant risk information. As HF risk features change, AI-enabled ECG or image analysis, wearable devices, and other data can be incorporated into the prediction algorithm to provide more accurate prediction in regions with unique HF risk factors and adjust over time.

HF risk assessment tools developed in the future should be accompanied by interventions aimed at reducing HF incidence a priori. To encourage clinicians to treat HF risk factors, clinicians could use a novel care model, a specific therapeutic agent, or smart decision support tools. For effective strategies to reduce HF incidence, clinical trials need to evaluate risk prediction and intervention strategies [74].

HF hospitalization prevention

A method for identifying patients at risk as well as a hospitalization prevention intervention are also necessary in order to prevent HF hospitalizations. It is unfortunate that AI-based models have been limited in their performance for readmission prediction, as well as traditional statistical models. Three studies have used supervised ML, including DL algorithms in large cohorts, to predict readmissions after HF hospitalization. AUCs ranged from 0.63 to 0.71. Consequently, different algorithms need to be improved to improve their predictions of HF readmissions. It is more difficult to prevent readmissions once increased risk has been recognized with ML, even though it may enhance risk prediction [3, 75]. Hospitals have adopted multiple strategies to reduce readmissions, but the impact has been minimal. It has proven ineffective to prevent admissions or readmissions by using remote monitoring using external telemonitoring systems or implanted devices (defibrillators or pacemakers), and the only effective remote monitoring strategy for HF hospitalizations is based on pulmonary artery pressure.

A significant increase in short- and long-term mortality after HF hospitalization has been linked to efforts to reduce readmissions. A clinical trial evaluating AI-enabled hospitalization risk prediction and novel AI-enabled intervention strategies is needed to ensure efficacy and safety.

HF population management

As a result of AI analytics, highly actionable information may be provided in real time to patients with HF, identifying those who are undiagnosed, eligible for medical therapy but not receiving optimal doses, non-adherent to their treatment plan, or most likely to benefit from certain specific HF therapies. The patient and physician could receive AI-generated information in novel and potentially AI-generated formats that may influence behavior and uptake of therapy (decision aids for patients, education tailored to specific issues, support group contacts, or other regional or health care system-specific resources) [76]. A similar approach is used in highly successful commercial applications of AI analytics, a level of success that hasn't been reached with the use of AI in health care.

Standard EHR CDS tools can identify a patient with a basic indication for a specific HF therapy; for example, patients with low EF and a prolonged QRS duration would be eligible for cardiac resynchronization therapy (CRT). However, AI techniques could vastly improve the value of CDS by determining whether the patient meets all other indications for CRT [77]. Further, given that a third of patients do not respond to CRT, AI techniques could identify patients with a higher likelihood of response to CRT, as 2 recent studies of AI analytics in CRT-eligible patients suggest. Ultimately, clinical trials documenting that AI-enabled HF population management strategies favorably impact therapy utilization and outcomes would be needed to justify the considerable resources needed to implement them, promote uptake by patients and physicians, and exclude adverse unintended consequences.

Role of AI in elucidating HF pathophysiology, precision medicine, and novel therapeutics

As of now, HF is typically defined by its EF and presumed etiology. Cluster analysis, for example, may identify unique HF phenotypes that can then be characterized using traditional statistical methods or supervised learning techniques to determine whether phenotypes have different prognoses or tolerances for or responses to therapy [78]. The HF with preserved EF (HFpEF) and HFrEF phenotypes have been identified using clinical data as input variables in patients with HFpEF and HFrEF. Phenotyping patients with HF and identifying precision or novel therapies for HF will likely require data beyond clinical features. It may be possible to identify unique pathophysiologic phenotypes with novel therapeutic targets, diagnostic/prognostic biomarkers for clinical trials by combining genomic and circulating proteomic data with new clinical data such as microbiome and AI-enabled ECG or image analysis.

Preventive cardiology

A number of concepts related to CAD are considered foundational to modern medicine, including the identification and addition of associated conditions called risk factors to overall models of risk stratification. As AI becomes more capable of analyzing variables, identifying nonlinear associations, and identifying novel risk factors, it will build on this foundational work.

It is a valuable yet imprecise tool that is commonly used today when assessing risk for CAD and other atherosclerotic diseases. Due to the identification of nonlinear relationships, an ML algorithm improved risk stratification dramatically for the same 9 traditional risk factors, detecting 13% more high-risk individuals and prescribing 25% less statin therapy for low-risk individuals [79]. Another study, however, emphasized the importance of including nontraditional risk factors in a pooled cohort risk calculator by using 735 variables per individual. The prognostic performance of the algorithm using hundreds of variables was no better than that using only standard CAD risk factors, contrary to what would be expected after including a wealth of data in the algorithms.

By incorporating nontraditional and unknown risk factors, ML is an innovative and robust tool for cardiovascular risk stratification. Using biosignals such as retinal fundus images obtained from the UK Biobank, cardiovascular risk factors were predicted without considering other clinical characteristics [80]. An ML algorithm has also been used to analyze voice recordings taken with a smartphone to identify features that may be related to CAD.

Digital biomarkers of information may become available in a variety of forms, such as these examples. A number of accepted paradigms may need to be changed in the approach to predicting atherosclerotic cardiovascular events, such as assessing outcomes with a time horizon lower than 10 years, using serial data collected over time, and evaluating unsupervised learning methods instead of selecting variables based on biologic plausibility.

CDS

With the proliferation of diagnostic and therapeutic options and ever-increasing medical knowledge, CDS at the point of care is an urgent necessity to ensure adherence to guideline recommendations, standardize care, and improve decision making and outcomes in an era of ever-increasing medical knowledge and complexity.

CDS systems are increasingly integrating with EHRs to provide up-to-date medical knowledge and evidence-based guidance to physicians at the point of care as part of the meaningful use requirements of the Health Information Technology for Economic and Clinical Health Act. Up until recently, most CDS systems used in health care could only access structured data within EHRs, such as laboratory results. It is possible to extract information from unstructured clinical narratives using natural language processing. It was previously not possible to generate automated input to CDS systems built into EHRs using NLP tools [3, 81].

In addition to searching digital EHRs with NLP, electronic tools can also provide automated inputs to CDS programs that deliver patient-specific individualized information to enable patient-centered decisions at the point of care. Data elements extracted from EHRs (e.g., laboratory test results) may be combined with patient information acquired by NLP.

Promising AI developments outside cardiology

An ophthalmology study found excellent accuracy (AUC of 0.989), sensitivity (97%) and specificity (91%) using convolutional neural networks trained on more than 100,000 retinal fundus images. Research from Google Health and academic institutions in radiology showed that DL models based on chest radiographs previously interpreted by radiologists performed similarly for pneumothorax (AUC, 0.95), nodule or mass (AUC, 0.72), airspace opacity (AUC, 0.91), and rib fractures (AUC, 0.86). According to a recent mammography study, conducted jointly by investigators from the United States and the United Kingdom, false-positive rates decreased by 5.7% and 1.2%, respectively, and false-negative rates decreased by 9.4% and 2.7%, respectively.

In an independent study involving 6 radiologists, the AI model outperformed all human readers, and the AI model's AUC outperformed the radiologists' AUC by a margin of 11.5% [82]. Algorithms have also been shown to be able to distinguish between benign and malignant skin lesions using pattern recognition, and to screen for autism by analyzing short videos of children.

Applications of AI to optimize cardiovascular research

In order to fully exploit data-rich platforms, such as whole-genome sequencing, mobile device biometrics, and electronic health records, AI applications, including ML and deep learning, are crucial. Cardiovascular diseases are being diagnosed, predicted, prevented, and treated using ML. As a result of these new methods, large volumes of data can be integrated quickly, diagnosis and treatment can be more personalized, and latent relationships can be detected more easily. However, they pose new methodological challenges. Standardizing phenotypes is necessary to maximize reliability, and integrating heterogeneous data with EHRs is essential. In order for data to be traceable, valid, and reproducible, workflows must be documented. When designing studies and interpreting results, new biases such as the digital divide and differential internet access by geography, population, and socioeconomic status must be taken into account. As a final consideration, missing data and variations in care delivery must be taken into account. The data contained in medical records, unlike primary data collection, relate directly to the patient's health status and care-seeking behavior, in addition to the clinician's care and documentation. The time of observation is determined by the patient and physician, rather than the researchers, so the inferences can vary. In order to establish the validity and reliability of these tools, clinicians, data scientists, and statisticians should work together in team science [83].

Phenotyping and risk prediction

As a result of the cumbersome nature of existing approaches and scoring systems and the fact that they are not reproducible well across populations, case identification and outcome prediction must be improved in order to increase accuracy and effectiveness.

Additionally, ML can be applied to other types of structured or unstructured data in addition to the data-rich environment of the EHR. In addition to ECG and echocardiography data, other imaging studies may also be considered.

A phenotyping application of ML is the characterization and prediction of survival of patients with HFpEF. HFpEF patients were divided into three distinct groups using unsupervised ML. Their next step was to examine the differences in death rates and hospitalizations among groups using supervised learning [84]. In addition to being validated with other cohorts, these promising data illustrate how AI can be incorporated into an HER's rich environment. Using AI for ECG data, 44,959 patients with left ventricular dysfunction despite having no symptoms. Convolutional neural networks were trained to identify patients with ventricular dysfunction based on ECG data alone, defined as an EF of 35% or less. According to an independent study of 52,870 patients, the network model yielded values of 0.93, 86.3%, 85.7%, and 85.7% for AUC, sensitivity, specificity, and accuracy. In this study, AI was applied to ECG data to identify ventricular dysfunction.

Clinical trials

Recruiting trial participants is widely recognized as inefficient and overly costly, which leads to delays in the identification of new treatments and ultimately patient care. By applying AI to the EHR, we can improve the efficiency of prescreening eligibility and matching patient characteristics to trial inclusion and exclusion criteria.

Wearable sensors

Wearable sensors are being extensively researched for their use in disease prevention and management, and AI has a unique position to help in this field. Smartwatch data can be used to detect atrial fibrillation, for example. When compared with a reference standard ECG, a deep neural network trained using heuristic pretraining showed promising performance. Study results showed that smartwatch photoplethysmography coupled with a deep neural network could passively detect atrial fibrillation with some loss of sensitivity and specificity compared with criterion-standard ECGs [3, 85].

Moving Forward: Addressing the Challenges When Implementing AI

There is a risk of bias, limited generalizability, low quality of data, and other limitations in publications, and how to find them. In light of the increasing likelihood of AI's application to medicine, it is important to consider the pitfalls in its implementation. Indeed, there have been many examples in the lay press of promising technologies that fell short of expectations after being tested on a broader scale. Among the examples are facial recognition software that fails to recognize diverse populations, AI that may reflect historical bias and perpetuate inequity in the criminal justice system, and even medical screening tests that are poorly generalizable.

Poor quality and limited diversity of data sets used to train the algorithms can cause such problems, as can disparities in outcomes or bias in human behavior. Garbage in, garbage out, as the old adage goes, applies just as much to AI technologies. When applied to comparatively imprecise data derived from billing codes or extracted from an EHR, a model derived from data from a randomized clinical trial is likely to perform poorly. In the same way, digital imaging approaches that analyze static images cannot distinguish pathophysiologically important features from those that result from image acquisition artifacts. A particular outcome may be spuriously associated with features associated with the type of image acquisition (pixel characteristics) if the type of image acquisition correlates with a disease state. In the case of systematic societal bias, these technologies can even reveal it; for instance, a risk prediction model may incorrectly determine that a particular subgroup of patients is less likely to benefit from a given lifesaving intervention (e.g., heart transplant). Thus, when developing or implementing an AI algorithm, it is important to be aware that poorly executed AI can mislead us and may even reflect, perpetuate, or exacerbate health care disparities, a factor that must be taken into consideration across all health systems of all economic backgrounds [86-88]. A hospital, region, or country with limited financial resources is likely to find it difficult to implement AI. If AI is only available in high-income settings, health care disparities may be exacerbated. Unlike errors relating to competence or judgment of a health care professional, errors in AI algorithms may apply to thousands or millions of people if they become widely implemented.

Interpreting literature and applying technologies in practice requires clinicians to recognize these pitfalls. From inception to application, tracing the development of a given technology may be a useful approach [89]. The training process was based on data input. Is the data of high quality? What methods were used to collect them? Is the data set and population similar to that of the target application? After examining the model's performance, we should consider its accuracy. The area under the curve must be considered in addition to this assessment. The findings seem to be robust, but how robust are they? Was there external validation and subgroup analysis by the investigators? After examining the model's application, we can examine how it is used. What is the similarity between the application and the derivation data sets? Is it possible to periodically test the model's performance against a criterion? Last but not least, we can put the model's results into their proper context [90]. What is the consistency of the findings with our own clinical intuition or other clinical guidance? Our ability to remain vigilant and ensure responsible use of AI in medicine depends on a systematic approach [91].

Challenges Managing and Publishing with AI Data

In the era of big data and open science, AI has flourished. Statistical models can now be produced that rival or surpass human performance by using large volumes of data and sophisticated algorithms. Crowdsourcing expensive research and development efforts for the chance to win substantial amounts of money has stimulated innovation through competitions like the Netflix Prize in 2009. As a result of limitations in data-sharing regarding health-related data, health care has been slower to adopt similar strategies. However, the Centers for Medicare and Medicaid Services launched an AI challenge in 2019 aimed at predicting unplanned hospital and skilled nursing facility admissions [92].

Unlike medical records, which contain a wealth of information, this challenge relies on claims data. A question arises, "What are the barriers to sharing the rich data contained in EHRs around the world?" There are many issues surrounding the sharing of health care-related data around the world, and they are constantly evolving. From a policy perspective, regulations such as the US Health Insurance Portability and Accountability Act and the European Union's general data protection regulation provide some frameworks for the importance of engaging the patient/consumer in the release of the information; many other countries have similar restrictions on data sharing related to health care [93].

There are, however, some academic journals that have adopted data-sharing policies that require open sharing of data that may conflict with such regulations. AI is now using large volumes of data that are much harder, possibly impossible, to identify, unlike traditional research studies [94]. Additionally, there are questions concerning the value and ownership of health care data outside the context of regulatory and ethical considerations. Annotating data sets for AI research may require substantial investments in technical personnel and equipment by health care organizations. Health care data ownership may be further clouded by the intellectual contribution in parallel with data resulting from direct patient contributions. The ownership of medical record information varies from state to state, ranging from the hospital/physician owning the data to the patient owning the information to the topic not being addressed at all from a legal standpoint. Health care institutions may be able to generate revenue streams as value-based payment models become more prevalent. Intellectual property may be lost if the data is shared publicly [95, 96]. Strategic partnerships may be the way forward. It will be up to each individual to decide how, and if, data will be shared. Also, partnering organizations may cease to exist or be acquired by another organization opportunistically. DeepMind's data archives were acquired by Google, which effectively ended a previous commitment not to release the data. The collaboration and availability of data will continue to be key to advancing health care. Data ownership (or data control) and data sharing will be refined through these collaborations.

Conclusion

Aside from regulatory and ethical considerations, there are questions regarding the ownership and value of health care data. Health care organizations may need to invest significantly in technical personnel and equipment to annotate data sets for AI research. Intellectual contributions to health care data may further cloud ownership of data resulting from direct patient contributions. States vary on who owns medical record information, ranging from hospitals/physicians to patients to not addressing it at all from a legal standpoint. With the advent of value-based payment models, health care institutions may be able to generate revenue streams. Public sharing of data may result in the loss of intellectual property. The future may lie in strategic partnerships. Every individual will be responsible for deciding how and if to share their data. It is also possible for partnered organizations to cease to exist or acquire another organization opportunistically. Data archives from DeepMind were acquired by Google, which effectively ended DeepMind's non-disclosure commitment. Health care will continue to advance through collaboration and data availability. These collaborations will refine data ownership (or data control) and data sharing.

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None.

Conflict of Interest

None.

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