Trends in Cardiovascular Medicine 32 (2022) 34–41

Contents lists available at ScienceDirect

Trends in Cardiovascular Medicine

journal homepage: www.elsevier.com/locate/tcm

Artificial intelligence in cardiology☆,☆☆

Dipti Itchhaporia

Hoag Hospital Newport Beach and University of California, 520 Superior Avenue, Suite 325, Newport Beach, Irvine, CA 92663, United States

ARTICLE INFO

Keywords:
Artificial intelligence
Machine learning
Cardiovascular medicine
Cardiology
Clinical decision making

ABSTRACT

This review examines the current state and application of artificial intelligence (AI) and machine learning (ML) in cardiovascular medicine. AI is changing the clinical practice of medicine in other specialties. With progress continuing in this emerging technology, the impact for cardiovascular medicine is highlighted to provide insight for the practicing clinician and to identify potential patient benefits.

Introduction

Since the last decade of the 19th century with the invention of the electrocardiogram (ECG), technology has played a significant role in cardiovascular medicine. The extensive use of technology in the clinical setting, coupled with the early adoption of guideline-directed-medical-therapy (GDMT) aimed at better patient outcomes, has prepared the specialty for the promising era of artificial intelligence (AI) and, more specifically, machine learning (ML).

In everyday clinical practice, the diagnosis and treatment of cardiovascular disease (CVD) relies on data in several formats. These formats include patient history, physical examination, laboratory data, non-invasive imaging diagnostics and invasive angiography. The introduction of newer data-rich technologies, including mobile telemetry devices, wearable and implantable recording devices, biometrics from the electronic health record (EHR), and research and other patient-generated health data, requires cardiologists to perform an increasingly sophisticated analysis [1–5]. Bonderman suggests that data and historical evidence may not be the only factors that influence the clinical decision-making process [6]. Further, inclusion of social bias and the prejudice of irrelevant factors characterized by Kahnerman et al. are also incorporated by clinicians [7].

Cardiovascular medicine, like other specialties, has faced pressure to achieve the triple aim: optimize patient care, reduce costs, and improve outcomes. The sheer volume of data required for this level of precise care is voluminous and changes too quickly to be used effectively without the help of a robust clinical decision support tool. Krittanawong et al. suggest that, without cognitive computing, our specialty faces practical challenges due to overutilization and inadequate patient care, affecting readmission and mortality rates [8].

Clinical decision-making is a challenging process, with the strain of data overload and the pressure to improve care and translate medical advances and knowledge into an actionable plan. AI tools, specifically ML tools, are poised to potentially extend and augment the effectiveness of the clinician and revolutionize patient care (Fig. 1).

Current state

Technology pervades our everyday lives, and there is no doubt that the future of healthcare is intimately intertwined with technological advancements. Although AI has existed for over five decades, only recently have we begun to truly realize the potential of its applications, in the form of ML, in medicine. This potential holds the promise of better patient care across all healthcare institutions by augmenting the work of clinicians.

The terms AI, ML, and deep learning (DL) are often used interchangeably but are essentially hierarchical. ML methods provide a set of tools to achieve AI and includes supervised, unsupervised and reinforcement learning [9,10].

AI is the overarching concept that refers to the use of specialized mathematical algorithms, which give machines the ability to perform problem solving functions, word or object recognition, and decision making. This rapidly applicable technique deals with complex problems by analyzing data using neural networks in an effort to mimic intelligent human behavior.

A subfield of AI, ML encompasses various techniques for solving complicated problems with big data by identifying interaction patterns among variables. It uses software that allows computers to learn from data, identify patterns and make decisions [1,6,9,10]. In contrast to traditional statistics, one of the applications of ML is building automated clinical decision systems (such as readmission and mortality score systems) that help doctors make more accurate

☆ Declaration of Competing Interest: None.

☆☆ Ethical Statement: None.

E-mail address: drdipti@yahoo.com

https://doi.org/10.1016/j.tcm.2020.11.007
1050-1738/

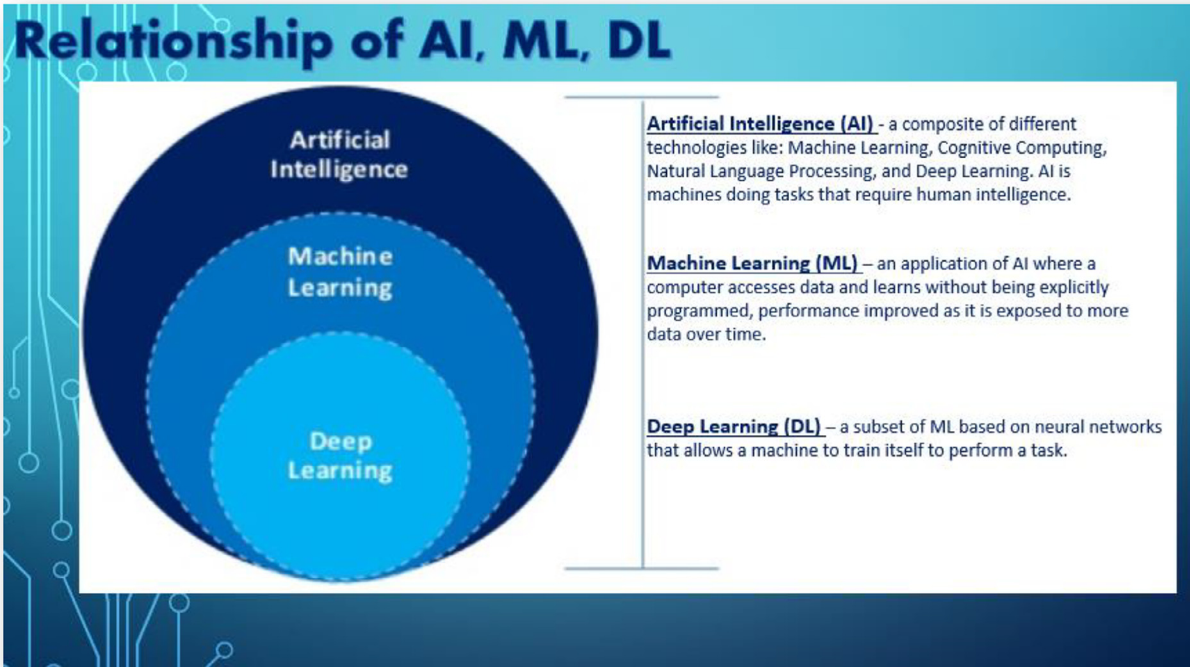

Fig. 1.. Framework of AI, ML, DL.

predictions, rather than simple estimated score systems. The ML community, which has seen increased computational power amidst the availability of big data, sees an opportunity in the healthcare sector to tackle complex tasks [11]. As noted above, ML can be categorized into three learning types: supervised; unsupervised; and reinforcement.

Supervised learning, which has the widest applicability to date, is an ML approach wherein a model is given both inputs and the corresponding ‘correct’ responses during the training [10]. It deals with classification and regression problems, and is used to develop a model for classifying future events or to find which variables are most relevant to the outcome. Although supervised learning benefits from having a clearly delineated relationship between the inputs and outputs, incorrect data labels may result in a less effective model, since the correct input-output link is determined entirely by the training data. AI has the ability to lessen social bias and noise, but is subject to bias when given a biased training set.

Unsupervised learning is a type of ML algorithm used to draw inferences from datasets consisting of input data without labeled responses [10]. The most common unsupervised learning method is cluster analysis, which is used for exploratory data analysis to find hidden patterns or grouping in data, data mining for sequence and pattern mining in medical imaging for image segmentation. Unsupervised learning seeks to identify novel disease mechanisms, genotypes, or phenotypes from hidden patterns present in the data; the objective is to find the hidden patterns in the data without feedback from humans.

In reinforcement learning, the model learns from trial and error and rewards via a feedback system [10]. This particular method has been used in selecting the optimal medication regimen for non-small cell lung cancer [12]. Reinforcement learning can be viewed as a hybrid of supervised and unsupervised learning; the objective of reinforcement learning is to maximize the accuracy of algorithms using trial and error [8].

A subset of ML is DL. DL attempts to imitate the workings of the human brain in processing data and creating patterns for use in decision making. It is inspired by the complex workings of the human brain and strives to find high-level abstract representations of a given data set. DL has enabled many practical applications of ML and, by extension, the overall field of AI. This method has emerged because of advances in computer processor power and the availability of big data [13]. It uses multiple layers of artificial neuronal networks that can generate automated predictions from input (training datasets). Benefits of this method over traditional ML include less data for training and ease of scale with more accuracy [14]. DL can be very powerful in image recognition and can potentially be used in cardiovascular imaging (e.g., 2D-speckle-tracking echocardiography, 3D-speckle-tracking echocardiography, angiography, cardiac magnetic resonance). It can also be trained in an unsupervised manner for unsupervised learning tasks (e.g., novel drug-drug interaction). It also works well with noisy data, such as 3D-speckle tracking echocardiography and strain imaging data. DL algorithms can facilitate the use of artificial real-time cardiovascular imaging with better spatial and temporal resolution [8].

Deep learning, as it is primarily used, is essentially a statistical technique for classifying patterns, based on sample data, using neural networks with multiple layers. Although DL is useful in certain tasks such as classifying medical images, DL is not suitable for all clinical data issues. Kingsbury and coworkers noted that “In our experience across several clinical problems, conventional, off the shelf ML methods can be trained faster and have overall better performance when compared to deep neural networks” [15]. However, the use of DL in every application that requires data analysis should not be done at the expense of other ML algorithms with less computation and memory requirements, which are capable of producing similar results. Despite the variety of recent successes of deep learning, there are limitations in the application of the technique. First, deep learning is not the optimal machine learning technique for all data analysis problems. For problems in which data are well structured or optimal features are well-defined, other simpler machine learning methods such as logistic regression, support vector machines, and random forests are typically easier to apply and more effective [16].

Convolution Neural Networks (CNNs) are a class of deep neural networks, most commonly applied to analyzing visual imagery. It has been postulated by Dilsizian and Siegel that CNNs are best optimized to the task of image pattern recognition or image analysis [18]. CNNs require little preprocessing and often use the raw images fed to them, making them a particularly powerful and versatile tool [18].The use of CNNs in this manner has increased drastically over the last several years, with researchers finding success in the use of CNNs to provide subtle features that a clinician may miss on a scan, aiding in the detection of a variety of pathologies. Abdolmanafi et al., for example, utilized a deep-learning CNN in the classification of coronary artery optical coherence tomography (OCT) images in patients with Kawasaki disease. However, they noted in order to fine tune the process, a considerable amount of time is required [21]. Additionally, imaging data can be particularly difficult to manage, especially given the wide array of different format types in which different imaging modalities are stored, such as JPEG and DICOM.

Cognitive computing

The term cognitive computing (CC) is used to describe AI systems that can synthesize data from various information sources, weighing context and conflicting evidence to suggest possible answers. In general, cognitive computing is used to assist humans in their decision-making process. A number of AI technologies are required for a computer system to build cognitive models, including machine learning, deep learning, neural networks, natural language processing (NLP) and sentiment analysis [8].IBM Watson is a well-known example of cognitive computing; it continuously learns from datasets and can help predict outcomes using multiple algorithms. CC is currently used at Memorial Sloan Kettering and MD Anderson, where it uses unstructured data, best practice data, and clinical study results to help make diagnosis and treatment decisions for patients [8].One example of this use in cardiology was illustrated by Dr. Partho Sengupta, who developed an associative memory classifier, a cognitive computing machine learning algorithmic approach, to differentiate constrictive pericarditis from restrictive cardiomyopathy, and demonstrated its feasibility for automated interpretation of speckle-tracking echocardiography data [20].

Natural language processing (NLP)

NLP is an example of machine learning systems with the ability to understand and interpret human speech and writing. They interface with subjective data used in electronic health records (EHRs) in order to extract useful information that can be used in algorithm generation. These algorithms can be used to carry out high-volume tasks formerly accomplished by physicians. A large amount of data are presented to the cognitive system in order to increase precision of decision making. Ng et al. have described guidelines that recommend the types and amount of data needed to effectively use disease prediction models using EHR data [21]. Sohn et al. demonstrated the feasibility of NLP in processing radiology reports and developed a model for identifying aneurysms [22]. Since NLPs can scan multiple databases, libraries and other data sources, they are useful in identifying critical valvular and vascular stenosis, hypertrophic cardiomyopathy, atrial septal defects, and other anomalies [22,23].

In 2018, Garvin et al. demonstrated the use of a novel NLP in collecting and classifying clinical data from more than 1000 patients with heart failure in order to determine the quality of inpatient care given [24]. Although this technology is still in its nascent stages, the potential to accurately and effectively utilize the vast stores of clinical data included in EHRs and leverage this information to assess present quality of care is a promising method in directing future improvements.

Applications of ML

The potential of ML, DL and CC to change the manner in which cardiac data is utilized –their accuracy, objectivity, and efficiency – is undeniable. With the development of increasingly powerful machines and as DL approaches gain traction, the diagnostic fields of radiology (computed tomography [CT], magnetic resonance imaging [MRI] and mammography interpretation), pathology (microscopic and cytological diagnoses), dermatology (rash identification and pigmented lesion evaluation for potential melanoma), and ophthalmology (retinal vessel examination to predict the risk for diabetic retinopathy and cardiovascular disease) can be further advanced in the interest of elevating patient care.

The potential applications of ML in medicine are numerous and represent various ranges of computational difficulty. The use of extracted data in the generation of algorithms to apply to a given problem is the most common application of ML in healthcare. The utility of such ML algorithms has already been established in numerous settings. For example, automated ML-driven algorithms have been helpful in the classification and early diagnosis of micromelanomas, the implications of which are reduced mortality and less intensive treatment requirements [25]. The efficacy of ML-developed algorithms heavily depends on the availability of data to build these predictive frameworks. In cardiology, these data sets can come from a variety of modalities. Data-rich sources include electrocardiograms (EKGs), echocardiograms and other myocardial imaging modalities; 'omics' technologies including genomics and proteomics that can aid AI in the profiling of particular molecular entities and help risk-stratify patients; and information recorded by clinicians in the EHR. However, not all data sets share equal potential in their applicability to AI systems. The data collected from EHRs is often subjective in nature and thus difficult for accurate AI utilization, therefore making NLP useful [26].

The efficacy of ML in the analysis of predefined tasks, such as image processing for border detection on a scan or recognizing suspicious areas on an image, is a crucial aspect of ML's utility in healthcare. Enhancing the process of visual pattern recognition has profound implications on the process of clinical diagnostics. It is important to understand the shortcomings of human visual pattern recognition. Two independent studies have found that 50–63% of U.S. women who receive regular mammograms over ten years will receive at least one false positive; additionally, one third of the time, two or more radiologists examining the same mammogram will disagree on the interpretation [27]. Analyzing images and performing diagnostic prediction tasks, for example, using ML to detect diabetic retinopathy, are harder than the simple aforementioned tasks but still possible with the present technology [28]. In this setting, visual pattern recognition software, which can store and compare tens of thousands of images while using the same heuristic techniques as humans, is estimated to be 5% to 10% more accurate than the average clinician [28]. So far, ML has exhibited demonstrable value in the analysis of different myocardial imaging modalities, from EKGs to MRI, and in utilizing that information to establish probabilistic frameworks whereby they may establish the presence or lack of disease in a given image.

AI, especially ML, has impacted healthcare in four overarching ways [9]. One is through computer vision. Computer vision is a field of AI that trains computers to process, analyze, interpret and understand digital images. Using digital images from photographs, videos and DL models, machines can accurately identify and classify objects. Applying this feature to medical images, computer vision can support disease detection and clinical decisions regarding classification for staging and prognosis. The second and third are predictive modeling and precision medicine-guided care recommendations. Predictive modeling is used for assessing genetic risk (genomics) and for predicting the course of chronic disease (phenomapping). This approach requires multiple datasets coupled with natural learning processing and machine learning. Precision medicine looks at an individual's health data (EHR data, wearable data), and omics data (i.e., genomics, proteomics, and metabolomics) and uses cluster analysis and other ML analytics to make individualized recommendations. The last way is a health system performance enhancer, which uses ML analytics to gain insights into healthcare system management and improve clinical care and patient safety.

Uncertainty is a fact of everyday medical practice, with complex variables and determinants that govern a patient's health and create diagnostic and therapeutic dilemmas. This uncertainty can be addressed by AI, specifically ML, as it augments the abilities of clinicians by helping them provide the highest standard of care. This aspect has the potential to create uniform medical care from different health-care providers.

AI offers the ability to further standardize the quality of care by working with clinicians by providing all the necessary and pertinent information and making predictions required to make the optimal diagnosis and the best plan of care for follow-up. For example, Hannun et al. demonstrate the efficacy of DL in the classification of various EKG rhythms, a powerful addition to every cardiologist's diagnostic toolkit [29]. AI performs the analysis of data from clinical notes, allowing clinicians to meet documentation standards while integrating societal, clinical, and personal context into the decision-making process. The use of AI in this regard may help standardize quality of care by helping to reduce two major elements of decision-making error: social bias and noise, factors that may affect a physician's judgment, such as mood, for example [7]. It is impossible to completely eliminate human biases, but using AI can significantly reduce such errors. Ultimately, the optimal role of ML will be to support clinicians, ensuring that the final decision regarding diagnosis and treatment falls on the clinician; it is hoped that the analysis and augmentation of information with ML will help ensure optimal clinical decisions.

Hospitals are also scrutinizing ML tools to increase capacities without expanding building space, improve clinician productivity without adding to work hours, and minimize patient wait-times while increasing the number of incoming patients. A growing number of medical centers are considering a new, innovative form of digital management called hospital command centers. These centers use advanced predictive analytic technology and ML to monitor and analyze real-time data on patient admissions, patient discharges, bed availability, and other hospital logistics to address their unique needs and strategic functions. As a result of the Affordable Care Act in 2010, health care organizations and providers have had to deal with increases in patient volumes and regulations with new documentation standards. This development has led to clinician burnout, a factor that makes the achievement of the quality goal of the quadruple aim impossible. As health organizations grapple with this issue, it is hoped that the hospital command centers may help simplify administrative burdens and optimize the practice of patient-centered care.

Limitations of ML in medical practice

While putting the power of ML to work in clinical settings presents a variety of exciting applications, as mentioned above, this endeavor is not without several crucial limitations. The algorithms developed by machine learning technologies are only as effective as the data used to frame them. There is a wide variety of sources from which important patient health information could be drawn –certainly cardiac parameters, such as heart rate, rhythm, etc. – much of which could be used by ML systems in the development of valuable analytic algorithms. Conversely, the lack of such data and large amounts of poor-quality data compromises the integrity of this process; the use of sparse or biased data sets could result in problematic algorithms that do not accurately represent the clinical situation in question. Additionally, many valuable sources of information, such as EHR data, as well as information regarding social, cultural and economic determinants, may be difficult to find or implement. Training issues also limit the success of ML. The models used also may change over time, requiring frequent updating. The algorithm may additionally become over tailored to the training sample rather than finding the relationships in the data.

Although ML – and AI in general – has become considerably more advanced in recent years, the technology is still in its early stages compared to many other, more established, modalities. This reality poses potential complications for its integration into medical practice. The application of ML into medicine may be costly, discouraging its widespread utilization. Although it is reasonable to assume that ML has the potential to revolutionize physician workflow in many positive ways, the initial implementation of these technologies may prove jarring for providers as they struggle to adjust day-to-day routine. According to Cucolo et al., the ‘black box" nature of the ML algorithm and the difficulty for clinicians to understand and trust the interpretation of the data may be the most difficult hurdle to overcome [30].

Applications in cardiology

Technology has been a mainstay in the field of cardiology for the past several decades, with successful integration into diagnostics and intervention. The efficacy of utilizing AI and specifically ML in cardiology has also been established in a variety of different settings, such as coronary artery disease with risk prediction, and cardiac imaging, including electrocardiography and echocardiography.

Cardiac imaging and imaging interpretation

Cardiac imaging is an area that shows early promise. DL systems such as CNNs have shown great potential as valuable tools in cardiac imaging. Many authors have published results highlighting the use of CNN and other methods for coronary calcium detection, thrombus volume characterization, left atrium segmentation, coronary stenosis, carotid artery characterization, detection of and classification of aortic aneurysm, and others.

Diagnostic support for cardiac imaging uses segmentation of known anatomical landmarks. In this application, the model is trained using deep reinforcement learning to quickly navigate through the volume of CT images to find and localize the anatomical landmarks [31]. Once the landmarks are identified, AI-powered segmentation methods can be used to quantify the structures. This application may be useful for modeling and segmentation of heart valves and, more specifically, for sizing implants. Its use may also facilitate the switching from real-time x-ray to 3D CT in the catheterization laboratory [32].

ML can have a positive impact on imaging reconstruction, analysis and interpretation. Its ability to analyze large amounts of imaging data and then couple with the use of dedicated imaging software can allow imaged displays to show more anatomic views, allowing for ease of image interpretation [33]. Du et al. tested DL technology for angiographic recognition of lesion characteristics, including diameter stenosis, calcification, thrombus and dissection

[34].Work done with DL to automate calcium scoring in patients following Rb-PET/CT showed good correlation for the classification with five categories, from very low to very high calcium scores [9]. DL algorithms have also been shown to diagnose obstructive coronary artery disease more accurately compared to conventional methods using myocardial perfusion imaging (MPI) [9].

Ciusdel et al. trained a deep neural network on 17,800 angiograms and evaluated 27,900 angiograms for fully automated cardiac phase and end diastolic frame detection on coronary angiograms, with an accuracy of 92.6%, a sensitivity of 92.4% and specificity of 92.9% [9]. An ML algorithm to evaluate intravascular ultrasound images and automatically calculate lumen area and plaque burden, showing tremendous agreement with expert analysis, was tested at Emory University [9].This method has potential for augmenting care in the cardiac catheterization laboratory.

Electrocardiography

Electrocardiogram (ECG) analysis is at the core of cardiovascular pathology diagnosis. Since 1996, when it was first described, the use of AI for electrocardiography continues to be refined [38]. ECG analysis is the most developed application of machine learning methods in cardiology, owing mostly to publically available databases for training and testing such as the MIT-BIH, Physionet's Physiobank, INCART, or the American Heart Association database [48]. The open access to ECG databases has led to the development of many methods and approaches for computer-aided ECG arrhythmia classification over the last decades.

The ECG reflects the electrical activity of the heart, and for a normal beat in sinus rhythm includes the P wave, the QRS complex, and the T wave. Heartbeat classification focuses on the automatic identification of normal beats and abnormal beats, and can be useful for detecting ectopic beats or arrhythmic events. Modern ML models can identify QRS complexes and P and T waves with high precision, thus allowing for calculations of clinically significant parameters such as HR [11]. The use of DL systems has improved the analytic power of EKGs; indeed, DL has been successful in accurately classifying the EKGs of cardiac patients into normal, abnormal, and life-threatening states [39].DL techniques to help automate the detection of atrial fibrillation (AFib) are occurring with EKGs and ambulatory EKG systems [40]. The Stanford Machine Learning Group used a form of DL, a 34-layer convolutional neural network to detect a range of arrhythmias which outperformed a board-certified cardiologist in recall and precision [41].ML is being rapidly implemented into wearable devices operating deep neural network (DNN) in ECG analysis. Kannathal et al. used a deep neural network to classify ECG signals of cardiac patients into normal, abnormal, and life-threatening states, and found the classification to be correct in approximately 99% of test cases [17].

Wearable devices for ECG monitoring are having an impact on the effort to move the clinic to the home. The Apple Watch and AliveCor are well known examples of such devices [48]. In the case of Alive-Cor, the wearable technology is integrated in a smart phone application and records ECG data from patients. These data are analyzed with a machine learning algorithm to help detect atrial fibrillation or other arrhythmias. Machine learning techniques provide accurate and automatic classifications of heartbeats to detect arrhythmias or unexpected changes in heart morphology. They may help in automatic disease diagnosis, monitoring and stratification by handling extended ECG recordings for which visual and manual inspections can be tedious and time consuming. Their real-time use, along with their adaptability to be embedded on wearable devices, can help with efficient and reliable monitoring of ECG activity at home.

Echocardiograms

Much work has also been done in the integration of ML systems in the analysis of echocardiography. In 2016, Sengupta and colleagues utilized a cognitive computing system to distinguish between constrictive pericarditis and restrictive cardiomyopathy, while also demonstrating its efficacy in the interpretation of speckle-tracking echocardiography data [35].

Echocardiograms are an important tool in the diagnosis and management of cardiovascular disease. ML has the potential to change the landscape of echocardiography with its complimentary tools that can help generate accurate, consistent and automated interpretation of echocardiograms, thus potentially reducing the risk of human error, as interpretations are presently done by clinician expertise. Automation with longitudinal strain and 3D echocardiography has shown great accuracy and reproducibility, allowing the incorporation of these techniques into daily workflow. These attributes can help decrease inter-operator variability and give experience to non-expert readers.

Research calls to mind the feasibility of applying ML models to provide rapid, highly accurate and consistent assessment of echocardiograms, comparable to the ability of clinicians. Algorithms are capable of accurately quantifying a wide range of features, such as the severity of valvular heart disease or the ischemic burden in patients with coronary artery disease. There is at least one innovative software solution, developed by Edwards Life-Sciences, that focuses on improving the quality of patient care and growing structural heart programs [36]. Artificial intelligence is the driving force behind its core capability of assessing diagnostic echocardiogram quality, following patients through the care pathway, and helping physicians and their clinical staff ensure their patients are receiving guideline directed care.

A recent study of over 14,000 echocardiograms showed promise for AI applications to automatically classify image orientation, perform image segmentation and assign a diagnosis [37]. Detection of wall motion abnormalities on echocardiography requires experience and can thus suffer from observer variability. AI solutions are emerging, which have good accuracy for this task [35,37].

ML in electrocardiography is routinely used in patient care, as opposed to ML in echocardiography, which is still in its infancy. Work such as that being undertaken utilizing Edward's software will further this field.

Clinical decision support

Clinical decision support systems with cognitive computing are being developed and use ML, pattern recognition, and NLP. In coronary artery disease (CAD), the capacity of ML systems to develop algorithms capable of making clinical predictions was demonstrated by Baxt in 1991, in which an artificial neural network was trained on more than 300 patients who were hospitalized with suspicion of myocardial Infarction (MI). Upon subsequent testing of new patients presenting to the Emergency Department with chest pain, the computer-derived protocol had a higher sensitivity in detecting MI compared to that of the clinicians caring for these patients [42]. In a pilot study published in 2018, an ML algorithm showed 94% accuracy for predicting a myocardial infarction in patients presenting with chest pain in the emergency department [43].

More recently, the Francis Crick Institute developed a model, using ML, which was found to be better at predicting risk of death in patients with heart disease than in models designed by medical experts. The model for coronary artery disease was designed using the electronic health data of over 80,000 patients, collected as part of routine care by scientists at the Crick, working collaboratively with colleagues at the Farr Institute of Health Informatics

Research and University College London Hospitals NHS Foundation Trust. They outperformed experts using self-taught ML techniques [44]. It should be noted here that, although this result may be statistically significant (C-index for AI algorithm 0.801 vs C-index for conventional risk prediction for death in CVD patients 0.793), it may not be clinically significant at this level of difference. This study illustrates an important issue of the difference between statistical vs. clinical significance. Whereas statistical significance indicates reliability of study results, clinical significance reflects its impact on clinical practice. Statistical significance testing has established traditionally accepted values, which is lacking for evaluation of clinical significance. Statistical significance is largely dependent on the study's sample size; in large sample sizes, even small treatment effects, which maybe clinically non-significant can appear statistically significant. Thus, it is important to interpret carefully whether statistically significance is clinically meaningful [45].

Recently, Dawes et al. developed an algorithm of three-dimensional systolic cardiac motion based on MRI; this algorithm allowed the researchers to more accurately predict survival rates of patients with newly diagnosed pulmonary hypertension [46]. In general, AI technologies are being utilized for CAD risk prediction, including machine, and coronary calcium scoring algorithms to make predictions regarding patient risk. Importantly, the machine-learning approach can address the limitations of conventional risk scores by taking into consideration multiple risk factors, determining the relationship between these factors and outcomes. Conventional prediction models take into account standard risk factors such as age, cholesterol levels and blood pressure but do not account for factors like medications, other medical conditions and non-traditional biomarkers [13].

ML algorithms are based on fewer assumptions and can, in some cases, provide superior and more robust predictions [8]. For example, Azzalini et al. used generalized boosted regression (an ML approach) to identify whether contrast media type was an independent predictor of contrast-induced acute kidney injury after percutaneous coronary intervention [9].

A clinical decision support system studied for interpretation and treatment of stable coronary artery disease is CEREBRIA-1 (Machine Learning vs Expert Human Opinion to Determine Physiologically Optimized Coronary Revascularization Strategies). In this study, an ML algorithm for analysis of 1008 instantaneous wave-free ratio pullback tracings were evaluated and compared with the analysis of a team of interventionalists, and it found that the ML program was non-inferior to the interventionalist for PCI decision making [9] (Table 1).

Table 1.
Applications of AI.

Clinical service	***AI application***	***Data source(s)***
-Chronic Care Management [14,44]	- Algorithms - GDMT - Unsupervised Machine Learning	- Patient–generated health data - Sociodemographics - "Omics" - Electronic Health Record (EHR) - Diagnostics - Remote Monitoring
- Clinical Decision Support - Decision Trees - Cross Validation [40–44,31]	- Algorithms - Supervised Machine Learning	- Big Data - EHR - Diagnostic Imaging – 3D - "Omics" - Precision Medicine Platforms
- Forecasting the spread of disease Example: ACS Risk [8,42,44]	- Algorithms - Supervised Machine Learning	- Big Data - EHR - Diagnostic Imaging - "Omics" - Precision Medicine Platforms - Large clinical databases (ACC)
- Precision Medicine-Customized Treatment [1,5,8,14]	- Unsupervised Machine Learning - Precision Medicine Platforms	- Precision Medicine Platforms - Large clinical databases (ACC) - Literature Knowledge - Multi-omic data
- Cardiac Imaging Interpretation - Hidden Patterns [9,29–35]	- Supervised Machine Learning Deep Learning - Unsupervised Machine Learning - Cognitive Learning	- Diagnostic Images: CT, MRI, Echo, Angiography, EKG

Precision cardiac medicine

Aside from imaging, assessment of CAD and interventional cardiology, AI has shown promise in the area of precision cardiac medicine. Giri et al. state in their paper, "To date, big data, such as 'omics' data, are too large and heterogeneous to be stored, analyzed, and used to their full potential"[9]. AI techniques may solve this issue as well as allow for automatic generation of new hypotheses, instead of requiring that physicians postulate them [5]. Unsupervised DL may facilitate exploration of novel factors in score systems and better prediction analysis, or add hidden risk factors to existing models [8,1]. This approach could lead to new models for antiplatelet/anticoagulant therapy, bleeding versus stroke risk, mortality risk with procedures, as examples [8]. ML-based techniques also can highlight long-term outcomes or late complications for patients who have undergone a specific procedure or are prescribed a specific drug.

In 2015, Shah et al. utilized several learning algorithms in the analysis of clinical, laboratory, ECG, and echocardiographic data of almost 400 patients with heart failure with preserved ejection fraction (HFpEF) and classified the patients into three distinct phenogroups based on a variety of different clinical characteristics and outcomes [14]. The success of this endeavor indicates that this approach could be used more extensively in the future to improve the manner in which heterogeneous pathologies are classified, thereby helping clinicians best make decisions regarding resource allocations. Krittanawong et al. also identify other complex cardiovascular disorders that could benefit from AI-driven precision medicine, such as pulmonary hypertension and cardiomyopathy [8].

Data sources: uses and limitations

Clinical cardiology offers an overabundance of different sources of data for use by AI in the formation of algorithms. This information includes phenotypic data, such as EKGs and other myocardial imaging modalities, many of which provide narrow data sets that are optimally suited for machine learning. What is especially interesting and exciting in the field of cardiology is the use of data-rich technology, such as implantable recording devices, or even everyday technology such as smart phones and smart watches that keep track of cardiac parameters like heart rate and are able to record tracings of an EKG. These technologies then present the potential for direct-to-patient applications of cardiology. The acquisition of these large and diverse datasets and patient-generated data streams from new wearable and implantable sensor technologies can provide a very granular view of the intra- and interindividual variations in health and disease. Making full use of these multidimensional data streams will require the computational and data analytic ability of ML to process these data meaningfully and rapidly.

Presently, clinicians often do not have time to review all of this information derived from these sources, since this task involves combing through numerous pages of a single patient's device data. ML has the potential to provide processed summaries of these data, which would be most useful in guiding therapy. As the connected self generates all kinds of data, for example, heart rates and ambient arrhythmias, we need to understand what is normal. For example, if someone has a run of atrial fibrillation, a technology has to first classify this event correctly, and then there has to be an evidence standard that can influence the clinical care. This issue of what is the right evidence standard for AI was discussed at length by Maddox et al.; they argued that an evidence standard is required to demonstrate outcomes and a lack of unintended consequences [26].Further, the need of machine learning to utilize data-rich pools in order to develop effective algorithms necessarily precludes them from being helpful in analyses of rare disorders for which we simply do not have enough data to train machine learning.

It is predicted that soon, health care organizations and providers will embrace algorithmic solutions on smart phones or tablets first, followed by pattern recognition software and, finally, machine-generated best practices for individual patients [4,6]. Patients will be able to use a variety of AI tools to care for themselves, just as they manage multiple other aspects of their lives today through ubiquitous usage of AI systems like Apple's Siri or Amazon's Alexa [4].

Those most excited about AI technology wonder whether AI could autonomously detect warning signs of disease or acute incidents through fine-tuned predictive algorithms and send that information directly to patients. Such an application may not only save lives, but also aid in managing patient behavior through active tracking of parameters such as weight, blood pressure, and activity level, and help warn patients. How the integration of AI can modify these behaviors is not known. It is important to note that presently this technology is designed to aid a clinician's decision making rather than be used by the patient directly for their healthcare management. Despite the efficacy that ML has exhibited in terms of forming predictive models by utilizing presently available data, an important dimension that is often missing from these predictions is the timeline. Although an algorithm may suggest that a patient is at higher risk for developing a myocardial infarction, it cannot define an accurate timeline of the event because presently available datasets do not adequately define such timelines. In spite of this issue, AI may continue to be useful in helping clinicians to make risk predictions.

Conclusion

AI and ML systems have initiated a paradigm shift in health care. Clearly, these systems are useful in the identification of clinically significant patterns in high volumes of heterogeneous data – be it from smart watches, EHRs or ECGs – even if the importance of these patterns is not causative, but rather purely correlational [19]. EHRs were not originally designed to predict disease risk or offer treatment options to consider. But when combined with ML, EHR data could potentially do both, transforming health care in the process [47,6,26].

In the day-to-day practice of cardiology, AI, specifically ML, is expanding its footprint, presently most suited to a spectrum of computational tasks with a range of difficulties, the best of which are narrow tasks, such as image processing, in which the system is working with a predefined context. Even tasks of pattern prediction and broad data analysis are conceivable today, if these endeavors are specifically asked for. In other words, the systems are not self-directed and require appropriate data sets. Therefore, the role of ML in cardiology is most likely to remain supportive for the foreseeable future, augmenting cardiologists with relevant information and predictions regarding diagnosis and best treatment but leaving the ultimate decision in the hands of the clinician. For AI, ML integration comes with the need for appropriate evidence standards; there is a lack of standardization across datasets, making optimal models for clinical integration challenging. According to a recent work by Maddox et al., developing task-appropriate standards, as well as an elucidation of the manner by which ML develop their predictive insights beyond the idea of a "black box" methodology, may prove helpful in assuaging some of the concerns that clinicians may have in integrating ML into their practice [26].

History has shown us that the forward progress of technological advancement is unlikely to slow down; medical technology is no exception. The forward momentum of AI and ML technology has demonstrated that the technology will not replace clinicians but will augment their care delivery. Ultimately, it is the clinician who has the capacity to demonstrate empathy, compassion, and complex reasoning under uncertain conditions, traits that patients want in their medical care. Indeed, ML could be the very thing that catapults American healthcare into the future, helping to clarify the best care approaches, creating new approaches for diagnosing and treating hundreds of complex medical problems, and measuring adherence. This outcome will not happen overnight, of course; recall that efforts to produce self-driving vehicles date back to the 1950s. There are certainly many challenges that remain ahead: Who will regulate this industry? Who will objectively assess the effectiveness of this new technology? Who will be held accountable for errors? These are questions being asked about autonomous driving technology today [11]. But sometime in the future, ML will disrupt healthcare as we know it.

In preparation for that day, health care providers need to actively engage to adapt their practice and to shape the technology. Rather than fearing that the ML technology will displace them, they should direct and craft the technology for end users. The anguish of the clinician's EHR experience drives the importance of creating the type of change that is needed and wanted. The favorable adoption of AI in the form of ML into medical practice can be further facilitated by its integration into medical school curricula. This feature will help develop future clinicians who are not only effective, empathetic healthcare providers, but who are also accomplished in the utilization of AI systems in their practice in a manner that improves diagnosis, care, and outcomes. AI, specifically ML, is guaranteed to be more closely intertwined with our lives, and the field of cardiology would do well to embrace this trend and the potential it presents.

Bibliography

[1] Johnson KW, Soto JT, Glicksberg BS, Shameer K, Miotto R, Ali M, et al. Artificial intelligence in cardiology. J Am Coll Cardiol 2018;71(23):2668–79.
[2] Kuo FC, Mar BG, Lindsley RC, Lindeman NI. The relative utilities of genome-wide, gene panel, and individual gene sequencing in clinical practice. Blood 2017;130:433–9.
[3] Muse ED, Barrett PM, Steinhubl SR, Topol EJ. Towards a smart medical home. Lancet 2017;10067:358–89.
[4] Steinhubl SR, Muse ED, Topol EJ. The emerging field of mobile health. Sci Transl Med 2015;7:283.
[5] Shameer K, Badgeley MA, Miotto R, Glicksberg BS, Morgan JW, Dudley JT. Translational bioinformatics in the era of real-time biomedical, health care and wellness data streams. Brief Bioinform 2017;18:105–24.
[6] Bonderman D. Artificial intelligence in cardiology. Wien KlinWochenschr 2017;129:866–8.
[7] Kahnerman D, et al. How to overcome the high, hidden cost of inconsistent decision making. Harv Bus Rev 2016;R10:36–43.
[8] Krittanawong C, Zhang HJ, Wang Z, Aydar M, Kitai T. Artificial intelligence in precision cardiovascular medicine. J Am Col Cardiol 2017;69(21):2657–64.

[9] Sardar P, Abbott JD, Kundu A, Aronow HD, Granada JF, Giri J. Impact of artificial intelligence on interventional cardiology: from decision-making aid to advanced interventional procedure assistance. JACC Cardiovasc Interv 2019;12:1293–303.
[10] Petersen SE, Abdulkareem M, Leiner T. Artificial intelligence will transform cardiac imaging-opportunities and challenges. Front Cardiovasc Med. 2019;6:133. doi:10.3389/fcvm.2019.00133.
[11] Al'Aref SJ, Anchouche K, Singh G, Slomka PJ, Kolli KK, Kumar Amit, et al. Clinical applications of machine learning in cardiovascular disease and its relevance to cardiac imaging. Eur Heart J 2019;40(24):1975–86.
[12] Rabbani M, Kanevsky J, Kafi K, Chandelier F, Giles FJ. Role of artificial intelligence in the care of patients with nonsmall cell lung cancer. Eur J Clin Investig 2018;48. doi:10.1111/eci.12901.
[13] Weng SF, Reps J, Kai J, Garibaldi JM, Qureshi M. Can machine-learning improve cardiovascular risk prediction using routine clinical data. PLoS One 2017;12:e0174944.
[14] Shah SJ, Katz DH, Selvaraj S, Burke MA, Yancy CW, Gheorghiade M, et al. Phenomapping for novel classification of heart failure with preserved ejection fraction. Circulation 2015;131:269–79.
[15] Chen D, Liu S, Kingsbury P, et al. Deep learning and alternative learning strategies for retrospective real-world clinical data. NPJ Digit Med 2019;2:43.
[16] Chartrand G, Cheng P, Vorontsov E, Drozdzal M, Turcotte S, Pal C, Kadoury S, Tang A. Deep learning: a primer for radiologists. RadioGraphics 2017;37:2113–31.
[17] Kannathal N, Acharya UR, Lim CM, Sadasivan P, Krishnan S. Classification of cardiac patient states using artificial neural networks. Exp Clin Cardiol 2003;8(4):206–11.
[18] Dilsizian ME, Siegel EL. Machine meets biology: a primer on artificial intelligence in cardiology and cardiac imaging. Nucl Cardiol 2018;20:139.
[19] Abdolmanafi A, Duong L, Dahdah N, Cheriet F. Deep feature learning for automatic tissue classification of coronary artery using optical coherence tomography. Biomed Opt Express 2017;8:1203–20.
[20] Sengupta PP, Huang YM, Bansal M, et al. Cognitive machine-learning algorithm for cardiac imaging: a pilot study for differentiating constrictive pericarditis from restrictive cardiomyopathy. Circ Cardiovasc Imaging 2016;9(6):e004330. doi:10.1161/CIRCIMAGING.115.004330.
[21] Ng K, Steinhubl SR, deFilippi C, Dey S, Stewart WF. Early detection of heart failure using electronic health records: practical implications for time before diagnosis, data diversity, data quantity and data density. Circ Cardiovasc Qual Outcomes 2016;9(6):649–58.
[22] Sohn S, Ye Z, et al. Identifying abdominal aortic aneurysm cases and controls using natural language processing of radiology reports. AMIA JT Summons Tranl Sci Proc 2013;2013:249–53.
[23] Sardar P, Abbott DJ, et al. Impact of artificial intelligence on interventional cardiology. JACC Cardiovasc Interv 2019;12(14):1293–303.
[24] Garvin J.H., Kim Y., Gobbel G.T., Matheny M.E., Redd A., Bray B.E., et al. Automating quality measures for heart failure using natural language processing: a descriptive study in the department of veterans affairs. 2018
[25] Jaworek-Korjakowska J. Computer-aided diagnosis of micro-malignant melanoma lesions applying support vector machines. J Biomed Biotech 2016;6:1–8.
[26] Maddox TM, Rumsfeld JS, Payne PRO. Questions for artificial intelligence in health care. JAMA 2018. doi:10.1001/jama.2018.18932.
[27] DeFrank JT, Rimer BK, Bowling JM, Earp JA, Breslau ES, Brewer NT. Influence of false-positive mammography results onsubsequent screening: do physician recommendations buffer negative effects? J Med Screen 2012;19:35–41.
[28] Gulshan V, Peng L, Coram M, et al. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. JAMA 2016;316:2402–10.
[29] Hannun AY, Rajpurkar P, Haghpanahi M, Tison GH, Bourn C, Turakhia MP, Ng AY. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. Nat Med 2019;25(1):65–9.
[30] Cuocolo R, Perillo T, De Rosa E, Ugga L, Petretta M. Current applications of big data and machine learning in cardiology. J Geriatr Cardiol 2019;16(8):601-607. doi:10.11909/j.issn.1671-5411.2019.08.002.
[31] Ghesu FC, Georgescu B, Zheng Y, Grbic S, Maier A, Hornegger A, et al. Multi-scale-scale deep reinforcement learning for real-time 3D landmark detection in CT scans. IEEE Trans Pattern Ana Mach Intell 2019;41:176–89.
[32] Dey D, Slomka PJ, Leeson P, Comaniciu D, Shrestha S, Sengupta PP, et al. Artificial intelligence in cardiovascular imaging. JACC 2019;73(11):1317–35.
[33] Al'Aref SJ, Anchouche K, Singh G, Slomka PJ, Kolli KK, Kumar A, et al. Clinical applications of machine learning in cardiovascular disease and its relevance to cardiac imaging. Eur Heart J 2019;40:1975–86.
[34] Du T, Xie L, Liu X, et al. Intelligent recognition of coronary angiography by deep learning technology: a novel computer-aided diagnostic system Paper presented at: transcatheter cardiovascular therapeutics symposium (TCT); 2018. September 21–25San Diego, CA.
[35] Sengupta PP, Huang YM, Bansal M, Ashrafi A, Fisher M, Shameer K, et al. Cognitive Machine-Learning Algorithm for Cardiac Imaging: A Pilot Study for Differentiating Constrictive Pericarditis From Restrictive Cardiomyopathy. Circ Cardiovasc Imaging 2016 Jun;9(6):e004330.
[36] Cardiocare program Edwards Life sciences, Edwards, Lifesciences. "CardioCare." *Edwards Lifesciences*. Edwards Lifesciences 2020.
[37] Zhang J, Gajjala S, Agrawal P, Tison GH, Hallock LA, Beussink-Nelson L, et al. Fully automated echocardiogram interpretation in clinical practice. Circulation 2018;138(16):1623–35.
[38] Itchhaporia D, Snow PB, Almassy RJ, Oetgen WJ. Artificial neural networks: current status in cardiovascular medicine. JACC 1996;28:515–21.
[39] Kannathal N, Acharya UR, Lim CM, Sadasivan PK, Krishnan SM. Classification of cardiac patient states using artificial neural networks. Exp Clin Cardiol 2003;8:206–11.
[40] Trahan, Ronald. "Cardiologs ECG Analysis Platform' Receives FDA Clearance." *VentureBeat*, VentureBeat, 5 July 2017, venturebeat.com/2017/07/05/cardiologs-ecg-analysis-platform-receives-fda-clearance/.
[41] Rajpurkar P, Hannun AY, Haghpanahi M, Bourn Ng AY. Cardiologist-level arrhythmia detection with convolutional neural networks. Comput Vis Pattern Recognit 2017;1:65–9.
[42] Baxt WG. Use of an artificial neural network for the diagnosis of myocardial infarction. Ann Intern Med 1991;115:843–8.
[43] Lindholm D, Holzmann M. Machine learning for improved detection of myocardial infarction inpatients presenting with chest pain in the emergency department (abstr). J Am Coll Cardiol 2018;140(Suppl: A22):899–909.
[44] Steele AJ, Denaxas SC, Shah AD, Hemingway H, Luscombe NM. Machine learning models in electronic health records can outperform conventional survival models for predicting patient mortality in coronary artery disease. PLoS One 2018;13(8):e0202344. doi:10.1371/journal.pone.0202344.
[45] Ranganathan P, Pramesh CS, Buyse M. Common pitfalls in statistical analysis: clinical versus statistical significance. Perspect Clin Res 2015;6(3):169–70. doi:10.4103/2229-3485.159943.
[46] Dawes TJW, de Marvao A, Shi W, Fletcher T, Watson GMJ, Wharton J, et al. Machine learning of three-dimensional right ventricular motion enables outcome prediction in pulmonary hypertension: a cardiac MR imaging study. Radiology 2017;283:381–90.
[47] Stead WW. Clinical implications and challenges of artificial intelligence and deep learning. JAMA 2018;11:1107–8.
[48] Lyon A, Mincholé A, Martínez JP, Laguna P, Rodriguez B. Computational techniques for ECG analysis and interpretation in light of their contribution to medical advances. J R Soc Interface 2018;15(138):20170821. doi:10.1098/rsif.2017.0821.