JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. 69, NO. 21, 2017
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2017.03.571

REVIEW TOPIC OF THE WEEK

Artificial Intelligence in Precision Cardiovascular Medicine

Chayakrit Krittanawong, MD,[a,b] HongJu Zhang, PhD,[c] Zhen Wang, PhD,[d,e] Mehmet Aydar, PhD,[b,f] Takeshi Kitai, MD, PhD[b,g]

ABSTRACT

Artificial intelligence (AI) is a field of computer science that aims to mimic human thought processes, learning capacity, and knowledge storage. AI techniques have been applied in cardiovascular medicine to explore novel genotypes and phenotypes in existing diseases, improve the quality of patient care, enable cost-effectiveness, and reduce readmission and mortality rates. Over the past decade, several machine-learning techniques have been used for cardiovascular disease diagnosis and prediction. Each problem requires some degree of understanding of the problem, in terms of cardiovascular medicine and statistics, to apply the optimal machine-learning algorithm. In the near future, AI will result in a paradigm shift toward precision cardiovascular medicine. The potential of AI in cardiovascular medicine is tremendous; however, ignorance of the challenges may overshadow its potential clinical impact. This paper gives a glimpse of AI's application in cardiovascular clinical care and discusses its potential role in facilitating precision cardiovascular medicine. (J Am Coll Cardiol 2017;69:2657–64) © 2017 by the American College of Cardiology Foundation.

In the near future, artificial intelligence (AI) techniques, such as machine learning, deep learning, and cognitive computing, may play a critical role in the evolution of cardiovascular (CV) medicine to facilitate precision CV medicine. CV clinical care currently faces practical challenges pertaining to cost reductions in prevention and treatment, low cost-effectiveness, overutilization, inadequate patient care, and high readmission and mortality rates. Productive interactions between physicians and data scientists are needed to enable clinically meaningful automated and predictive data analysis. To date, big data, such as "omics" data, human gut microbiome sequencing, social media, and cardiac imaging, are too large and heterogeneous, and change too quickly, to be stored, analyzed, and used. AI has the potential to exploit big data and be used in advanced patient care. In fact, cardiovascular diseases (CVDs) are complex and heterogeneous in nature, as they are caused by multiple genetic, environmental (e.g., air pollution), and behavioral factors (e.g., diet and gut microbiome). At present, many more advancements need to be made to predict outcomes accurately and effectively, rather than assessing a simple score system or traditional CV risk factors. Deep-learning AI is a new machine-learning technique that plays a vital role in areas such as image recognition (e.g., Facebook's facial recognition system [Menlo Park, California], self-driving cars, speech recognition (e.g., Apple's Siri [Cupertino, California], Google Brain [Mountain

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Department of Internal Medicine, Icahn School of Medicine at Mount Sinai St. Luke's and Mount Sinai West, New York, New York; [b]Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio; [c]Division of Cardiovascular Disease, Department of Medicine, Mayo Clinic, Rochester, Minnesota; [d]Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery; [e]Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota; [f]Department of Computer Science at Kent State University, Kent, Ohio; and the [g]Department of Cardiovascular Medicine, Kobe City Medical Center General Hospital, Kobe, Japan. The authors have reported that they have no relationships relevant to the contents of this paper to disclose. Bijoy K. Khandheria, MD, served as Guest Editor for this paper.

Manuscript received March 12, 2017; accepted March 22, 2017.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

AF = atrial fibrillation

AI = artificial intelligence

ANN = artificial neural network

AUC = area under the curve

CV = cardiovascular

CVD = cardiovascular disease

ECG = electrocardiographic

EHR = electronic health record

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

HTN = hypertension

RNN = recurrent neural network

SCAD = spontaneous coronary artery dissection

STE = speckle-tracking echocardiography

SVM = support vector machine

View, California], Amazon's Alexa Voice [Seattle, Washington]), Google DeepMind AlphaGo, mobile apps (e.g., Cardiogram app [San Francisco, California]), machine vision software in cameras, IBM Watson (North Castle, New York), and robots. Deep-learning AI using big data can be used in pattern recognition in heterogeneous syndromes and image recognition in CV imaging. For example, AI can classify new genotypes or phenotypes of heart failure (HF) with preserved ejection fraction (HFpEF), and novel diagnostic echocardiographic parameters could potentially lead to novel targeted therapy. In addition, to date, 2-dimensional speckle-tracking echocardiography (2D-STE) quantitation cannot sufficiently assess left ventricular ejection fraction because left ventricular ejection fraction is commonly calculated by manually tracing boundaries or via the time-honored "eyeball" method, which lack reproducibility and precision. Therefore, AI may improve the accuracy of 2D-STE quantitation and other cardiac imaging methods. In the 21st century, the paradigm is shifting from traditional statistical tools to the use of AI in CV medicine to enable precision CV medicine. Big data can be used to automatically generate new hypotheses, instead of physicians having to initiate hypotheses. In our opinion, rather than replacing physicians, AI will assist them in making better clinical decisions. The objective of this paper is to outline the role of AI applications, such as machine learning, deep learning, and cognitive computing, in enabling precision CV medicine, and discuss the potential future direction of AI in clinical practice. Going forward, future studies in CV research should focus on more complex and heterogeneous diseases using AI by moving beyond traditional statistical tools. To illustrate some of the points addressed here, this paper focuses on examples of AI algorithms in CV medicine.

BIG DATA

The term *big data* refers to extremely large datasets that cannot be analyzed, searched, interpreted, or stored using traditional data-processing methods. Big data include data from mobile phone applications, wearable technology, social media, environmental and lifestyle-related factors, sociodemographics, "omic" data (e.g., genomics, metabolomics, proteomics), and data from standardized electronic health records (EHRs) or precision medicine platforms. Whereas big data by themselves are useless, the processing of big data to make predictions or decisions using AI has the potential to transform the current practice of clinical care. Big data analytics using AI may potentially facilitate identification of novel genotypes or phenotypes of heterogeneous syndromes, such as HFpEF, Takotsubo cardiomyopathy, hypertrophic cardiomyopathy, primary pulmonary hypertension (PH), hypertension (HTN), and coronary artery disease, leading to personalized, targeted therapy. Big data analytics using AI can also support important clinical decisions, such as selection of antiplatelet agents in individuals who are post-percutaneous coronary intervention, anticoagulant agents in individuals with nonvalvular atrial fibrillation (AF), and pharmacogenomics in individuals. Furthermore, big data analytics has the potential to identify unknown risk factors for acute coronary syndrome (ACS), spontaneous coronary artery dissection (SCAD), or Brugada syndrome, and even the controversial issue of statins in the older population (age >75 years). Although big data utilization in CV medicine is still in its infancy, big data analytics have recently been implemented in CV medicine.

TRADITIONAL STATISTICS VERSUS MACHINE LEARNING. In the big data realm, AI techniques, such as machine learning, are revolutionizing the way physicians make clinical decisions and diagnosis, and have the potential to improve the estimated CVD risk scores to automate prediction. In traditional statistics, such as the logistic regression model, the c-statistic is a standard measure of predictive accuracy. However, current predictive scores, such as congestive HF, hypertension, age ≥75 years, diabetes mellitus, and prior stroke, vascular disease, age 65 to 74 years, and sex category (CHA_2DS_2-VASc), dual antiplatelet therapy, and the Framingham risk score, were developed using large trials or cohorts with ill-defined moderated values of c-statistics (e.g., 0.79 for men in Framingham risk score, 0.83 for women in Framingham risk score, 0.65 for CHA_2DS_2-VASc score, 0.66 for Anticoagulation and Risk Factors in Atrial Fibrillation, 0.70 and 0.68, respectively, in the ischemic and bleeding models in dual antiplatelet therapy) (1–4). Although the dual antiplatelet therapy study involved 25,682 patients at 452 sites in 11 countries, big data analytics using precision medicine platforms could involve millions of patients for exploration and validation. In 2013, the American Heart Association/American College of Cardiology guideline was developed by estimating atherosclerotic CVD using the pooled cohort equations from sex- and race-specific proportional hazards models, but its c-statistics are not well-defined in African

Americans (0.713 in men and 0.818 in women) (5). Cook et al. (6) reviewed the guideline and found overestimation of the pooled cohort equations in primary prevention external cohorts. They subsequently suggested that real-time calibration of risk prediction equations is feasible with big data analytics (6). Therefore, the increasing availability of automated real-time decision support tools using AI applications in EHRs will likely reduce the need for simple scoring systems such as these.

MACHINE LEARNING

Machine learning, a popular subdiscipline of AI, represents various techniques for solving complicated problems with big data by identifying interaction patterns among variables. In contrast to traditional statistics, machine learning is focused on building automated clinical decision systems (such as readmission and mortality score systems) that help physicians make more accurate predictions, rather than simple estimated score systems.

Machine learning can be categorized into 3 learning types: supervised; unsupervised; and reinforcement. In supervised learning, algorithms use a dataset labeled by humans to predict the desired and known outcome. Supervised learning is great for classification and regression problems, but it requires a lot of data and is time-consuming because the data have to be labeled by humans. Conversely, unsupervised learning seeks to identify novel disease mechanisms, genotypes, or phenotypes from hidden patterns present in the data. In unsupervised learning, the objective is to find the hidden patterns in the data without feedback from humans. For example, teaching medical residents (labels) before they see the patients can be termed *supervised learning*. In contrast, allowing medical residents to see patients (no labels), then allowing them to learn from their mistakes (errors) and come up with their own plans (optimize) can be termed *unsupervised learning*. Some algorithms, such as artificial neural networks (ANNs), can be trained using supervised or unsupervised learning to optimize the accuracy of automated prediction. Last, reinforcement learning can be viewed as a hybrid of supervised and unsupervised learning. The aim of reinforcement learning is to maximize the accuracy of algorithms using trial and error.

Learning curves and area under the curve (AUC) are important considerations in the choice of a machine-learning algorithm, whereas c-statistics are important in the choice of traditional data-processing methods. As with traditional statistics, machine learning requires sufficient training datasets (also known as sample size in traditional statistics) and the right algorithms to optimize its performance on the training dataset before testing. In traditional statistics, alpha should not be more than 0.05, whereas in machine learning, there should be no underfitting (suboptimal data) or overfitting (noisy data). Overfitting commonly occurs when a model is excessively complex relative to the size of the training dataset (i.e., too many parameters) that may not be valid for the testing dataset. For example, for a machine trying to learn what SCAD or acute myocardial infarction is, we start by training it with keywords such as "chest pain," "female," "age 30 to 50," "physical/emotional factors," and "h/o fibromuscular dysplasia"; the machine detects in the initial phase that all SCAD features have "chest pain," "female," "age 30 to 50," "physical/emotional factors," and "h/o fibromuscular dysplasia." If training continues with the same key words, the machine may also falsely deduce that all SCAD features must have "chest pain," "female," "age 30 to 50," and "h/o fibromuscular dysplasia," and that all "chest pain," "female," "age 30 to 50," and "history fibromuscular dysplasia" are SCAD. This may potentially include atherosclerotic acute myocardial infarction or Takotsubo cardiomyopathy, which is called overfitting to data. In contrast, AI may potentially exclude SCAD in men, SCAD without fibromuscular dysplasia, or 51-year-old women with SCAD. This problem is called underfitting to data.

An excellent example of the use of machine learning is the prediction of the survival of patients with HFpEF. Shah et al. (7) created an unsupervised learning model across 46 different variables to identify intrinsic structures within patients with HFpEF; they identified 3 distinct groups. Subsequently, they performed supervised learning to predict the difference in desired outcomes (mortality and hospitalization) among the groups. However, the limitation of unsupervised learning is that the initial cluster pattern needs to be corrected without bias; therefore, the study needs to be validated with other cohorts.

SUPERVISED LEARNING. Supervised learning algorithms have been successfully applied to problems in the prediction, diagnosis, and treatment of CVD as well as image analysis in CV imaging. Various algorithms can be trained using supervised learning. For example, we trained a machine for 30 potential variables (such as C-reactive protein, erythrocyte sedimentation rate, cysteine, QTc interval, E/A ratio, and SYNTAX score [an angiographic tool]). Subsequently, the algorithms generated a prediction model using weighted variables from the training dataset. Next,

we applied the algorithms to a new dataset (testing dataset) to predict ACS risk; the machine then calculated the ACS risk from the 30 potential variables in the new dataset. The prediction accuracy depends on the algorithm, dataset, and hypothesis. Different algorithms are appropriate for different hypotheses, and so an understanding of the advantages and disadvantages of each algorithm is required to apply it in the optimal manner and potentially test the hypotheses. Knowing the goals and the appropriate techniques for hypotheses is critical for machine learning to be carried out effectively and accurately.

Algorithms that can be used in supervised learning include ANN, support vector machine (SVM), decision tree, random forests, naive Bayes classifier, fuzzy logic, and K-nearest neighbor (KNN). Each algorithm has its own advantages and disadvantages. Supervised learning problems can be categorized into classification (predict categories), regression (predict values), and anomaly detection (predict unusual patterns) problems. Factors for selecting optimal algorithms include data characteristics, training time, learning curves, and number of parameters and features. ANN and SVM are the 2 most popular algorithms because they are compatible with large and complex data (e.g., "omic" data) and can process data with higher accuracy than other supervised learning algorithms.

ANNs, which mimic the human neuron concept, perform well for image processing of electrocardiographic (ECG) and echocardiographic data. ANNs: 1) can be used in nonlinear relations; 2) conditions where traditional statistical analyses fail; 3) have a higher predictive accuracy than linear or logistic regression; 4) are very flexible in various data types; and 5) can be used with deep-learning algorithms. Their limitations include: 1) data overfitting; 2) lengthy computation time; and 3) having more parameters than most supervised learning algorithms.

In contrast to ANNs, SVMs are less prone to overfitting and need less memory. They have been shown to perform well for text classification in EHRs and pattern recognition in echocardiographic imaging to stratify CV risk and help physicians make decisions (8,9). In addition, an SVM is feasible for nonlinear data or large and complex data, such as "omic" data, because kernel functions, a shortcut to expedite learning process, can be applied to SVMs to enhance their accuracy and reduce processing time (10,11). However, selection of kernel functions is very important, as the wrong choice can lead to an increase in the error percentage. Other algorithms, such as decision tree, naive Bayes classifier, and random forest, have lower accuracy than ANN and SVM, but are relatively easy to use and can be used with small datasets. The decision tree algorithm is easy to understand and is unlikely to encounter overfitting because of the relatively small dataset. It can be used with a series of yes/no questions to classify data into categories and also be used in clinical decision-making or CV risk prediction in simple tasks (12). The random forest algorithm is an extension of the decision tree algorithm, in which decision trees are combined and each decision tree is independently trained. Random forest algorithms have been used in coronary computed tomography angiography, readmission for HF patients, and HF risk and survival prediction models (13–17). In addition, random forests can easily perform leave-1-out predictions (i.e., sensitivity analysis in meta-analysis) and are relatively robust to selection bias.

The naive Bayes classifier is a simple probabilistic classifier derived from Bayes' theorem. It performs very well on small training datasets and can be used in text classification problems, such as in CV risk factor identification and decision-making systems (18,19). Fuzzy logic functions are similar to human reasoning and decision-making in which logic returns values (e.g., 10% possibility of SCAD, 30% possibility of acute myocardial infarction, 15% possibility of pericarditis) instead of straight true/false or yes/no answers (e.g., definitely SCAD and not SCAD). Fuzzy logic has been used in various areas, such as for prediction of early-stage coronary artery disease, mortality prediction after cardiac surgery, and cardiac arrhythmia detection (20–23). K-nearest neighbor is one of the simplest nonparametric methods. It executes quickly on small training datasets and can be used in ECG interpretation problems (24,25); however, K-nearest neighbor requires more space and time for large datasets.

LIMITATIONS OF SUPERVISED LEARNING. In supervised learning, small training datasets can lead to inaccurate decisions in testing datasets if the training datasets are biased; therefore, supervised learning requires large datasets to train the model and validation by other datasets. Supervised learning also requires the training datasets to be manually labeled to predict only known output results (e.g., mortality and readmission rate). Furthermore, even though multiple functions can fit a given training dataset on which supervised learning subsequently makes assumptions about the "best" function that fits the data, it can cause bias that guides the learning algorithm to prefer to one hypothesis or function over another.

UNSUPERVISED LEARNING. In unsupervised learning, unlabeled data are used to predict unknown

results and the algorithm has to determine how to discover the hidden patterns in the dataset. Unsupervised learning is often used in deep learning, and has been implemented in self-driving vehicles and robots as well as being used in speech- and pattern-recognition applications. In CV clinical care, unsupervised deep learning with 2D- and 3-dimensional (3D)-STE data may enable identification of novel phenotypes of cardiomyopathy or HFpEF, and can potentially be used in precision medicine platforms or the National Heart, Lung, and Blood Institute's TransOmics for Precision Medicine program to identify genotypes of HTN or ACS. The algorithms used in unsupervised learning can be classified into: 1) clustering algorithms; and 2) association rule-learning algorithms. Clustering algorithms can be used to cluster unlabeled data into different groups. A cluster is a collection of data items that are "similar" to 1 cluster and "dissimilar" to other clusters and is used when there are no obvious natural groupings, in which case the data may be difficult to explore. For example, Google News can be shown to customers in different ways to match their online lifestyles. Association rule-learning algorithms help to uncover relationships between seemingly unrelated data items. For example, 70% of patients who had angioedema with angiotensin-converting enzyme inhibitors also have angioedema with angiotensin receptor-neprilysin inhibitors. Another example of an association rule is novel drug-drug interaction.

LIMITATIONS OF UNSUPERVISED LEARNING. One major limitation of unsupervised learning is difficulty identifying the initial cluster pattern, which could potentially lead to biases. Because the final cluster pattern is dependent on the initial cluster pattern, this could result in inaccurate decisions. Therefore, it needs validation in several cohorts. In addition, some complex problems lead to limitations that are not easily overcome without supervised training; thus, it may require manually labeled data to identify the optimal algorithm. For example, noisy data, such as 3D-STE images, have to be manually denoised before predictions can be successful. Thus, for the best results, unsupervised learning may require manual hand coding in some parts, unsupervised algorithms in other parts, and subsequent validation.

DEEP LEARNING

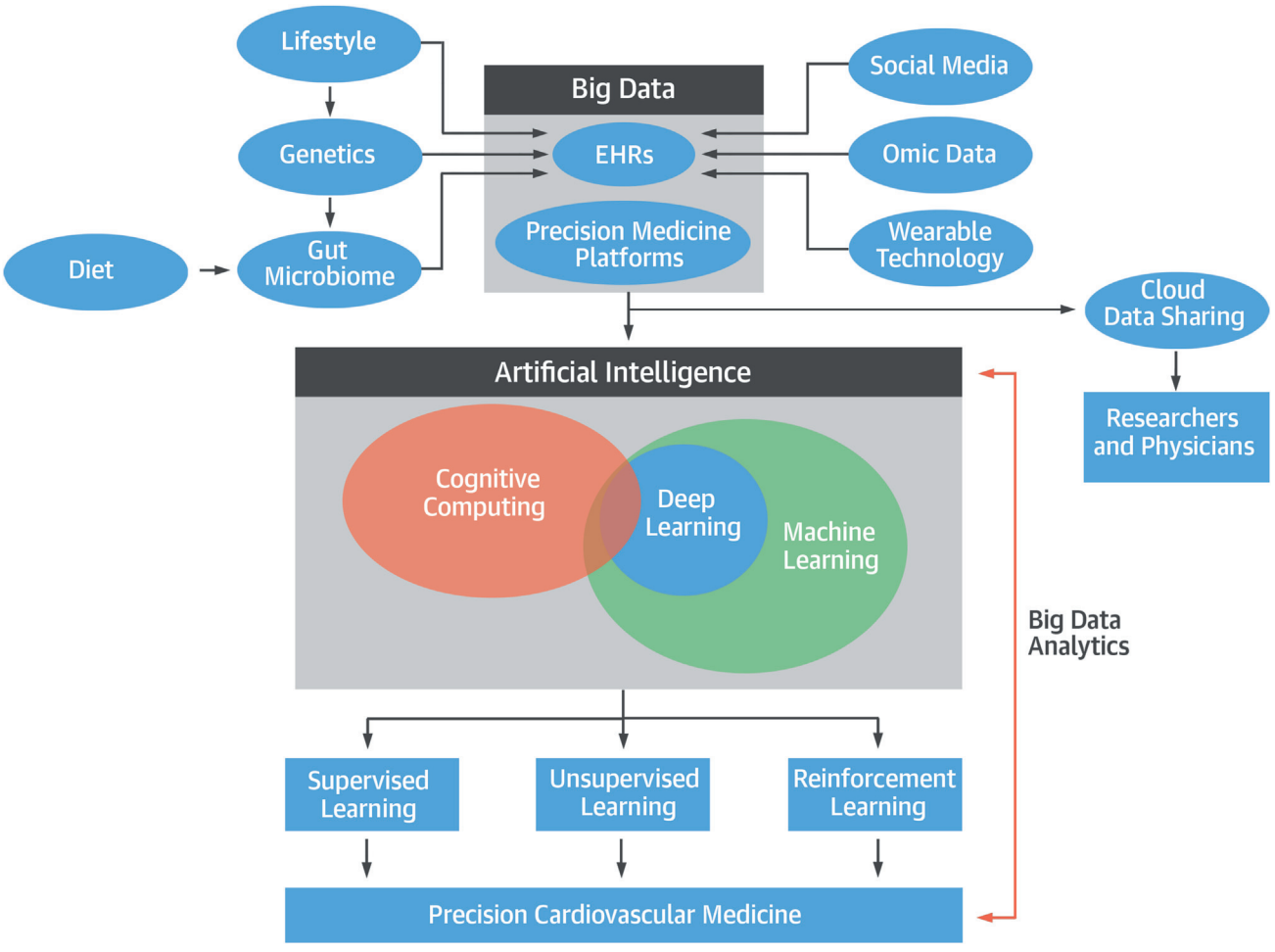
Deep learning mimics the operation of the human brain using multiple layers of artificial neuronal networks that can generate automated predictions from input (training datasets). Deep learning has become a hot topic in AI because it is a growing field and appears promising. Deep learning can be very powerful in image recognition (e.g., facial recognition in Facebook, image search in Google), and can potentially be used in CV imaging (e.g., 2D-STE, 3D-STE, angiography, cardiac magnetic resonance). It can also be trained in an unsupervised manner for unsupervised learning tasks (e.g., novel drug-drug interaction). Furthermore, there is no limitation on working memory. It also works well with noisy data, such as strain imaging and 3D-STE data. Deep-learning algorithms will facilitate use of artificial real-time CV imaging with better spatial and temporal resolution, potentially improving the quality of care and reducing costs.

Deep learning has recently been implemented in CV medicine, more specifically, in CV imaging. Deep learning with neuronal network algorithms can be recurrent neural networks (RNN), convolutional, and deep neural networks. Wang and Kong (26) used a supervised convolutional neural network model to predict end-systolic and end-diastolic volumes in cardiac magnetic resonance. Convolutional neural networks and RNN are dominant in image and speech recognition. RNNs have proven effective in many difficult machine-learning tasks, such as image captioning (27) and language translation (28). Choi et al. (29) used an RNN to predict HF 9 months before diagnosis made by physicians and found that the RNN (AUC: 0.777) was superior to supervised machine-learning algorithms. Google developed a deep neural network known as Google DeepMind AlphaGo that defeated human champions in the Go game in March 2016. Kannathal et al. (30) used a deep neural network to classify the 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.

Deep learning has proven to be better than other machine-learning techniques, such as SVM, because deep learning can use multiple layers and transformations, compared with the 2 layers used by SVM.

LIMITATIONS OF DEEP LEARNING. Deep learning is usually nonlinear analysis and has many parameters and multiple layers; thus, overfitting may be a major challenge that could lead to poor predictive performance. Increasing the size of the training dataset or decreasing the number of hidden layers may help to avoid overfitting. Deep learning also requires a large training dataset, which necessitates collaboration between institutions and EHR linkage (e.g., the American Heart Association Precision Medicine Platform). Furthermore, deep-learning analysis requires deep-learning-capable machines, such as graphics processing unit-accelerated computing, for example,

CENTRAL ILLUSTRATION **Artificial Intelligence in Precision Cardiovascular Medicine**



Krittanawong, C. et al. J Am Coll Cardiol. 2017;69(21):2657–64.

Big data (genetics, social media, environmental, and lifestyle-related factors, or "omic" data) can be stored through EHRs or precision medicine platforms, and can be shared for data analysis with other physicians or researchers through secure cloud systems. Big data analytics using artificial intelligence (machine learning, deep learning, or cognitive computing) and 3 main types of learning algorithms (supervised, unsupervised, and reinforcement learning) will enable precision cardiovascular medicine. EHR = electronic health record.

NVIDIA DIGITS DevBox (Santa Clara, California) and Amazon EC2. Setting up a neural network using deep-learning algorithms is also time-consuming. Finally, deep learning with multiple layers may increase the training time without improvement in precision.

CLINICAL IMPLICATIONS OF DEEP LEARNING. Deep learning can perform tasks without human assistance in industry (e.g., self-driving, playing Go, learning math to write math textbooks, reading scientific publications to answer questions, watching movies to answer questions, machine vision software in cameras, phones, and robots). Implementation of deep learning in CV medicine includes the following. First, unsupervised deep learning may facilitate exploration of novel factors in score systems or add hidden risk factors to existing models. Second, deep learning can be used to classify novel genotypes and phenotypes from heterogeneous CVDs, such as HFpEF, HTN, pulmonary hypertension, and cardiomyopathy. Third, automated deep-learning prediction models can predict risk of bleeding and stroke by weighting between CHA_2DS_2-VASc and the hypertension, abnormal renal function, abnormal liver function, stroke, bleeding, labile international normalized ratios, elderly, drug therapy, and alcohol intake (known as HAS-BLED) scores to facilitate optimal doses and

anticoagulant therapy duration in nonvalvular AF patients. Fourth, deep learning may also help to identify additional stroke risk factors (e.g., left atrial appendage, left atrial strain on echocardiography, real-time risks from wearables) and incorporate those factors into new models for anticoagulant therapy. Last, with deep learning, left ventricular ejection fraction may be predicted from ECG patterns or coronary calcium score from echocardiography.

COGNITIVE COMPUTING

Cognitive computing involves self-learning systems using machine learning, pattern recognition, and natural language processing to mimic the operation of human thought processes. In cognitive computing, a system or device is trained by machine-learning or deep-learning algorithms. The goal of cognitive computing is to create automated computerized models that can solve problems without human assistance (**Central Illustration**).

IBM Watson, a well-known example of cognitive computing, continuously learns from datasets (e.g., EHR, social media, stock market) and can predict outcomes using multiple algorithms more accurately than humans. Sengupta et al. (31) developed an associative memory classifier, a cognitive computing machine-learning algorithmic approach, to classify constrictive pericarditis from restrictive cardiomyopathy, and demonstrated its feasibility for automated interpretation of STE data. An associative memory classifier (accuracy: 93.7%; AUC: 96.2%) proved to be better than random forest (accuracy: 88.3%; AUC: 94.2%) and SVM (accuracy: 87.4%; AUC: 92.2%). With a set of select STE variables, the associative memory classifier achieved an AUC of 89.2%. Four echocardiographic variables (e′, E/e′, and septal and posterior wall thickness) had an AUC of 94.2%. Fifteen STE and 4 echocardiographic variables (e′, E/e′, septal, and posterior left ventricle wall thickness) showed incremental diagnostic value in distinguishing constrictive pericarditis from restrictive cardiomyopathy.

Cognitive computing systems can also reason creatively about data, patterns, and situations, and extend models with new pieces. Cognitive computing can leverage machine learning to extend the ability of HF diagnosis efficiently by helping physicians discover diagnosis patterns that they may not observe by themselves. Therefore, implementation of deep learning in cognitive computing systems can be used for classification of novel diseases, genotypes, phenotypes, or unknown drug-drug interaction.

CONCLUSIONS

The implementation of deep learning with unsupervised features for big data analytics holds significant potential for identifying novel genotypes and phenotypes in heterogeneous CV diseases, such as Brugada syndrome, HFpEF, Takotsubo cardiomyopathy, white-coat hypertension, HTN, pulmonary hypertension, familial AF, and metabolic syndrome. Furthermore, the development of AI application and precision medicine platforms will facilitate precision CV medicine. In the future, cognitive computers, such as IBM Watson, will be standard in health care facilities and assist physicians with their decision making and prediction of patient outcomes. Many technology companies, such as IBM, Apple, and Google, are investing heavily in health care analytics to facilitate precision medicine. We believe that AI will not replace physicians, but it is important that physicians know how to use AI sufficiently to generate their hypotheses, perform big data analytics, and optimize AI applications in clinical practice to bring on the era of precision CV medicine. However, ignorance of the challenges of AI may overshadow the impact of AI on CV medicine. Machine learning, deep learning, and cognitive computing are promising and can potentially change the way in which medicine is practiced, but physicians need to be prepared for the upcoming AI era.

ADDRESS FOR CORRESPONDENCE: Dr. Chayakrit Krittanawong, Department of Internal Medicine, Icahn School of Medicine at Mount Sinai, St. Luke's and Mount Sinai West, 1000 10th Avenue, New York, New York 10019. E-mail: Chayakrit.Krittanawong@Mountsinai.org.

REFERENCES

1. Harrell FE Jr., Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 1996;15:361–87.

2. D'Agostino RB Sr., Pencina MJ, Massaro JM, Coady S. Cardiovascular disease risk assessment: insights from Framingham. Glob Heart 2013;8:11–23.

3. van den Ham HA, Klungel OH, Singer DE, Leufkens HG, van Staa TP. Comparative performance of ATRIA, $CHADS_2$, and CHA_2DS_2-VASc risk scores predicting stroke in patients with atrial fibrillation: results from a national primary care database. J Am Coll Cardiol 2015;66:1851–9.

4. Yeh RW, Secemsky EA, Kereiakes DJ, et al., DAPT Study Investigators. Development and validation of a prediction rule for benefit and harm of dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention. JAMA 2016;315:1735–49.

5. Goff DC Jr., Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. [Published

correction appears in J Am Coll Cardiol 2014;63:3026.]. J Am Coll Cardiol 2014;63:2935–59.

6. Cook NR, Ridker P. Calibration of the pooled cohort equations for atherosclerotic cardiovascular disease: an update. Ann Intern Med 2016;165:786–94.

7. Shah SJ, Katz DH, Selvaraj S, et al. Phenomapping for novel classification of heart failure with preserved ejection fraction. Circulation 2015;131:269–79.

8. Berikol GB, Yildiz O, Özcan IT. Diagnosis of acute coronary syndrome with a support vector machine. J Med Syst 2016;40:84.

9. Balasubramanian V, Gouripeddi R, Panchanathan S, Vermillion J, Bhaskaran A, Siegel R. Support vector machine based conformal predictors for risk of complications following a coronary drug eluting stent procedure. 2009 36th Annual Computers in Cardiology Conference (CinC), Park City, UT; 2009:5–8.

10. Furey TS, Cristianini N, Duffy N, Bednarski DW, Schummer M, Haussler D. Support vector machine classification and validation of cancer tissue samples using microarray expression data. Bioinformatics 2000;16:906–14.

11. Brown MP, Grundy WN, Lin D, et al. Knowledge-based analysis of microarray gene expression data by using support vector machines. Proc Natl Acad Sci U S A 2000;97:262–7.

12. Wang Y, Simon MA, Bonde P, et al. Decision tree for adjuvant right ventricular support in patients receiving a left ventricular assist device. J Heart Lung Transplant 2012;31:140–9.

13. Motwani M, Dey D, Berman DS, et al. Machine learning for prediction of all-cause mortality in patients with suspected coronary artery disease: a 5-year multicentre prospective registry analysis. Eur Heart J 2017;38:500–7.

14. Panahiazar M, Taslimitehrani V, Pereira N, Pathak J. Using EHRs and machine learning for heart failure survival analysis. Stud Health Technol Inform 2015;216:40–4.

15. Guidi G, Pettenati MC, Melillo P, Iadanza E. A machine learning system to improve heart failure patient assistance. IEEE J Biomed Health Inform 2014;18:1750–6.

16. Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. Ann Appl Stat 2008;2:841–60.

17. Zolfaghar K, Meadem N, Teredesai A, Roy SB, Chin SC, Muckian B. Big data solutions for predicting risk-of-readmission for congestive heart failure patients. 2013 IEEE International Conference on Big Data, Silicon Valley, CA; 2013:64–71.

18. Miranda E, Irwansyah E, Amelga AY, Maribondang MM, Salim M. Detection of cardiovascular disease risk's level for adults using naive Bayes classifier. Healthc Inform Res 2016;22:196–205.

19. Letian W, Han L, Zhang L, Guo S. GW27-e0397: an analysis and diagnosis system of coronary heart disease based on big data platform. J Am Coll Cardiol 2016;68:C82.

20. Pal D, Mandana KM, Pal S, Sarkar D, Chakraborty C. Fuzzy expert system approach for coronary artery disease screening using clinical parameters. Knowl-Based Syst 2012;36:162–74.

21. Borracci RA, Arribalzaga EB. Fuzzy logic-based model to stratify cardiac surgery risk. Rev Argent Cardiol 2015;83. Available at: http://ppct.caicyt.gov.ar/index.php/rac/article/view/6730. Accessed March 23, 2017.

22. Anuradha B, Reddy VCV. Cardiac arrhythmia classification using fuzzy classifiers. JATIT 2008;4:353–9.

23. Muthukaruppan S, Er MJ. A hybrid particle swarm optimization based fuzzy expert system for the diagnosis of coronary artery disease. Expert Syst Appl 2012;39:11657–65.

24. Arif M, Malagore IA, Afsar FA. Detection and localization of myocardial infarction using K-nearest neighbor classifier. J Med Syst 2012;36:279–89.

25. Saini I, Singh D, Khosla A. QRS detection using K-nearest neighbor algorithm (KNN) and evaluation on standard ECG databases. J Adv Res 2013;4:331–44.

26. Wang K, Kong Y. Diagnosis of heart disease via CNNs (CS231n). Stanford University. Available at: https://www.studocu.com/en-au/document/stanford-university/convolutional-neural-networks-for-visual-recognition/practical/practical-diagnosis-of-heart-disease-via-cnns/751944/view?auth=0&auth_prem=0&new_title=0&has_flashcards=true. Accessed March 26, 2017.

27. Karpathy A, Li FF. Deep visual-semantic alignments for generating image descriptions. CVPR 2015:3128–37.

28. Cho K, Van Merriënboer B, Gulcehre C, et al. Learning phrase representations using RNN encoder-decoder for statistical machine translation. arXiv 2014:1406.1078.

29. Choi E, Schuetz A, Stewart WF, Sun J. Using recurrent neural network models for early detection of heart failure onset. J Am Med Inform Assoc 2017;24:361–70.

30. 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.

31. 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:e004330.

KEY WORDS big data, cognitive computing, deep learning, machine learning