



Artificial intelligence and its application for cardiovascular diseases in Chinese medicine

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ABSTRACT

Cardiovascular diseases (CVDs) are major disease burdens with high mortality worldwide. Early prediction of cardiovascular events can reduce the incidence of acute myocardial infarction and decrease the mortality rates of patients with CVDs. The pathological mechanisms and multiple factors involved in CVDs are complex; thus, traditional data analysis is insufficient and inefficient to manage multidimensional data for the risk prediction of CVDs and heart attacks, medical image interpretations, therapeutic decision-making, and disease prognosis prediction. Meanwhile, traditional Chinese medicine (TCM) has been widely used for treating CVDs. TCM offers unique theoretical and practical applications in the diagnosis and treatment of CVDs. Big data have been generated to investigate the scientific basis of TCM diagnostic methods. TCM formulae contain multiple herbal items. Elucidating the complicated interactions between the active compounds and network modulations requires advanced data-analysis capability. Recent progress in artificial intelligence (AI) technology has allowed these challenges to be resolved, which significantly facilitates the development of integrative diagnostic and therapeutic strategies for CVDs and the understanding of the therapeutic principles of TCM formulae. Herein, we briefly introduce the basic concept and current progress of AI and machine learning (ML) technology, and summarize the applications of advanced AI and ML for the diagnosis and treatment of CVDs. Furthermore, we review the progress of AI and ML technology for investigating the scientific basis of TCM diagnosis and treatment for CVDs. We expect the application of AI and ML technology to promote synergy between western medicine and TCM, which can then boost the development of integrative medicine for the diagnosis and treatment of CVDs.

1 Introduction

Cardiovascular diseases (CVDs), dominated by atherosclerotic vascular diseases, are age-related heart and blood vessel disorders, including ischemic heart disease, hypertensive heart disease, valvular heart disease, and cardiomyopathies. The World Health Organization

(WHO) estimates that CVDs cause approximately 17.9 million deaths annually^[1]. The prevalence and mortality rates associated with CVDs are increasing owing to the aging population and lifestyle changes. Premature death and chronic disability are burdensome to society^[2, 3]. In this regard, CVDs are major disease burdens to affect life expectancy and quality^[4].

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Advanced hardware and exceptional computing power have enabled the development of artificial intelligence (AI), which can be used to simulate human intelligence to investigate the intrinsic relationships and rules of data, thereby providing extensive and powerful data-analysis capability for mining medical big data. The rapid development of AI technology is providing a foundation for the early diagnosis and treatment of CVDs [5]. AI offers significant potential in risk prediction, clinical assistance, chronic disease management, and drug development [6-9]. The applications of AI and big data approaches might offer resolutions for systematically analyzing the results of network pharmacology, molecular biology, metabolomics, and other advanced methods for cardiovascular diseases and other human diseases. More importantly, the development of AI has provided novel insights into understanding the principles of traditional Chinese medicine (TCM) for disease treatment from clinical and basic science perspectives. Herein, we present the recent progress in the application of AI technology for the diagnosis and treatment of CVDs in Chinese medicine.

2 Current progress of AI technology for CVDs

Breakthrough in computer science offers significant opportunities for humans to manage data intelligently to enhance communication capacity and handle complex matters effectively. AI was developed to optimize computer algorithms and perform tasks similar to those requiring human intelligence [10]. Herein, we briefly introduce the history of AI development, the basic concepts of AI technology, and their application in disease treatment.

2.1 Three waves and two winters of AI development

AI technology has experienced three waves and two winters. In 1956, the term “artificial intelligence” was introduced at the Dartmouth Conference. Since then, theories regarding knowledge processing and formal reasoning have been established. However, owing to computer performance bottlenecks, inadequate data volume, and rapid growth in computational complexity, the development of AI has resulted in issues pertaining to knowledge acquisition and processing. In 1977, Edward A. Feigenbaum introduced the concept of “knowledge engineering”, leading a new wave of the rapid development of expert systems [11]. However, in the 1990s, because expert systems can only perform specific tasks, AI development entered a cold winter. Meanwhile, in 1990, the emergence of the Internet resulted in a significant increase in the amount of data. In this regard, manually predefined rules are impractical; thus, researchers have attempted to allow computers to learn by themselves. Consequently, data-driven statistical machine learning (ML) became representative of AI technology. In 2006, HILTON et al. [12]

proposed the concept of deep learning (DL), which propelled another significant advancement in ML. Subsequently, the development of computer hardware and unprecedented data scales significantly accelerated the advancement of AI. In 2016, Alpha Go Lee defeated the world Go master Lee Sedol, thus extending the capability of AI to a new level [13]. The storm of the advanced AI technology reminds of us that “Future world is on board”. Under such circumstances, whether medicine is ready for the AI era?

2.2 Brief concepts of ML and its application for CVDs

AI comprises six primary research areas: computer vision, automated reasoning, robotics, natural language processing, knowledge representation, and ML [14]. ML and its subset, DL, are the most widely used AI techniques in medicine. ML combines classical statistics and computer science. In 1997, Mitchell defined ML as a technology that allows computer programs to improve automatically through experience [15]. Classical statistical methods are inaccurate for managing large, multitype, and complex-structured data. By contrast, ML can manage such data effectively and provide appropriate explanations or predictions using various algorithms and learning features. ML model construction generally includes data preprocessing, feature engineering, model selection, model training and tuning, and model validation [16]. The dataset is typically categorized into training and validation sets for model development and a test set for model evaluation [17]. Nevertheless, the classical ML is unsuitable for managing significant amounts of data. In addition, manual feature extractors can only accomplish specific and simple tasks that are laborious and inconsistent with human intelligence. However, owing to its high interpretability, DL can be used to perform regression prediction and solve problems efficiently, objectively, and precisely for big data analysis.

Based on feedback type, ML can be classified into supervised learning, unsupervised learning, semi-supervised learning, and reinforcement learning. Supervised and unsupervised learning is widely used in the medical field. In supervised ML, the ML algorithm is trained by providing data comprising input features and the corresponding data labels (output). The algorithm fits the ML model by learning the relationships between features and data labels. After the ML model is trained, the machine can provide predictions based on the new data obtained. Supervised ML algorithms can be used to perform regularized regression as well as provide ensembles of decision trees and support vector machines. Furthermore, they can learn linear and non-linear relationships from labeled data, which does not rely on successful engineering. Unlike supervised ML, which requires labeled cases to predict outcomes, unsupervised ML does not require

marked observations. Unsupervised ML can reveal the hidden structure in a dataset and effectively uncover the relationships of different variables via DL algorithms, matrix or tensor factorization, topological data analysis, etc. DL has emerged as a state-of-the-art ML method for making efficient decisions through analyzing complex data. Using unlabeled raw input data, unsupervised ML reveals the underlying intrinsic structures and patterns of data through downscaling and clustering. Thus, ML can be used to identify novel disease mechanisms, genotypes, and phenotypes [18, 19].

Neural networks typically include an input layer, multiple hidden layers, and an output layer, where each layer contains many nodes (or neurons) connected to a specific topology. Artificial neural network (ANN) constitutes a nonlinear adaptive information processing system that identifies potential relationships in a dataset by simulating and integrating the neuronal network process and transmitting information, which simulates the process of the human brain in decision making. ANNs can be used to investigate the implicit features of data while affording high learning and self-organization capabilities. Owing to the different connection methods, typical neural networks can be classified as multilayer perceptron neural networks, convolutional neural networks (CNNs), and recurrent neural networks (RNNs). In addition to ANNs, DL reveals the representations of high-dimensional data by building neural networks with sufficient hierarchical depth to perform layer-by-layer abstraction analysis [20]. CNNs and RNNs are the most typically used ML models. CNNs are representative neural networks comprising neurons with learnable weights and biases; they can be used to create local connectivity across images or signals. The connections have nonlinear activation functions, and hidden layers are applied to learn complex functions. Meanwhile, RNNs use an additional hidden state vector containing “memory” regarding the previous data observed. RNNs are particularly suitable for sequential data such as speech and language data.

Both supervised and unsupervised ML have been adopted extensively in cardiology. The application of supervised ML for processing cardiovascular images, analyzing electrocardiogram (ECG) data, predicting cardiovascular event risk, predicting acute myocardial infarction, etc., has been reported [21, 22]. Owing to its good fitting of high-dimensional data and high recognition accuracy, unsupervised ML can effectively identify complex patterns in large-scale clinical and molecular data. Unsupervised ML-based AI can assist in the precise classification of CVDs by integrating various medical data from patients and characterizing subgroups of heterogeneous diseases [23]. In current medical practice, ML is widely used to analyze raw clinical data for different purposes, including CVD risk prediction [24, 25], medical image interpretation [26, 27], clinical decision-making assistance [28],

prognosis prediction [29], and detection device identification enhancement [30]. For example, a typical case of ML is the use of adaptive CNNs for the rapid and accurate monitoring of patient-specific ECG classification [31]. ML can be used to develop a lightweight wearable device for real-time ECG monitoring and an early alert system for patients with CADs [32]. In particular, unsupervised ML exhibits significant potential in precise medical practice, such as the precision phenotyping identification of CVDs [33, 34]. A series of studies have revealed that unsupervised ML is applicable for analyzing the complex pathological mechanisms of heart failure, differentiating the subtypes of heart failure, and improving outcomes [35, 36]. Using multiple tensor factorization, LUO et al. [37] identified the subtyping of heart failure with preserved ejection fraction by integrating deep phenotypic measurements, trans-omics modalities of data, and interactions between genetic variants. Thus, ML systems exhibit significant potential in solving complex medical problems, such as predicting the risk of heart attack and stroke, and allowing the early diagnosis of cancer.

Nevertheless, ML for healthcare systems is still being developed, and its applications in healthcare and medicine are limited when compared with other technological fields. The use of AI and ML systems in medical practice presents several limitations and challenges. First, the performance of all ML systems relies significantly on the quality of raw data and features for training electronic health records. Accurate datasets with minimal missing values and precise parameters are extremely important. However, big data obtained for ML systems are typically acquired from different sources. Medical imaging data and clinical biochemical results for ML are typically obtained by different medical professionals with diverse training backgrounds and experiences, using various models of medical instruments under different acquisition parameters and conditions. Second, the “black box” containing multiple hidden layers in ML systems provides minimal insight into the logic of the algorithm used, which may result in inaccurate data interpretations in complicated clinical cases. Hence, the final diagnosis and therapeutic decisions are to be made by physicians. Owing to their substantial workloads, physicians are often constrained by time to update their knowledge for managing ML-based medical information. Hence, medical professionals and clinicians must update themselves with knowledge regarding the most recent AI and ML technology such that they can make unbiased and rapid decisions for precision healthcare.

Recent progress in reinforcement learning algorithms has significantly enhanced the capacity of AI and ML to manage complex and dynamic environmental factors for decision-making and the subsequent responses. Reinforcement learning algorithms are capable of developing the learning behaviors via “trial-and-error” using input

data and provide results for optimizing data analysis. In a relevant breakthrough study published in Nature (2015) [38], the capability of using a network based on reinforcement learning algorithms, which is named the deep Q-network, was demonstrated on various classic Atari 2600 video games. Although the model used only pixels and game score as inputs, it surpassed the performance of all previous algorithms and achieved a level comparable to that of a professional human game tester across a set of 49 games, using the same algorithm, network architecture, and hyperparameters [38]. In other words, the model can self-learn and develop an optimal method to maximize the final score, which bridges the gaps between high-dimensional sensory inputs and actions, thus artificially achieving the capacity to excel in challenging tasks. Another example is a study on Google, in which a reinforcement learning model was trained to defeat the world champion in the Chinese board game, Go. The algorithm was based solely on reinforcement learning; in particular, no human data, guidance, or domain knowledge was involved, except for game rules. AlphaGo is its own teacher. A neural network was trained to predict AlphaGo's move selections and became the winner of AlphaGo games. AlphaGo Zero achieved superhuman performance, winning 100-0 against the previous champion-defeating AlphaGo [39]. Although reinforcement learning is currently rarely used in healthcare and medicine, we believe that reinforcement learning algorithms and other advanced AL technologies will soon be applied to medicine and healthcare.

3 Application of AI technology for CVDs in TCM

AI and ML are poised to significantly impact on almost every aspect of human life, TCM should not be an exception to this trend. TCM has over 2000 years of history for the prevention and treatment of human diseases, including CVDs. The TCM theoretical system is characterized by holism (整体观念) and syndrome differentiation and treatment (辨证论治). As a holistic medical system, TCM states that human health is closely related to the natural environment, intrinsic spirit, psychological status, lifestyle, and constitutions. Syndrome differentiation and treatment involves the analysis of core symptom groups to identify diseases and patterns for treatment. Syndromic elements, which are the constituent components of syndromes, are the smallest dialectical units inferred from symptoms or signs. TCM emphasizes the complexity, dynamics, and development of understanding the pathology of diseases and designing therapeutic approaches on a personalized basis. In fact, TCM systems have been developed for centuries via trial-and-error approaches whose process is similar to reinforcement learning algorithms. Based on close observations and the analysis of a patient's input symptoms and body signs,

TCM practitioners estimate the Yin-Yang and Qi-blood status in the "black box," termed Zang Xiang (a core functional unit and concept in TCM theory), and design the appropriate therapeutic approaches to restore the balance of Yin-Yang and Qi-blood. Based on changes in the output symptoms and body signs in patients after treatment, TCM practitioners dynamically optimize the diagnosis for syndrome differentiation and adjust the therapeutic approaches based on the outcome of the treatments. In the "learning" process, TCM practitioners integrate the parameters and conditions of seasoning factors, geographic environments, and constitution statuses to provide personalized therapeutic treatments for patients. Owing to their accumulated experience, TCM practitioners have developed the "learning" ability to optimize "data analysis" based on TCM theory, which is formed under the instruction of ancient Chinese philosophy and through long-term clinical practice. Owing to its "open field" and "long-time" calibration and modification, TCM has become a unique and effective medical system for healthcare and disease treatment. Recent studies provide promising data to verify the efficacy of TCM for the treatment of various human diseases. For instance, several recent randomized controlled trials provide promising evidence to support the use of TCM formulae for CVDs with proven efficacy and safety [40-42]. However, the pharmacological mechanisms and active ingredients of TCM formulae remain unclear. Recent progress in network pharmacology provides a systematic approach for understanding the molecular targets and network regulation of different TCM formulae for CVDs [43]. However, the application of network pharmacology remains superficial. Meanwhile, the use of wearable devices and electronic medical records generates significant amounts of data [44], thus rendering general statistical methods insufficient for analyzing the complexity of TCM diagnosis and treatment. The development of advanced AI technology provides novel insights into the scientific basis of TCM in disease diagnosis and treatment, thereby providing an objective basis for evidence-based medicine. In the following section, we highlight the primary achievements in using AI technology to investigate the scientific basis of TCM treatments for CVDs.

3.1 AI-guided integrative TCM inspection for risk prediction and early screening

Hypertension is a risk factor for heart attack and stroke. Early detection of combined coronary heart disease (CHD) in patients with hypertension can prevent more severe events. In TCM theory, the heart's orifice is the tongue. Information based on the tongue can reveal various physiological and pathological features of the heart [45]. ZHAO et al. [46] segmented 154 tongue images into five regions (the tip, left side, middle, right side, and root of the

tongue) and used hyperspectral images to compare the tongue spectra of hypertensive patients with and without CHD. The two groups showed significant differences in the tip and middle regions. A neural network was constructed to perform classification, which afforded a prediction accuracy, sensitivity, and specificity of 84.78%, 86.95%, and 82.61%, respectively. In a recent study, ML was utilized to classify and predict pulse waves in patients with hypertension and in healthy subjects [47]. The risk of hypertension was assessed by observing the dynamic changes in the pulse wave. A total of 450 hypertensive patients and 479 healthy volunteers were recruited to test a self-developed H20 questionnaire and pulse wave information acquisition system. Features with significant changes were h1/t1, w1/t, t, w2, h2, t1, and t5, whereas typical variables for ML and classical statistics were h1/t1, h5, t, Ad, BMI, and t2. The feasibility of digital pulse wave diagnosis and the dynamic evaluation of hypertension was considered in a previous study [47]. Using the multitask interaction attention learning model, WANG et al. [48] analyzed translational palm images and proposed the detection of metacarpophalangeal joints and palmar thenar to assist in the detection of acute myocardial infarction. Therefore, the integration of AI technology and classic TCM diagnostic methods would provide novel insights into the diagnosis of CVDs.

3.2 AI-guided TCM diagnosis and syndrome differentiation

TCM practitioners generally use four diagnostic inspection methods, i.e. visual inspection (望), auscultation and olfaction (闻), inquiry (问), and palpation (切), to obtain clinical information for the diagnosis of syndrome pattern recognition. Among the diagnostic methods, pulse diagnosis is an essential component of palpation. According to classical TCM concepts, arterial pulses at different locations of both wrists, named cun (寸), guan (关), and chi (尺), reflect the health conditions of the internal Zang Xiang and its related Qi-blood and Yin-Yang status. Changes in Zang and its related functions affect the pulse status, thus forming a unique diagnostic basis. Experienced TCM practitioners can sense changes in pulse patterns when performing diagnosis. Pulse diagnosis in TCM depends significantly on the experience of TCM practitioners. The standardization and digitization of arterial pulse are important for reliable and consistent diagnoses. To mimic experienced TCM practitioners in pulse diagnosis, pulse parameters under different pressure levels at the cun, guan, and chi points must be obtained accurately to classify 28 types of arterial pulses. Recently, we developed a pulse-sensing platform to investigate and digitalize arterial pulse patterns. This platform comprises a robotic hand with three pressure feedback-controlled robotic fingers (each comprising 4×6 sensing pixel arrays)

for pulse data acquisition and an ANN system for pulse pattern recognition. We identified three consistent pulse patterns described by TCM doctors in healthy human subjects. The classification rates were 99.1% and 97.4% for the training and testing processes, respectively, for the three basic pulse patterns [49, 50]. We are currently developing a high-level AI system to simultaneously record pulse parameters obtained by TCM practitioners. AI-guided pulse diagnosis can be incorporated with TCM constitutions to facilitate health evaluation and disease diagnosis. According to the TCM theory of “heart governing blood and vessel”, pulse diagnosis can be utilized to inspect physiological and pathological changes of the heart and blood vessels. XU et al. [51] obtained clinical information from 528 CHD patients and extracted variables via inquiry, inspection, the pulse time domain, and pulse recurrence quantification analysis. Using a support vector machine algorithm, they established a CHD diagnostic model that can map from symptoms and signs to syndromes. The pulse time-domain parameters obtained were used for syndrome differentiation in patients with CHD. The nonlinear dynamic characteristics of the pulse signal significantly increased the accuracy of the average recognition by 82.83%. This implies that AI can capture slight changes in the pulse signal, which reflect the health status of a human. AI analysis facilitates the accurate acquisition of pulse data and enhances objective pulse-based syndrome identification. In a recent study, a neural network correlation model was constructed to investigate the relationship between TCM syndrome elements and clinical physical and chemical indexes in patients with unstable angina pectoris complicated with anxiety, which provided a biological basis for TCM syndrome differentiation [52]. In addition, a back propagation neural network model based on the Quasi-Newton method was developed to analyze the tongue and pulse features of 3233 DM-CHD patients in a large-scale clinical study. The accuracy rates were 75.6% and 99.31% for the Qi-Yin deficiency with blood stasis (1353 cases) and Qi-Yin deficiency (836 cases), respectively. The AI model demonstrated superior performance in syndrome classification. However, the accuracy rate of Yin-Yang deficiency (480 cases) was only 46.32%. This suggests that neural network modeling requires numerous samples for learning to obtain a well-fitting model. As for the Qi-Yin deficiency with blood stasis syndrome, the additional symptoms will increase the complexity of the model computation, thus decreasing the model accuracy. Therefore, complex CVDs may require more intricate model structures to reveal the internal rules and features of TCM syndrome differentiation. A recent study pertaining to dynamic changes in CHD syndromes provided a good example [53], where 20 cases in each of the four categories were analyzed, including critical coronary stenosis and pre-intervention, based on a study period of 12 weeks

and more than one year of post-intervention for reduced cardiac functions. After performing a hierarchical processing of the symptoms, a non-linear mapping of symptoms to syndrome elements was simulated using a DL algorithm (transformer) in conjunction with the dropout method to construct a diagnostic system for CHD syndrome elements. The self-attentive mechanism in the transformer focused on the core symptoms and revealed the significance of core symptoms in diagnosing the syndrome elements. The dropout layer underwent regularization to address the general symptoms associated with the syndrome elements, thus increasing the model's flexibility and avoiding overfitting [54]. The average accuracy of the model was $96.46\% \pm 8.957\%$ when the specialist's diagnosis was regarded as the gold standard. Subsequently, the diagnostic system was applied to 1 221 hospitalized CHD cases. The DL-based system significantly reduced the amount of manual tasks and simultaneously classified syndrome elements efficiently and accurately. Furthermore, decision trees were adopted to analyze the rules and identification patterns for diagnosing TCM syndromes using physical and chemical indicators. Thus, advanced AI technology is particularly beneficial for disease diagnosis and syndrome differentiation.

3.3 AI-guided TCM treatment and efficacy evaluation

TCM is characterized by syndrome-based medications, which involve different TCM formulae for different syndromes. AI applications in TCM treatment primarily rely on therapeutic experience based on data mining and are geared toward achieving clinical efficacy. In a recent study, network pharmacology and ML were used to investigate the underlying mechanisms of eight classic TCM formulae for CHD treatment. By screening 669 potential bioactive compounds and 581 targets, the researchers showed that the formulae affected nine classes of CVD-associated drug targets. Network clustering and hierarchical clustering were performed to evaluate these formulae at five levels: herbs, symptoms, compounds, targets, and pathways. The results showed that three formulae used specifically for Qi stagnation and blood stasis, Qi deficiency and blood stasis, and Qi deficiency syndromes exerted anti-inflammatory and immune-enhancing effects by modulating the tumor necrosis factor (TNF) and nuclear factor kappa-B (NF- κ B) signaling pathways. Two formulae for heart-kidney Yin deficiency and heart-kidney Yang deficiency regulated the peroxisome proliferator-activated receptors (PPAR) and thyroid hormone signaling pathways in the endocrine system to improve renal function. This study provides a scientific basis for syndrome-based medications using TCM formulae for different CHD types [55].

Traditional Chinese medicine injections (TCMIs) have indicated significant benefits for heart failure with a

reduced ejection fraction. LIN et al. [56] performed a Bayesian network meta-analysis on 107 randomized controlled trials to evaluate the efficacy of conventional treatment with or without TCMIs. The results showed that treatments combined with Xinmailong injection (心脉隆注射液) or Shenmai injection (参麦注射液) yielded better effects than conventional treatment alone. Xinmailong injection improved cardiac function and reduced the levels of brain natriuretic peptide and N-terminal pro-brain natriuretic peptide. By contrast, Shenmai injection enhanced the 6-min walking test and left ventricular end-diastolic and end-systolic functions.

Data mining involves querying and extracting significant amounts of data stored in databases to obtain implicit information, patterns, and rules for decision making and generalizing information [57, 58]. TCM data mining primarily involves clustering analysis, association rules, and logistic regression. Additionally, ML algorithms have been used to investigate TCM syndrome distribution, medication regularity, and acupuncture point selection rules as well as to analyze the clinical experiences of well-known TCM practitioners [59]. BI et al. [60] analyzed 715 Chinese herbal prescriptions for CHD treatment. Using association rules (Apriori algorithm) in conjunction with the "top-N group" method [61], they analyzed the typical herbal combinations and summarized the empirical prescriptions. Subsequently, they applied network pharmacology to identify the bioactive components and their targets in core prescriptions.

3.4 AI-guided inheritance of TCM practical experience

Data mining techniques can be used to inherit the clinical experience of senior TCM practitioners. AI-guided TCM inheritance can objectify, structure, and visualize the experiences of renowned TCM practitioners. By combining pharmacology, pathophysiology, bioinformatics, and other knowledge, AI analysis can reveal the intrinsic logical strategies and mechanisms of TCM diagnosis and treatment [62]. LIAN et al. [63] retrieved the experiences and experimental cases of 90 TCM masters treating heart palpitations. They analyzed the herb grouping pattern using the Apriori algorithm and complex system entropy clustering method. The TCM heritage assistance platform has accelerated the progress of TCM data-mining. LI et al. [64] adopted an improved mutual information method, association rules, complex system entropy clustering, and unsupervised entropy hierarchical clustering to analyze the medication experience and herbal grouping rules of prescriptions for 122 cases involving frequent ventricular premature complexes; subsequently, they visualized the core prescription herbal associations using Cytoscape. Notably, studies regarding AI-guided TCM inheritance are limited. Hence, well-designed clinical trials should be performed using advanced AI technology to further

develop personalized treatments for CVDs that are similar to those afforded by senior TCM practitioners.

4 Challenges and perspectives

The goal of AI is to equip machines with human intelligence to perform various tasks, including perceptions and movements (physical tasks) as well as complex reasoning, decision-making, and learning (mental tasks). Currently, in some tasks, AI has demonstrated performance far exceeding that afforded by humans [65]. The autonomous learning, inductive deduction, and low error rate of AI has resulted in more convenience and fresh perspectives to TCM. Thus, AI technology can promote synergy between TCM and multiple disciplines/fields, thus realizing more significant achievements.

Nevertheless, several challenges must be overcome in the development and application of AI technology. Extensive data analysis and the execution of large models require high computing power, which inevitably necessitates high-performance computer hardware. Data are the primary impetus that promote the development of AI for achieving better recognition rates and accuracy. Electronic case structurization and data acquisition standardization must be enhanced to form a large-scale, high-quality, and comprehensive CVD database of TCM [66]. Furthermore, the breadth and depth of the dataset must be increased by acquiring samples containing multilevel modern medical data from various regions and periods of disease [67, 68]. Moreover, the underlying algorithms must be further developed to enhance the algorithm performance and adaptability for managing small-sample and multimodal medical data with noise [69]. Additionally, the advanced application of AI necessitates professional insights and the ability to utilize AI techniques. Suitable feature extraction methods and algorithms must be selected in conjunction with the data type and task purpose of specific application scenarios. To illustrate, decision trees and clustering methods are more frequently applied owing to their high interpretability, whereas artificial neural networks are less interpretable but can solve complicated problems with an excellent fit to complex functions. Hence, the interpretability and accuracy of AI algorithms must be balanced [70]. Furthermore, insufficient comparison and integration among multiple modeling algorithms have been reported. Finally, although AI has demonstrated impressive progress in tongue imaging [71], the application of AI in studies pertaining to TCM treatment is premature. More importantly, to validate the capability of AI, close collaborations with domain experts must be realized and research achievements must be applied to disease-oriental clinical studies or healthcare systems [72].

The advent of the information age has promoted the intersection of Chinese medicine, modern medicine, computer science, and other disciplines. Although AI

must be further developed before it can be fully applied in clinical practice, it has accelerated the era of individualized and precision medicine hitherto. The construction of an AI-based comprehensive diagnosis and treatment system with TCM characteristics will provide more accurate and objective support for the prevention, diagnosis, and treatment of CVDs. More efforts are to be expended to integrate AI technology with Chinese medicine.

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Competing interests

The authors declare no conflict of interest.

References

- [1] HUANG ML, WU YS. Classification of atrial fibrillation and normal sinus rhythm based on convolutional neural network. *Biomedical Engineering Letters*, 2020, 10(2): 183-193.
- [2] ZHANG G, YU C, ZHOU M, et al. Burden of Ischaemic heart disease and attributable risk factors in China from 1990 to 2015: findings from the global burden of disease 2015 study. *BMC Cardiovascular Disorders*, 2018, 18(1): 1-13.
- [3] ROTH GA, JOHNSON C, ABAJOBIR A, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. *Journal of the American College of Cardiology*, 2017, 70(1): 1-25.
- [4] The Writing Committee of the Report on Cardiovascular Health and Diseases in China. Report on cardiovascular health and diseases in China 2021: an updated summary. *Chinese Circulation Journal*, 2022, 37(6): 553-578.
- [5] WEIKANG B, DAIMIN Z, XIAOXIN J, et al. Application of artificial intelligence in the diagnosis and treatment of cardiovascular diseases. *Chinese Journal of Hypertension*, 2020, 28(2): 124-131.
- [6] AMBALEVENKATESH B, YANG X, WU CO, et al. Cardiovascular event prediction by machine learning: the multi-ethnic study of atherosclerosis. *Circulation Research*, 2017, 121(9): 1092-1101.
- [7] AMIN MS, CHIAM YK, VARATHAN KD. Identification of significant features and data mining techniques in predicting heart disease. *Telematics and Informatics*, 2019, 36: 82-93.
- [8] ASAN O, BAYRAK AE, CHOUDHURY A. Artificial intelligence and human trust in healthcare: focus on clinicians. *Journal of Medical Internet Research*, 2020, 22(6): e15154.
- [9] NAMASIVAYAM V, SENGUTTUVAN N, SARAVANAN V, et al. Artificial intelligence and its application in cardiovascular disease management. *Machine Learning and Systems Biology in Genomics and Health*, 2022: 189-236.
- [10] HE J, BAXTER SL, XU J, et al. The practical implementation of artificial intelligence technologies in medicine. *Nature Medicine*, 2019, 25(1): 30-36.
- [11] ZHENG W, YAN L, GOU C, et al. Computational knowledge

- vision: paradigmatic knowledge based prescriptive learning and reasoning for perception and vision. *Artificial Intelligence Review*, 2022: 1–36.
- [12] HINTON GE, OSINDERO S, TEH YW. A fast learning algorithm for deep belief nets. *Neural Computation*, 2006, 18(7): 1527–1554.
- [13] HOLCOMB SD, PORTER WK, AULT SV, et al. Overview on deepmind and its Alphago Zero AI. Proceedings of the 2018 International Conference on Big Data and Education, 2018: 67–71.
- [14] RUSSELL SJ, NORVIG P. Artificial intelligence: a modern approach. 3rd ed. Upper Saddle River: Prentice Hall, 2010.
- [15] MITCHELL TM. Machine learning. New York: McGraw-Hill, 1997.
- [16] HAKAK S, ALAZAB M, KHAN S, et al. An ensemble machine learning approach through effective feature extraction to classify fake news. *Future Generation Computer Systems*, 2021, 117: 47–58.
- [17] XU Y, GOODACRE R. On splitting training and validation set: a comparative study of cross-validation, bootstrap and systematic sampling for estimating the generalization performance of supervised learning. *Journal of Analysis and Testing*, 2018, 2(3): 249–262.
- [18] HEDMAN ÅK, HAGE C, SHARMA A, et al. Identification of novel pheno-groups in heart failure with preserved ejection fraction using machine learning. *Heart*, 2020, 106(5): 342–349.
- [19] SSHAH SJ, KATZ DH, SELVARAJ S, et al. Phenomapping for novel classification of heart failure with preserved ejection fraction. *Circulation*, 2015, 131(3): 269–279.
- [20] LECUN Y, BENGIO Y, HINTON G. Deep learning. *Nature*, 2015, 521(7553): 436–444.
- [21] KOLEK MJ, GRAVES AJ, XU M, et al. Evaluation of a prediction model for the development of atrial fibrillation in a repository of electronic medical records. *JAMA Cardiol*, 2016, 1(9): 1007–1013.
- [22] PAVLOU M, AMBLER G, SEAMAN SR, et al. How to develop a more accurate risk prediction model when there are few events. *British Medical Journal*, 2015, 351: h3868.
- [23] SHU S, REN J, SONG J. Clinical application of machine learning-based artificial intelligence in the diagnosis, prediction, and classification of cardiovascular diseases. *Circulation Journal*, 2021, 85(9): 1416–1425.
- [24] POPLIN R, VARADARAJAN AV, BLUMER K, et al. Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. *Nature Biomedical Engineering*, 2018, 2(3): 158–164.
- [25] YING A, NENGJUN H, RONG Y, et al. Deep learning-based model for risk prediction of cardiovascular diseases. *Chinese Journal of Medical Physics*, 2019, 36(9): 1103–1112.
- [26] CHEN W, HUANG H, HUANG J, et al. Deep learning-based medical image segmentation of the aorta using XR-MSF-U-Net. *Computer Methods and Programs in Biomedicine*, 2022, 225: 107073.
- [27] LITJENS G, CIOMPI F, WOLTERINK JM, et al. State-of-the-art deep learning in cardiovascular image analysis. *JACC: Cardiovascular Imaging*, 2019, 12(8 Part 1): 1549–1565.
- [28] XIAOTONG Z, CHUNYING P, HAN Z. Prediction model of cardiovascular disease based on deep learning. *Journal of Computer Applications*, 2021, 41(S2): 346–50.
- [29] BELLO GA, DAWES TJ, DUAN J, et al. Deep-learning cardiac motion analysis for human survival prediction. *Nature Machine Intelligence*, 2019, 1(2): 95–104.
- [30] YU S, TIAN Z. Research on application of artificial neural network in HRV analysis. *Computer Technology and Development*, 2017, 27(09): 141–144, 149.
- [31] JOHNSON KW, TORRES SOTO J, GLICKSBERG BS, et al. Artificial intelligence in cardiology. *Journal of the American College of Cardiology*, 2018, 71(23): 2668–2679.
- [32] MALIK J, DEVECIOGLU OC, KIRANYAZ S, et al. Real-time patient-specific ECG classification by 1D Self-Operational Neural Networks. *IEEE Transactions on Biomedical Engineering*, 2021, 69(5): 1788–1801.
- [33] ANTMAN EM, LOSCALZO J. Precision medicine in cardiology. *Nature Reviews Cardiology*, 2016, 13(10): 591–602.
- [34] JOHNSON KW, SHAMEER K, GLICKSBERG BS, et al. Enabling precision cardiology through multiscale biology and systems medicine. *Basic to Translational Science*, 2017, 2(3): 311–327.
- [35] SHAH SJ, KITZMAN DW, BORLAUG BA, et al. Phenotype-specific treatment of heart failure with preserved ejection fraction: a multiorgan roadmap. *Circulation*, 2016, 134(1): 73–90.
- [36] YASMIN F, SHAH SMI, NAEEM A, et al. Artificial intelligence in the diagnosis and detection of heart failure: the past, present, and future. *Reviews in Cardiovascular Medicine*, 2021, 22(4): 1095–1113.
- [37] LUO Y, AHMAD FS, SHAH SJ. Tensor factorization for precision medicine in heart failure with preserved ejection fraction. *Journal of Cardiovascular Translational Research*, 2017, 10(3): 305–312.
- [38] MNIH V, KAVUKCUOGLU K, SILVER D, et al. Human-level control through deep reinforcement learning. *Nature*, 2015, 518(7540): 529–533.
- [39] SILVER D, SCHRITTWIESER J, SIMONYAN K, et al. Mastering the game of Go without human knowledge. *Nature*, 2017, 550(7676): 354–359.
- [40] LI X, ZHANG J, HUANG J, et al. A multicenter, randomized, double-blind, parallel-group, placebo-controlled study of the effects of Qili Qiangxin capsules in patients with chronic heart failure. *Journal of the American College of Cardiology*, 2013, 62(12): 1065–1072.
- [41] HAO PP, JIANG F, CHEN YG, et al. Traditional Chinese medication for cardiovascular disease. *Nature Reviews Cardiology*, 2015, 12(2): 115–122.
- [42] HAO P, JIANG F, CHENG J, et al. Traditional Chinese medicine for cardiovascular disease: evidence and potential mechanisms. *Journal of the American College of Cardiology*, 2017, 69(24): 2952–2966.
- [43] YANG HY, LIU ML, LUO P, et al. Network pharmacology provides a systematic approach to understanding the treatment of ischemic heart diseases with traditional Chinese medicine. *Phytomedicine*, 2022, 104: 154268.
- [44] DINHLE C, CHUANG R, CHOKSHI S, et al. Wearable health technology and electronic health record integration: scoping review and future directions. *JMIR mHealth and uHealth*, 2019, 7(9): e12861.
- [45] HAIYUN S, LING W, YIQIN W, et al. Progress of the correlation study between tongue information and clinical test indicators of coronary artery disease. *Modernization of Traditional*

- Chinese Medicine and Materia Medica-World Science and Technology, 2021, 23(3): 834-838.
- [46] ZHAO J, MA B, LIU M, et al. Screening for combined coronary artery disease in hypertensive patients with hyperspectral imaging of tongue. *Spectroscopy and Spectral Analysis*, 2022, 42(2): 512-516.
- [47] LUO ZY, CUIJ, HU XJ, et al. A study of machine-learning classifiers for hypertension based on radial pulse wave. *BioMed Research International*, 2018, 2018: 2964816.
- [48] WANG Q, ZHAO C, QIANG Y, et al. Multitask interactive attention learning model based on hand images for assisting Chinese medicine in predicting myocardial infarction. *Computational and Mathematical Methods in Medicine*, 2021, 2021: 6046184.
- [49] KONG KW, CHAN HY, HUANG Q, et al. Sphygmopalpation using tactile robotic fingers reveals fundamental arterial pulse patterns. *IEEE Access*, 2022, 10: 12252-12261.
- [50] LEUNG YLA, GUAN BH, CHEN S, et al. Artificial intelligence meets traditional Chinese medicine: a bridge to opening the magic box of sphygmopalpation for pulse pattern recognition. *Digital Chinese Medicine*, 2021, 4(1): 1-8.
- [51] XU WJ, PAN L, YAN HX, et al. Application of syndrome diagnosis model with 528 cases of coronary heart disease based on TCM pulse nonlinear dynamics characteristics. *China Journal of Traditional Chinese Medicine and Pharmacy*, 2014, 29(5): 1661-1665.
- [52] CHEN X, WANG Y, ZHANG L, et al. Construction and evaluation of neural network correlation model between syndrome elements and physical and chemical indexes of unstable angina pectoris complicated with anxiety. *Computational and Mathematical Methods in Medicine*, 2022, 2022: 6217186.
- [53] LI HZ, WANG J, ZHANG ZP, et al. Study on distribution and combination rule of syndrome elements in coronary artery disease based on modified transformer algorithm. *World Science and Technology-Modernization of Traditional Chinese Medicine and Materia Medica*, 2021, 23(9): 3086-3094.
- [54] SRIVASTAVA N, HINTON G, KRIZHEVSKY A, et al. Dropout: a simple way to prevent neural networks from overfitting. *The Journal of Machine Learning Research*, 2014, 15(1): 1929-1958.
- [55] YANG J, TIAN S, ZHAO J, et al. Exploring the mechanism of TCM formulae in the treatment of different types of coronary heart disease by network pharmacology and machining learning. *Pharmacological Research*, 2020, 159: 105034.
- [56] LIN S, SHI Q, GE Z, et al. Efficacy and safety of traditional Chinese medicine injections for heart failure with reduced ejection fraction: a bayesian network meta-analysis of randomized controlled trials. *Frontiers in Pharmacology*, 2021: 12.
- [57] ISHAQ A, SADIQ S, UMER M, et al. Improving the prediction of heart failure patients' survival using SMOTE and effective data mining techniques. *IEEE access*, 2021, 9: 39707-39716.
- [58] LASHARI SA, IBRAHIM R, SENAN N, et al. Application of data mining techniques for medical data classification: a review. *MATEC Web of conferences*, 2018. doi: 10.1051/mateconf/201815006003.
- [59] QIAN L, HAO X. Visualization analysis of literature of TCM data mining based on CiteSpace software. *Chinese Journal of Integrated Traditional and Western Medicine*, 2020, 40(1): 46-51.
- [60] BI SL, XU L, CHEN SQ, et al. Detection of herbal combinations and pharmacological mechanisms of clinical prescriptions for coronary heart disease using data mining and network pharmacology. *Evidence-Based Complementary and Alternative Medicine*, 2021, 2021: 9234984.
- [61] XU L, CHEN SQ, BI SL, et al. editors. The "top N groups" method used to mine the empirical formula based on Apriori algorithm. 2019 10th International Conference on Information Technology in Medicine and Education (ITME), 2019. doi: 10.1109/ITME.2019.00172.
- [62] MI HY, WEI C, LI HR, et al. Bayesian-algorithm-based study of coronary heart disease angina pectoris cases treated by Professor WU Yi-ling. *Chinese Journal of Integrated Traditional and Western Medicine*, 2018, 38(5): 534-538.
- [63] LIAN WJ, LI HZ, LIU JL, et al. The rule of prescription for treating heart palpitation by masters of traditional Chinese medicine. *Chinese Journal of Integrative Medicine on Cardio-cerebrovascular Diseases*, 2022, 20(5): 820-825.
- [64] LI HZ, ZHAO X, WANG J, et al. Research on inheritance of Professor WANG Jie's experience in treatment of frequent ventricular premature complexes based on inheritance support system of traditional Chinese medicine. *Chinese Journal of Experimental Traditional Medical Formulae*, 2021, 27(7): 161-168.
- [65] RUSSELL SJ. *Artificial Intelligence: A Modern Approach*. New York: Pearson Education, 2010.
- [66] ISLAM MS, HASAN MM, WANG X, et al. A systematic review on healthcare analytics: application and theoretical perspective of data mining. *Healthcare*, 2018, 6(2): 54.
- [67] BI Y, WANG X, ZHAO Z, et al. Clinical epidemiological investigation of the regional characteristics of TCM syndrome in coronary heart disease. *Journal of Traditional Chinese Medicine*, 2020.
- [68] WU Y, ZHANG F, YANG K, et al. SymMap: an integrative database of traditional Chinese medicine enhanced by symptom mapping. *Nucleic Acids Research*, 2019, 47(D1): D1110-D1117.
- [69] ZEYE L, XIANGBIN P. Application of artificial intelligence in prevention and treatment of cardiovascular diseases. *Chinese Journal of Clinical Thoracic and Cardiovascular Surgery*, 2022, 29(9): 1230-1235.
- [70] ADADI A, BERRADA M. Explainable AI for healthcare: from black box to interpretable models. *Embedded Systems and Artificial Intelligence*, 2020: 327-337.
- [71] FENG L, HUANG ZH, ZHONG YM, et al. Research and application of tongue and face diagnosis based on deep learning. *Digital Health*, 2022, 8: 20552076221124436.
- [72] ALLEN JRB, SELTZER SE, LANGLOTZ CP, et al. A road map for translational research on artificial intelligence in medical imaging: from the 2018 National Institutes of Health/RSNA/ACR/The Academy Workshop. *Journal of the American College of Radiology*, 2019, 16(9): 1179-1189.

人工智能及其在中医心血管疾病中的应用

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【摘要】心血管疾病是全球主要的高致死性疾病, 早期预测心血管事件的风险可以降低急性心肌梗死的发生率, 降低心血管疾病患者的死亡率。由于心血管疾病复杂的病理机制和多因素参与心血管病的发生和发展过程, 传统的数据分析无法有效处理心血管疾病和从多维数据层面预测心血管疾病风险、解读医学影像、提出治疗决策和预测疾病预后。另一方面, 中医药已被广泛用于治疗心血管疾病, 中医药在心血管疾病的诊治方面具有独特的理论和实践体系。多学科技术探索中医诊断方法产生的大数据难以用传统方法进行分析, 同时, 中医配方含有多种草药成分, 阐明活性化合物和网络调节的复杂相互作用也需要先进的数据分析能力。人工智能技术的最新进展为解决这些挑战提供了强大的工具, 极大地促进了发展中西医结合诊断和治疗策略以及理解中药复方治疗心血管病的科学原理。我们简要介绍了人工智能和机器学习技术的基本概念和最新进展, 并总结了先进的人工智能和机器学习在心血管疾病诊断和治疗中的应用。此外, 我们还回顾了利用综合人工智能和机器学习技术研究心血管疾病中医诊治科学依据的主要进展。我们预期人工智能和机器学习技术的应用将促进中西医对话以及为发展现代中西医结合诊治心血管疾病创造巨大机遇。

【关键词】 中医; 心血管疾病; 人工智能; 机器学习; 深度学习