Impact of artificial intelligence and digital twin technology on cardiovascular disease diagnosis and management challenges and future directions (Review)

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Abstract. The incidence of cardiovascular disease (CVD) is rising steadily and continues to be the major cause of mortality worldwide. The pressing requirement is to develop personalised healthcare solutions. Digital twin (DT) and artificial intelligence (AI) technology can change the treatment of CV through personal disease modelling, risk stratification, diagnosis and prediction. AI-powered DT technologies develop patient-specific simulations that aid in early diagnosis, optimized treatment and post-intervention monitoring. Machine learning algorithms and deep neural networks enable real-time data identity from electronic health records, portable sensors and medical imaging to continuously update digital twins to represent physiological changes. AI-powered DT models also help in better clinical decision-making by modelling disease progression and accurately predicting treatment outcomes. However, its universal adoption is hampered by issues of data privacy concerns, computational power requirements, and regulatory compliance. Strengthening these capabilities using good data stewardship, interdisciplinarity and next-generation computational architectures will accelerate the use of DT technology in cardiovascular medicine. The present review emphasizes the applications of AI-based DT models to correct the future of accurate cardiology, pursue the patient's results and reduce the burden of health care.

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Contents

1. Introduction

Cardiovascular diseases (CVDs) are heart and blood vessel disorders. Among these are hypertension (high blood pressure), coronary artery disease (CAD; expressed as heart attacks), cerebrovascular diseases (such as strokes), heart failure and other vascular-related ailments. CVD comprises heart muscle and circulatory system diseases that supply the heart, brain and other organs (1,2). Despite being a non-communicable disease, CVD continues to be the number one cause of mortality worldwide, as well as the leading cause of high morbidity and mortality rates worldwide (3,4). Hypertension is a chronic condition characterized by consistently elevated arterial blood pressure, which exerts excessive force on the vascular walls. It is often asymptomatic during the early stages, but progressively damages the cardiovascular system, contributing to complications such as left ventricular hypertrophy, atherosclerosis, renal dysfunction, and increased risk of stroke and myocardial infarction. CAD arises due to the accumulation of atherosclerotic plaques within the coronary arteries, leading to restricted blood flow to the myocardium. Clinically, it manifests as angina pectoris and, in the advanced stages, as myocardial infarction (heart attack), which occurs when a plaque ruptures and forms a thrombus, causing complete arterial occlusion. Cerebrovascular diseases, such as ischemic and haemorrhagic strokes, result from disruption of blood supply to the brain. Ischemic stroke is caused by arterial blockage, whereas haemorrhagic stroke is due to vessel rupture. Both can lead to irreversible neurological damage and are often precipitated by longstanding hypertension or atherosclerosis. Heart failure is a clinical syndrome in which the heart becomes unable to pump sufficient blood to meet the metabolic demands of the body. It may arise from chronic hypertension, myocardial infarct, or cardiomyopathies. Affected patients usually present with fatigue, dyspnoea and oedema. Heart failure reduces the quality of life of patients and has a high potential for hospitalization and mortality (5).

CVD is the number one cause of mortality globally. Estimates by the World Health Organization (WHO) indicate that CVDs are the cause of ~17.9 million deaths eachyear, which translates to ~32% of total global deaths (6). Of note, >75% of such deaths occur in low- and moderate-income countries, reflecting intensive differences in access to healthcare and preventive interventions (7). The burden is complemented by those modifiable risk factors such as unhealthy eating habits, physical inactivity, smoking and excessive alcohol consumption. In addition, the incidence of diseases such as hypertension, diabetes and overweight, heart attack and stroke also increases. The Global Burden of Disease Study also reported that global deaths due to CVD increased from 12.4 million in 1990 to 19.8 million in 2022, underscoring the escalating nature of this public health challenge (8).

Ischemic heart disease (IHD), stroke, and Congestive heart failure (CHF) collectively contribute to ~80% of CVD-related deaths, while other conditions are presented in Fig. 1. IHD, also known as CAD, is characterized by a low blood supply to the heart muscle due to the narrowing or blockage of coronary arteries. This leads to chest pain (angina) and, if left untreated, can result in myocardial infarction (heart attack). It is the most common form of CVD and a major contributor to sudden cardiac death globally. Stroke is a cerebrovascular disorder that occurs when the blood supply to part of the brain is interrupted or reduced, depriving brain tissue of oxygen and nutrients (9). It can be classified into ischemic stroke (caused by blockage of a cerebral artery) and haemorrhagic stroke (caused by rupture of a blood vessel). Stroke is a main cause of disability and mortality, particularly among the aging population.CHF, also referred to simply as heart failure, is a chronic, progressive disease where the heart cannot effectively pump blood enough to meet the needs of the body. It usually results in conditions, such as IHD and high blood pressure. CHF is characterized by the presence of signs and symptoms such as fatigue, shortness of breath and fluid overload, and an important cause of entry into the hospital among the elderly (10,11).

There is a significant requirement for more accurate, effective and individual clinical and medical strategies with the increasing stress and diversity of heart disease, such as IHD, stroke and heart failure. The conventional risk models are usually inadequate in representing the heterogeneity of CVD presentations and patient outcomes. In the current context, novel technologies, such as artificial intelligence (AI) and digital twin (DT) technology have the potential to transform cardiovascular care by facilitating data-driven, patient-specific treatment. The present review discusses the inclusion of AI and DT technologies within cardiovascular medicine, and their ability to enhance diagnosis, individualize treatment and meet the significant challenges in CVD management.

Genetic aetiology for CVD is currently regarded as being crucial to its pathogenesis, both with monogenic and polygenic input determining the susceptibility of the individual. It has been found that a number of 'key genes' have contributed to different CVD conditions. Apolipoprotein E is associated with lipid metabolism and the risk of atherosclerosis, specifically with the ε4 allele, increasing levels of low-density lipoprotein (LDL) cholesterol and contributing to the development of CAD (12). LDL receptor gene mutations are associated with familial hypercholesterolemia, a disease-causing premature atherosclerosis. Proprotein convertase subtilisin/kexin type 9, another gene of lipid metabolism, regulates LDL receptor degradation, and gain-of-function mutations lead to hyperlipidaemia, but loss-of-function variants are protective against CAD (13). In addition, endothelial nitric oxide synthase, which controls vascular tone and endothelial function, is implicated in hypertension and endothelial dysfunction (14). Angiotensin-converting enzyme gene polymorphisms affect blood pressure control and myocardial remodelling, and the I/D polymorphism is most significantly associated with hypertensive heart disease and myocardial infarction (15). Additionally, myosin heavy chain 7 and troponin T2 are critical sarcomeric genes implicated in cardiomyopathies and heart failure. The discovery of these genetic determinants is critical for understanding disease pathophysiology, risk stratification and further developing precision medicine strategies in cardiovascular diseases (16).

Personalized medicine is a strategy aimed at personalizing treatment and interventions tailored to the individual by different factors, such as the genetic makeup, lifestyle habits and environmental exposures of the patient, since these significantly determine outcomes and responses to treatment (16). Personalized medicine in cardiology has immense potential for the identification and treatment of various conditions, such as cardiomyopathies and arrhythmias. Additionally, it can improve drug selection and assist in reducing adverse drug reactions. In the age of personalized medicine, digital twin technology is an innovative strategy with huge potential to transform the delivery of health services (17).

DT technology originated from the aviation industry and is currently applied to numerous industries, such as medicine.

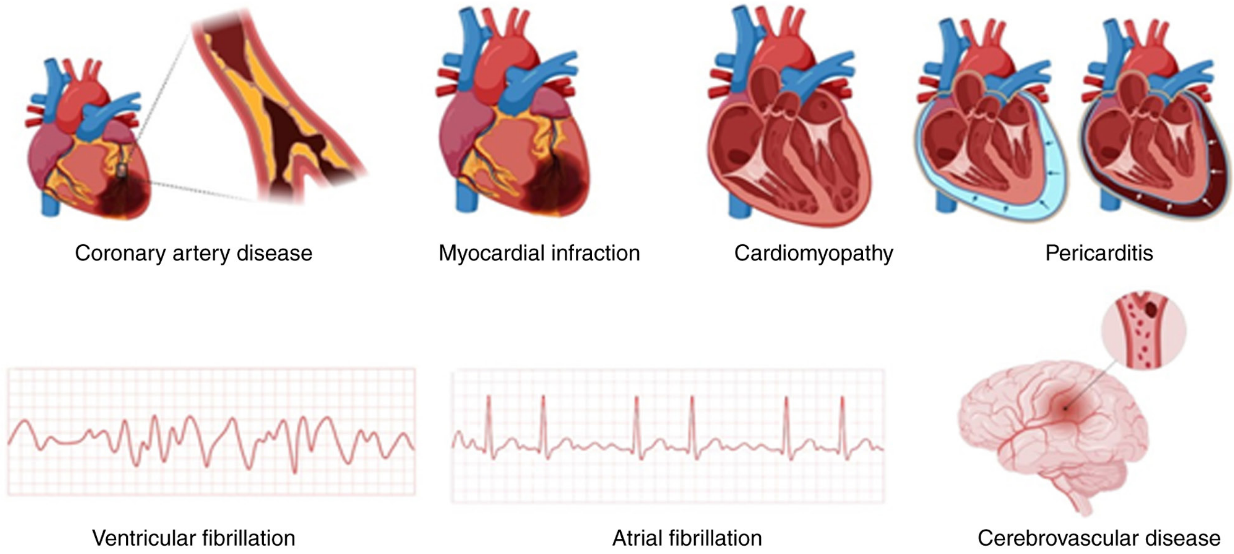

Figure 1. Major cardiovascular diseases.

A DT a computer model of a real counterparty, used for predicting treatment outcomes and prognosis for the physical twin. DTs provide doctors with a image of the patient's health, making it possible to have personalized treatment plans and interventions. AI-powered DT technology can refine accuracy in the treatment of CVDs (18,19). DT technology is continuously reinforced with information from its physical counterpart. Perhaps the greatest strength of DT technology is their capacity to incorporate and process various datasets, such as wearable devices, genetic information, electronic health records (EHRs) and patient-reported data (20,21).

2. Digital twin technology

Definition and origins of DTs. DT technology is rapidly evolving and is used across numerous industries and domains. A digital twin is a multi-dimensional virtual representation of a physical object or system (real-life twin) that integrates data to enable stimulation, monitoring, optimization and predictive maintenance (22-24). DT technology was first introduced by Michael Grieves in 2002 and was initially applied in the aerospace industry at NASA for product lifecycle management (24,25). Over time, this technology has evolved and diversified across numerous industries, becoming a cornerstone of the Fourth industrial Revolution (Industry 4.0) (26). The integration of cutting-edge technologies, such as internet of things (IoT), AI and big data has driven the growth and widespread application of digital twins across various industries (27,28). The development of DTs for CVDs is illustrated in Fig. 2.

General applications in healthcare and other industries. DT technology has been widely and efficiently employed in various sectors, including healthcare system management, public health and disease management, and personalized medicine. It aids in developing patient-specific models that support accurate diagnosis and tailored treatment planning, thereby advancing the effectiveness of personalized medicine. Additionally, DTs are used to model public health processes, predict disease spread, and managing resources during pandemics (29-33). Furthermore, this technology is employed in urban planning, manufacturing products, logistics and supply chain by optimizing production processes, resource use, and infrastructure modelling, reducing downtime in manufacturing operations and improving urbanization. It also enhances logistics operations by simulating processes, predicting disruptions and optimizing delivery routes (34,35).

A growing body of research is currently applying DT technology across various medical specialties, including cardiovascular medicine. Several case studies have highlighted DT application and potential clinical impact. For instance, researchers from King's College London, Imperial College London, and the Alan Turing Institute created >3,800 anatomically accurate digital heart models using real patient data to examine how age, sex and lifestyle factors affect cardiac function (36). These digital twins are being used to improve treatments and guide drug development. Another case study from the Carle Illinois College of Medicine involved building DTs of patients with heart failure by integrating genomic and proteomic data, enabling personalized simulations of treatment responses (37). At Johns Hopkins University, patient-specific DTs of the heart have been developed to improve the precision of catheter ablation in atrial fibrillation. Additionally, the Turing Institute is working on cardiovascular DTs for patients with pulmonary arterial hypertension to simulate heart and blood flow dynamics for better monitoring and intervention planning. These studies underscore the growing clinical relevance of DT technology in cardiovascular care (38).

Relevance of DTs in cardiovascular medicine. DTs in cardiovascular medicine provide immense potential for advancing personalized care, enhance disease predication, and optimizing clinical decision making. DTs are virtual twins that replicate the anatomy and physiology of an individual's heart and circulatory system. DTs in cardiovascular medicine have exceptional applications including enhanced diagnostic

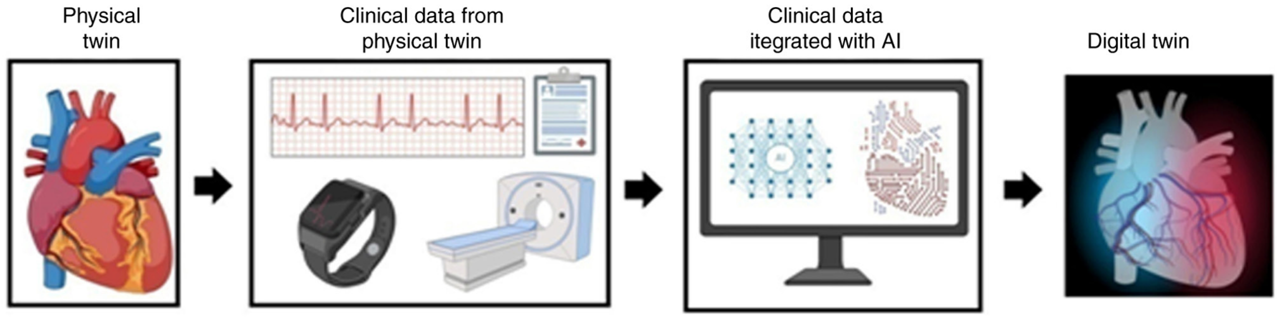

Figure 2. Digital twin technology in cardiovascular diseases. AI, artificial intelligence.

workflows by generating precise replicas to enhance disease phenotyping and diagnostic processes, personalized stimulations and prognostication to predict disease risk and improve procedural planning, clinical decision support and non-invasive planning using Electrocardiographic Imaging (ECGI) to guide interventions such as ablations (34,39,40).

Rationale for applying DTs to CVDs. DTs can mimic how cardiovascular systems operate in real-time, facilitating data-driven decision-making and the development of personalized treatment strategies. This technology is essential for tailoring patient-specific solutions and cost-effective treatment, rendering it an asset in the management of CVDs. The integration of big data analytics with DTs will significantly improve the monitoring of cardiovascular health and help anticipate complications before they arise, enabling timely interventions and effective management of CVDs (41,42). DT technology applications in CVD are illustrated in Fig. 3.

Methodology for DT technology in CVDs. The development of a DT for cardiovascular applications begins with the collection of different patient data, including electronic health records, medical imaging, wearable sensor data and genetic information. These data are then pre-developed and integrated through cleaning, harmonization and standardization. High-level modelling, such as physiological modelling and machine learning-based modelling, is utilized to establish a virtual twin (DT) of the cardiovascular system of the patient. The model is calibrated and validated by comparing its predictions with actual patient outcomes. Following validation, the DT is employed for clinical use, such as diagnosis support, risk prediction and personalized treatment planning. Over time, a feedback loop is maintained by updating the model with new patient data to increase accuracy over time (43).

3. Personalized disease modelling

To create patient-specific disease models based on DTs, patient data are originally obtained from different sources, including cardiac imaging [magnetic resonance imaging (MRI), CT scans], ECG data, genetic information and clinical history. This information is combined in computer simulations with the help of sophisticated tools such as AI and machine learning (ML). These technologies provide researchers and physicians with an electronic copy of the cardiovascular system of the patient to model heart functions, predict the development of the disease and use it with customized treatment options. The models are able to change the future with new information, give them dynamic and more accurate (44).

Creation of patient-specific cardiovascular models. DTs are the virtual model that accepts different types of modalities, such as imaging data, genomics data, or physiological monitoring make simulations representing cardiac function and disease progression accurately. The creation of a DT can be categorized into active, passive and semi-active. Thus, the first type of active DT model tracks the systemic circulation continuously at points that can be accessed and updates itself in real-time through the integration of data obtained in real-time. A passive DT describes the model of which creation had been offline, using a set of pre-collected data. A semi-active DT includes elements that exhibit a degree of dynamism. Recent innovations and advances in AI and ML have enhanced the capabilities of DT models, paving the way for real-time patient-specific simulations (45). Automated pipelines can efficiently extract fibre orientations and anatomical annotations of the heart from clinical data, streamlining the process, minimizing manual effort and reducing errors. Patient-specific models can also aid in optimizing procedures, such as cardiac ablation by forecasting long-term recurrence rates based on unique anatomical and physiological features. The integration of these models into broader healthcare systems is being investigated, particularly in relation to collaborative frameworks that could enable a virtual human twin project (46-48).

Risk prediction for myocardial infarction and arrhythmias. Myocardial infarction is defined as the death of myocardial cells due to prolonged ischemia. Worldwide, myocardial infarction presents as a silent killer, taking the lives of patients within seconds in the case that no medical attention reaches the victim. For diagnostic purposes, an ECG can serve to confirm a myocardial infarction, followed by ST-segment shifts or T-wave inversions, and elevated biochemical markers such as cardiac troponin, representing myocardial injury. Together with these, diagnosis is aided by other imaging techniques, such as radionuclide ventriculography, myocardial perfusion scintigraphy employing single photon emission computed tomography, and MRI (49,50). DTs couple clinical data with mechanistic models and data-driven approaches to improve training, optimally with personalized diagnosis and treatment planning. They further refine the inferred precision of myocardial tissue properties by taking cardiac MRI and

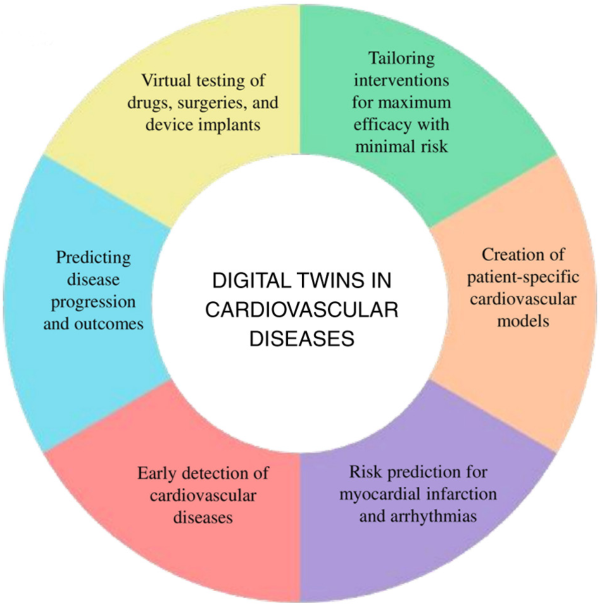

Figure 3. Applications of digital twin technology in cardiovascular diseases.

ECG as examples of multi-modal data, which are instrumental to building accurate models of myocardial infarction (51). Cardiac arrhythmias are irregularities or disruptions in the electrical activity of the heart. DTs allow for the analysis of electrical signals by simulating how arrhythmias develop based on the anatomy and physiology of an individual. DTs have the potential to predict the occurrence and pathways of ventricular tachycardia in patients with ischemic cardiomyopathy, as well as the risk of arrhythmia in patients with myocardial infarction. By evaluating the likelihood of arrhythmias, personalized heart models built from cardiac imaging data can predict future arrhythmic occurrences more accurately than current clinical measurements. This capability could enhance the identification of patients suitable for preventive ablation, ultimately lowering mortality and morbidity rates (40,52-54).

4. Diagnosis and predictive analytics

Early detection of CVDs. DTs create a virtual entity, not only of the physiological conditions of the real twin, but also of environmental and behavioural factors affecting heart health (55). An ECG is a widely used traditional method for diagnosing CVDs. DTs can simulate specific heart diseases using personalized ECG data. This method enhances early diagnosis and intervention by producing high-fidelity, patient-specific ECG signals; DTs improve the sensitivity of cardiac disease detection models (56). The integration of AT and ML with DTs enables real-time patient predictions and dynamic simulations, enhancing disease detection accuracy and clinical outcomes. Advanced techniques are employed to model blood flow and detect conditions, such as abdominal aortic aneurysms, including inverse analysis using recurrent neural networks. This approach enhances the identification and treatment of cardiovascular disorders through on-invasive data analysis (57).

Predicting disease progression and outcomes. DT technology exhibits promising results in predicting disease progression by integrating various data sources. The SynTwin method builds DTs to help precision medicine using network science and synthetic data. The notion that this approach improves clinical endpoint predictions by studying patient similarities and putting such similarities into a network community structure is proved. It demonstrates a higher predictive value with synthetic data than obtaining results directly from real datasets (58). In a previous observational study, a DT of patients with type 2 diabetes mellitus over a period of1year demonstrated significant changes in cardiovascular risk markers, including body weight, QRISK3 scores and A1c values. With personalized health counselling, digital twins can assist patients in migrating into lower-risk categories for cardiovascular conditions (59).

5. Treatment simulation and optimization

Virtual testing of medications, surgeries and implanted devices. DTs have been used to successfully test anti-arrhythmic medications (AADs) on patients with atrial fibrillation, including amiodarone, sotalol, dronedarone, flecainide, and propafenone. Digital twins may be able to assess the effectiveness of different AADs that could lessen the likelihood that atrial fibrillation would return following catheter ablation, according to research. This method opens the door for controlled and economical research into different drug combinations (60). Surgeons can model and plan surgical procedures based on the anatomy of each patient using the digital twin technique. Through simulation, the method enables healthcare professionals to anticipate possible challenges or issues that may arise during the procedure, enabling them to develop plans that lower risks and improve surgical results. In order to evaluate the impact that anatomical variations have on the functioning of cardiovascular devices, DTs are also utilized to model their deployment. This capability helps with medical device design and testing in terms of risk reduction and outcome optimization. DTs use simulation to maximize procedural planning and optimize the diagnostic process. To better understand the features of DTs and how they may be incorporated into clinical practice, further empirical research required (61,62).

Customizing interventions for optimal effectiveness, while minimizing risks. Through modelling how various drugs interact with the cardiovascular system of a patient, clinicians can determine the optimal dosing regimens, while minimizing side-effects. For example, DTs can estimate the way a patient will respond to various antihypertensive agents and thus prescribed pharmacotherapy to optimize blood pressure control without complications (63). DTs provide the benefit of testing intervention in a virtual environment before delivery. This capacity enables strict assessment of all possible treatment effects and risks and thus leads to ensuring clinical practice. DTs can be used to make accurate risk assessments of a variety of possible future health courses based on multiple treatment options. This strong predictive ability is crucial for determining the myriad of factors that can lead to adverse health outcomes, enabling healthcare professionals to anticipate and create strong contingency plans specific to the needs of each individual patient (64).

6. AI techniques integrated with digital twins for CVDs

Combining AI methods with DT technology for cardiovascular conditions yields substantial improvements in personalization, predictive analytics and decision-making in healthcare. This integration enables more advanced patient care through the early detection of risk factors, the simulation of disease progression, personalized treatment strategies, adaptive treatment monitoring and preoperative stimulations (65-67). By employing ML and deep learning methods, DTs are set to revolutionize cardiovascular patient care (68). AI powered DTs are automated, providing objective assessments and continuous health monitoring, which can help with early diagnosis and intervention, and reduce the dependence on human interpretation. For instance, the lung-DT framework classifies chest X-rays and tracks lung health in real-time using AI, providing insight that complement traditional diagnostic workflows, but do not replace them (69). DTs are utilized for synthesizing complex clinical data in CVDs to produce personalized models that guide therapy and inform prognosis. In order to support clinical decisions, these models provide a more thorough image of the patient's state by estimating parameters that are otherwise impossible to measure and addressing discrepancies in clinical measurements (70). Current research highlights that DTs can enhance and supplement present healthcare practices rather than completely replace them even though they can automate some diagnostic procedures and increase productivity. They are not considered stand-alone substitutes for conventional diagnostic techniques, but rather instruments to maximize resource allocation, enhance patient outcomes and lower expenses (71).

ML. ML is a branch of AI that focuses on the development of algorithms and statistical models to enable computers to learn from experience and create predictions (72). ML techniques are crucial in speeding up the efficiency of DT models. Through systematic processing and analysis of the huge amounts of data produced by monitoring patients, ML algorithms are able to identify key patterns and insights as a guide and improve clinical decision making. The capability of ML algorithms to predict CVD has been highly promising. Support vector machines and boosting algorithms have shown high predictive power for heart failure, cardiac arrhythmias, coronary artery disease and stroke, with combined area under the curve (AUC) values of 0.92 and 0.93, respectively (73,74). The two major areas of cardiovascular medicine where ML is widely used are echocardiography and electrocardiography, which are used to create predictive models for early disease identification and treatment optimization. These models enable timely interventions by assisting physicians in identifying individuals at higher risk of developing heart failure. The integration of machine learning algorithms with wearable sensors and digital stethoscopes further enhances the identification and treatment of cardiovascular diseases (75).

Supervised learning for predictive modelling. Supervised learning algorithms are trained using input data paired with their respective labels, which allows them to identify and model the underlying associations within the data. Bzdok *et al* (76) explored the impact of sample size and predictor count on logistic regression, random forests, and other supervised learning algorithms. Baessler *et al* (77) identified ML-based texture analysis that enabled the diagnosis of myocardial infarction on non-contrast-enhanced cardiac cine MRI, despite the absence of visible signal abnormalities. Ali *et al* (78) demonstrated the high accuracy of ML algorithms, including random forest (RF), decision tree (DT) and K-nearest neighbors (KNN), in heart disease prediction. Notably, RF, DT and KNN demonstrated exceptional performance on certain datasets, achieving 100% accuracy, sensitivity, and specificity, highlighting their potential for early and accurate heart disease diagnosis (79). Gosling *et al* (80) demonstrated the feasibility of using coronary CT angiography with fractional flow reserve (CT-FFR) to create DTs of patient-specific coronary arteries. These 3D models, combined with hemodynamic simulations, allow for the non-invasive assessment of coronary artery stenos is and virtual planning of percutaneous coronary interventions, providinga potential paradigm shift in cardiovascular care (80).

Unsupervised learning for pattern recognition and anomaly detection. The fundamental strength of unsupervised learning lies in its ability to autonomously explore data and identify hidden structures without the need for predefined labels or human intervention, rendering it a powerful tool for exploratory data analysis (81). Unsupervised learning can be divided into four categories: Association, auto encoders, clustering and anomaly detection. Finding data points in a dataset that considerably differ from expected or typical behaviour is the goal of anomaly detection (82). A new temporal convolutional network (TCN) auto encoder (TCN-AE) architecture was presented by Thill *et al* (83) for the automated identification of cardiac arrhythmias in ECG recordings. TCN-AEs reliably identify cardiac arrhythmias by recording the temporal dependencies in heartbeats using dilated convolutions. This innovative method outperformed current methods in arrhythmia diagnosis, exhibiting greater accuracy and efficacy (83). Using a modified DBSCAN (density-based spatial clustering of applications with noise) algorithm with adaptive parameter selection, Nanehkaran *et al* (84) presented a novel unsupervised method for the diagnosis of heart disease. Their approach effectively distinguishes between healthy and ill individuals by finding patterns in patient data. With a high accuracy of ~95%, their results demonstrated how well this method works to find patterns and anomalies in the patient data (84). Using only normal images for training, Nakao *et al* (85) successfully implemented an unsupervised auto-encoding generative adversarial network (AE-GAN) based method to detect anomalies, such as cardiomegaly and pleural effusion, in chest radiographs. Unsupervised ML for coronary artery disease was investigated by Flores *et al* (86) in 2021. Their approach discovered the subgroups hidden in patient by analysing both genetic and phenotypic data. This method may outperform conventional risk stratification models since it offers a more complex understanding of the illness and risk factors (86).

Deep learning. As an advanced development of ML, deep learning uses sophisticated algorithms to simulate human cognitive processes. To analyse data and make inferences, these algorithms create deep neural networks that are modelled after the structure of the human brain and nervous system. The most popular and effective deep learning models in clued convolutional neural networks (CNNs), recurrent neural networks (RNNs) and GANs, each suited for different types of data and tasks (87-89). Deep learning has shown promise in medical imaging, particularly in tasks, such as cardiac image classification, segmentation and anomaly detection with a higher accuracy from cardiac images generated from MRI, CT and ultrasound (90-92). Subramani *et al* (93) reported 96% accuracy in predicting cardiovascular disease outcomes using a combined deep learning and machine learning approach. Deep learning algorithms are being utilized more in predicting CVDs; however, addressing the biases, particularly for diverse populations remains a critical challenge. These models employ several strategies to reduce bias; however, effectiveness varies and disparities can persist across sex and racial groups. Bias in cardiovascular datasets often arises from imbalanced data, underrepresentation of minority groups, and systematic differences in data collection (94). The strategies to address bias include data balancing using techniques such as the synthetic minority over-sampling technique (SMOTE) and resampling are used to address class imbalance, improving model performance for underrepresented group. Synthetic data generation can supplement scarce patient records, improving model generalizability and performance across diverse populations (95). The use of data from multiple centres and varied populations is recommended to reduce bias and improve model robustness.

CNNs for segmenting and analysing images. CNNs are commonly used to analyse images, detect objects and segments in cardiovascular diseases. CNNs have been applied to various imaging modalities, including X-rays, CT and MRI, and they have been shown to increase the precision and effectiveness of the diagnosis of cardiovascular disease (96). In order to enhance cardiac image segmentation, more complex CNN architectures have been proposed, such as residual convolutional neural networks and dual-stream convolutional neural networks. These models use both intra-slice and inter-slice information to increase the segmentation accuracy of cardiac magnetic resonance (CMR) images. They have demonstrated encouraging outcomes in cardiac anatomy segmentation and disease diagnosis. Deep Dual-Stream Confusion Network Court has increased the accuracy of the cardiac image segmentation in the left and right ventricular cavity and myocardium compared to other techniques (97). The effectiveness of a fully convolutional neural network (FCN) in the automated evaluation of right atrium and left atrium CMR images in both long-axis and short-axis CMR images was demonstrated by Bai *et al* (98). FCN-based myocardial segmentation in CMR images has been proposed by Romaguera *et al* (99). Integrating image saliency and shape priors with CNNs has significantly improved segmentation results. Methods improve visual clarity in heart tissue and help with accurate location of cardiac areas, both are necessary for an accurate diagnosis (100,101).

RNNs for prediction and analysing time-series. A class of deep learning algorithms known as RNNs is designed to process sequential data efficiently. The ability to incorporate the memory of previous inputs when processing input sequences is the primary characteristic that sets RNNs apart (102,103). In a new predictive modelling framework for the early detection of heart failure, Choi *et al* (104) demonstrated the effectiveness of gated recurrent unit (GRU) deep learning techniques (104). An RNN model termed the deep heart failure trajectory model (DHTM) was developed by Lu *et al* (105) to forecast the long-term course of recurrent heart failure. An RNN-based method for predicting disease onset and risk based on EHR data was introduced by Rasmy *et al* (106) as the REverse Time AttentIoN (RETAIN) model. Shahi *et al* (107) proved the efficacy of RNNs in conjunction with echo state networks from reservoir computing in cardiac action potential predictions for at least 15-20 beats. The models, important for the comprehension of arrhythmic conditions, are of high accuracy in forecasting cardiac voltage time series, allowing for potential early intervention strategies (107). RNNs, particulalry bidirectional GRUs, have been used to classify ECG signals for biometric authentication and abnormal cardiovascular rhythm detection with high classification accuracy (108,109). The principal branches of AI utilized in the development and improvement of digital twins for the heart are illustrated in Fig. 4.

7. Challenges in digital twin technology

DT technology holds particular promise in transforming the delivery of CVD care through personalized medicine. Yet various critical challenges currently stand in the way of its universal acceptance. These are technical constraints in combining heterogeneous and multiform datasets, ethical considerations related to patient confidentiality and data integrity and a dearth of universal confidence based on inadequate verification of the digital twin models. The resolution of these critical issues, such as enhancing data integration, having stringent privacy controls and establishing trust through stringent validation is imperative for the adoption of this revolutionary technology in cardiovascular medicine. Conventional inverse analysis techniques fail to work for non-linear systems such asblood circulation in the cardiovascular system and require the use of more sophisticated techniques like recurrent neural networks (29). The exchange of real-time data among physical and virtual twins is a major challenge, demanding highly advanced technological infrastructure and expertise. In addition, the skilled hands necessary for operating and interpreting digital twin systems are a barrier to universal adaptation, restricting the target user base and enhancing the need for specialized education. Moral concerns regarding patient information privacy and monitoring also pose significant hurdles to the use of digital twin technologies. Overcoming this concern involves strict verification, validation, and uncertainty quantification to ensure that the simulations by the DTs are trustworthy (62).

Practical challenges. AI-powered DTs hold ample promise for improved patient outcomes and tailored therapy when incorporated into clinical procedures. Before these technologies can be extensively and successfully implemented in actual healthcare settings, a number of practical issues need to be resolved. DTs require the seamless integration of diverse data sources including electronic health records, wearable devices,

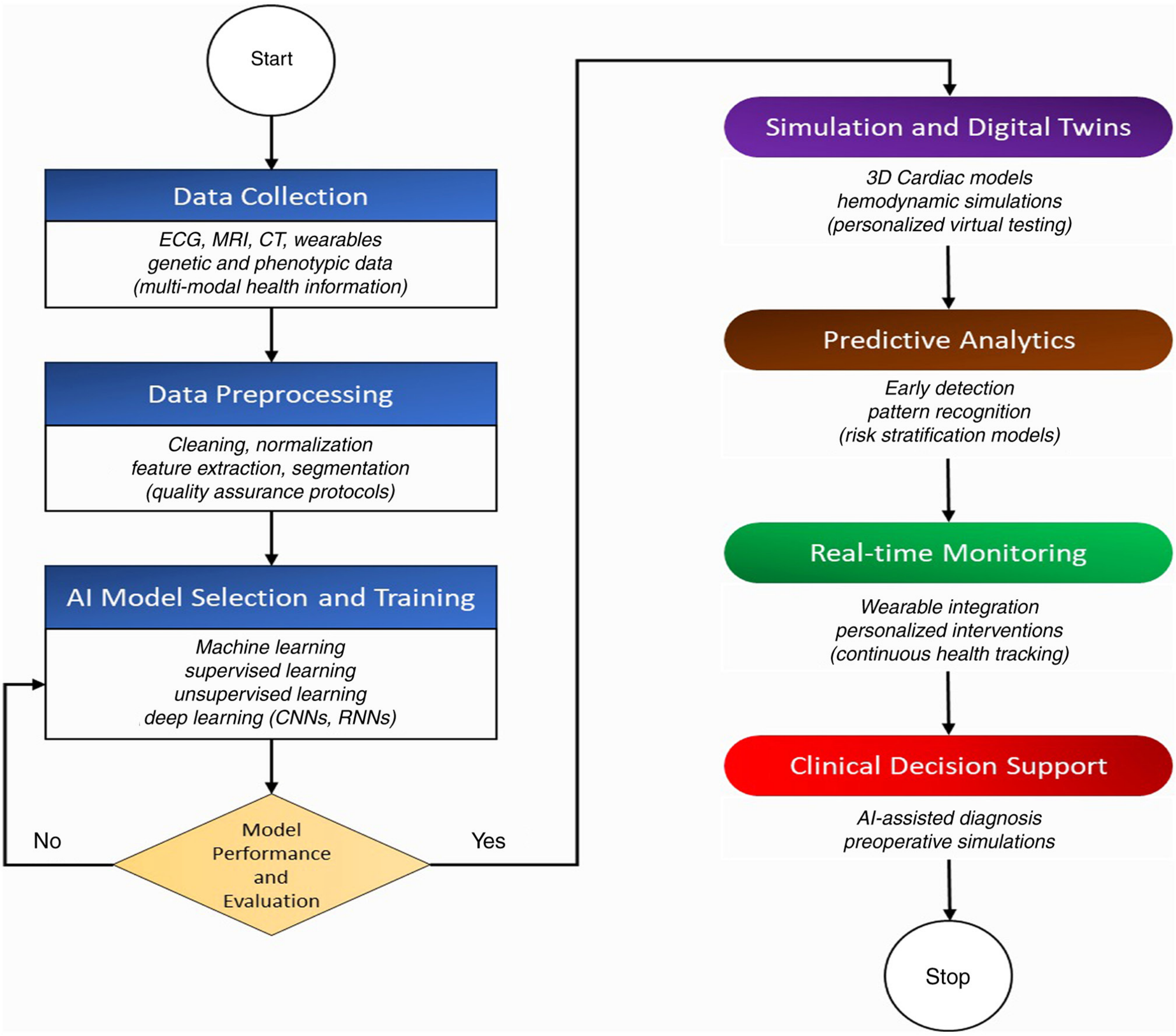

Figure 4. Flowchart of AI-driven cardiac digital twin development, from data collection to real-time monitoring and decision support. CNNs, convolutional neural networks; RNNs, recurrent neural networks.

imaging and multi omics data. The process of establishing interoperability among these disparate systems is difficult and frequently complicated by disparate data formats and standards. Especially in the context of current healthcare IT infrastructures, real-time data interchange and dynamic digital twin updating are crucial yet technically challenging. Ensuring accuracy and reliability of AI-driven DTs is critical. Strict validation studies are required to confirm that DT predictions and recommendations are clinically safe for patient care and building trust among clinicians and patients require transparent algorithms and clear-cut demonstration of clinical benefits (110-112).

Technical limitations. The technical limitations include data integration, real-time exchange, model robustness, validation and computational demands. The integration of vast, intricate and varied data streams such as imaging, physiological, and environmental data is necessary for digital twins. Real-time data interchange and system interoperability is difficult to achieve technically and continue to be a significant obstacle. Accuracy, dependability, and validation of digital twin models for clinical usage are difficult to achieve. Empirical studies on the characteristics and effectiveness of the paradigm in various patient populations are scarce. Advanced techniques and substantial computational resources are needed to create high-fidelity digital twins, and they may not always be accessible in clinical settings (113).

Ethical considerations. The use of patient data in DT raises concerns about privacy, data protection and potential misuse. Strong security measures are essential to maintain patient trust. When data are utilized for purposes other than direct clinical care, ongoing data collecting and monitoring may raise ethical concerns about patient permission and the possibility of surveillance. If DT technology is only available to well-resourced organizations or individuals, there is a chance that it will exacerbate health inequities (114).

Training and usability. DT implementation and interpretation frequently require for specific knowledge that may not be widely available among today's healthcare practitioners. It is a realistic difficulty to integrate digital twins into current healthcare workflows without causing disturbance. Adoption must be facilitated by user-friendly interfaces and precise clinical guidelines. In clinical practice, training and consistent use may be hindered by the lack of established protocols for the creation and use of digital twins (113).

8. Synopsis and considerations

The integration of multi-modal data, sophisticated computational infrastructure and specialized software and hardware, such as GPU-accelerated systems for real-time cardiac modelling are among the significant upfront expenditures associated with implementing digital twin technology. Maintaining the model, managing data and hiring qualified staff to run and interpret DT outputs are ongoing costs. DTs can reduce the need for physical clinical trials which would potentially lower long-term costs and improve cost effective patient management. Some of the digital health initiatives have shown cost savings in cardiovascular care. DT technology is more likely to be affordable and used by high-resource hospitals and research facilities because it requires sophisticated IT infrastructure and knowledge. Widespread adoption in lower resource settings is currently limited by technical, financial and workforce barriers. Integration with the existing healthcare systems and data privacy are the main challenges.

The ability of DT technology to integrate behavioural and environmental factors with physiological and clinical data in cardiovascular disease is growing. For precise disease phenotyping, risk assessment and individualized treatment, these elements are acknowledged as essential. DTs can better replicate real-world effects on cardiovascular health by incorporating information about a patient's surroundings, including climate, air quality and pollution exposure. By combining ambient data with physiological and medical data, advances in generative AI and ML make it possible to create more dynamic and customized simulations and predictions. Additionally, DT models are being used to incorporate lifestyle elements including food, exercise and other health-related habits. For instance, models that diagnose and predict CVDs using patient lifestyle information, observed symptoms and medical history have been developed, enabling users to self-monitor and receive tailored advice. Continuous monitoring of behavioural patterns and environmental exposures is made possible by real-time information from wearable technology and IoT sensors, promoting proactive and preventive care.

9. Conclusion and future perspectives

The application of DT technology in cardiovascular medicine is a paradigm shift towards personalized healthcare. Through the use of AI and ML, DTs facilitate accurate diagnosis, optimized treatment plans, and real-time monitoring of patients. Nevertheless, overcoming current challenges with data integration, privacy, and validation is essential for wider clinical adoption. Future research is required to focus on developing robust AI-driven models, which will enhance interoperability, and establish ethical frameworks for DT implementation. Collaborative efforts between academia, healthcare institutions and industry will be crucial part in translating DTs from research prototypes into accessible clinical tools. DTs could revolutionize the treatment and management of CVDs.

Collecting and analysing datasets which includes the patient specific cardiovascular parameters is the key to advance research in this field. The Cancer Imaging Archive (TCIA), UK Biobank and PhysioNet, are publicly available repositories which provide valuable imaging and physiological datasets. The clinical data from EHRs and real-time data from wearable devices will further enhance DT models. Collaborations with hospitals and research institutions can facilitate access to clinical data, while computational modelling tools like OpenSim and SimVascular can assist in synthesizing data. With the integration of these sources of information with machine learning will make DTs more predictive, leading to more accurate, patient-specific cardiovascular treatment.

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Authors' contributions

All authors (ASSJ, SA, BS, MKMR, KS, SR, PVC, NR and SS) were involved in the writing of the original draft, and in the reviewing and editing of the manuscript. ASSJ, SA, BS and SS were also involved in the investigative aspects of the study. All authors have read and approved the final manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

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Not applicable.

Competing interests

The authors declare that they have no competing interests.

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