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Integrating Artificial Intelligence in the Pathology of Major Cardiovascular Diseases: From Atherosclerosis to Heart Failure

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Abstract

The growing burden of cardiovascular diseases (CVDs) highlights the need for more accurate, efficient, and standardized diagnostic and prognostic approaches. This review aims to explore the integration of artificial intelligence (AI) in the pathology of major CVDs, emphasizing its potential to enhance diagnostic precision, improve patient risk stratification, and support clinical decision-making. By evaluating recent advancements, this review underscores the transformative impact of AI in cardiovascular pathology and its role in shaping future healthcare practices. AI-powered algorithms, particularly machine learning and deep learning, have significantly improved the accuracy of CVD diagnosis by detecting subtle pathological changes in histopathology slides, imaging data, and molecular profiles. In cardiovascular imaging, AI enhances image interpretation, enabling precise detection of atherosclerotic plaques, myocardial fibrosis, and valvular abnormalities, reducing inter-observer variability. AI-based predictive models are revolutionizing risk stratification by analyzing patient-specific data, aiding in early disease detection and personalized treatment plans. The review also highlights AI's role in drug discovery and clinical trials, where it accelerates candidate selection, optimizes trial design, and personalizes therapeutic interventions. Despite its potential, the widespread adoption of AI in CVD pathology faces challenges, including data standardization issues, algorithm interpretability, and the need for clinical validation. Future research should focus on developing more transparent and interpretable AI models to foster trust among clinicians and ensure their seamless integration into routine cardiovascular care. The incorporation of multimodal AI systems, combining imaging, genomic, and clinical data, holds promises for creating highly personalized diagnostic and therapeutic strategies. Continuous collaboration between AI developers, pathologists, and clinicians will be essential to address technical challenges, ensure ethical deployment, and maximize AI's clinical utility in CVD pathology.

Keywords: Artificial intelligence, Cardiovascular diseases, Clinical pathology, Deep learning, Diagnostic imagining, Risk stratification

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Introduction

CVD remains the leading cause of morbidity and mortality worldwide, accounting for nearly 18 million deaths annually [1, 2]. These diseases encompass a broad spectrum of conditions, including atherosclerosis, coronary artery disease (CAD), heart failure, arrhythmias, and valvular disorders. Early and accurate diagnosis is critical for effective treatment and improved patient outcomes [3, 4]. However, conventional diagnostic techniques in pathology, such as histopathology, molecular analysis, and imaging, often rely on manual interpretation, which can be time-consuming, prone to human error, and limited by inter-observer variability [5]. With the advent of AI, particularly machine learning and deep learning algorithms, the landscape of CVD pathology is undergoing a transformative shift [6, 7]. AI offers the potential to enhance diagnostic accuracy, improve prognostic assessments, and streamline pathological workflows by identifying complex patterns and subtle changes that may elude the human eye [8].

The integration of AI into CVD pathology is driven by its ability to analyze vast amounts of data from diverse sources, including digital pathology slides, genomic datasets, and multi-modal imaging (Table 1) [9]. AI-powered tools can automate tissue classification, detect biomarkers, and predict disease progression with remarkable precision. Moreover, AI models can assist in personalized medicine by correlating pathological findings with clinical data to optimize treatment strategies [10, 11]. Despite its promising potential, the adoption of AI in CVD pathology also presents challenges, including data standardization, validation, and the need for interpretability of AI-generated outputs (Figure 1) [12]. Nevertheless, as technology advances, AI is poised to play an increasingly vital role in the early detection, classification, and management of major CVDs, ultimately improving patient care and

Table 1: Applications of AI in CVD pathology.

Application	AI techniques used	Key benefits	Examples
Disease detection	Machine learning, deep learning	Improved accuracy and early diagnosis	Identification of atherosclerosis plaques, myocardial fibrosis
Risk stratification	Predictive modeling, neural networks	Personalized patient risk profiles	Early detection of high-risk individuals
Cardiovascular imaging	Convolutional neural networks, deep learning	Enhanced image interpretation	Automated analysis of scans and images
Drug discovery and design	Generative AI, knowledge graphs	Accelerated drug development	Identification of novel therapeutic targets
Clinical trial optimization	Natural language processing, machine learning	Faster recruitment and protocol design	Improved patient matching and outcome prediction

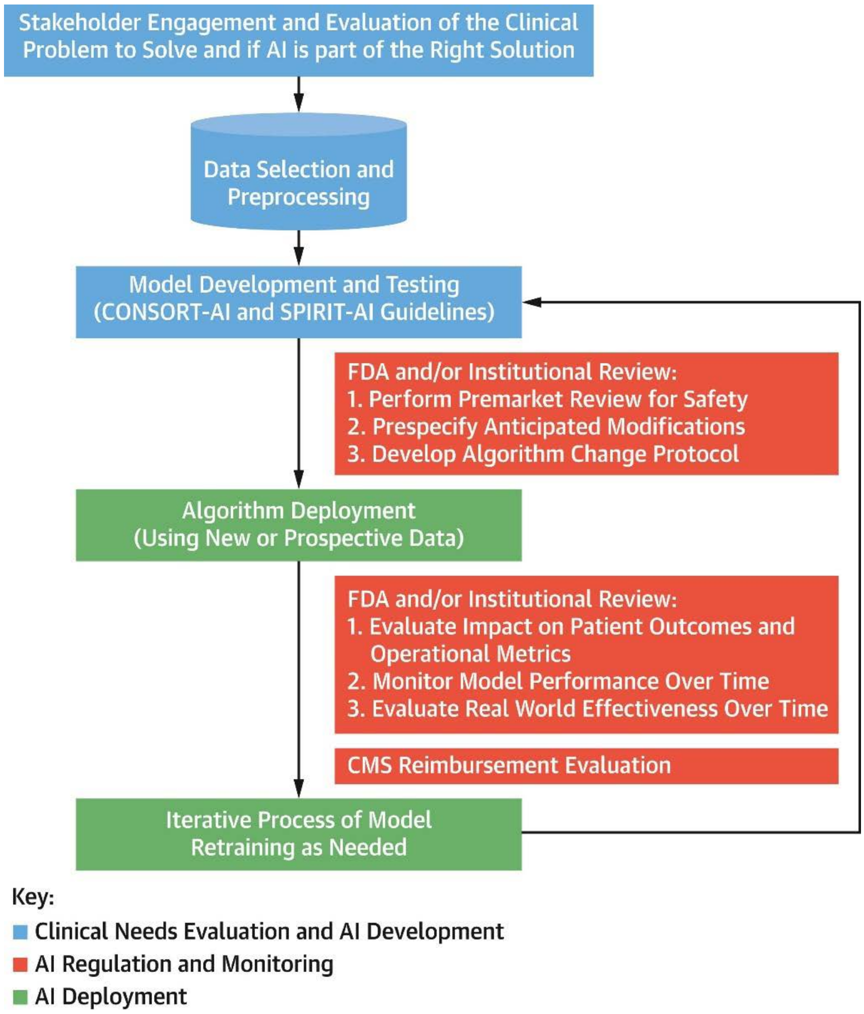

Figure 1: Framework for the development and deployment of clinically relevant AI model [12].

clinical outcomes [13]. The integration of AI into the pathology of major CVDs represents a transformative approach in the field of medicine. AI technologies, particularly machine learning and deep learning, have shown significant promise in enhancing diagnostic accuracy, treatment planning, and disease prevention [14, 15]. This review explores the various applications of AI in cardiovascular pathology, highlighting its potential to revolutionize patient care and improve outcomes.

The integration of AI in the pathology of major CVDs has been a topic of interest in recent literature. Opincariu et al. [16] discussed the role of coronary computed tomography angiography (CCTA) in detecting and quantifying vulnerable plaques, emphasizing the potential of radiomics-based machine learning for assessing plaque-associated risk. Sun et al. [17] focused on using machine learning to predict CVDs based on existing functional dependencies. Slart et al. [18] highlighted the application of machine learning algorithms, including deep learning, in cardiovascular imaging to enhance diagnosis and prognostication for patients with CVDs. Hahn et al. [19] explored the foundational concepts of AI and its recent applications in aortic disease, including the analysis of flow dynamics with advanced imaging techniques.

Furthermore, Wang et al. [20] discussed the use of medical knowledge graphs in cardiology and cardiovascular medicine, emphasizing their importance in effective clinical decision-making. Alqahtani et al. [21] proposed an ensemble-based approach using machine learning and deep learning models for CVD detection, considering multiple health variables. Nedadur et al. [22] highlighted the potential of AI in echocardiographic assessment of valvular heart disease, focusing on image acquisition and automated analysis. Lareyre et al. [23] discussed AI-based predictive models in vascular diseases, while Armoundas et al. [24] emphasized the importance of AI tools in improving outcomes in CVDs, although challenges remain in their widespread adoption. Overall, the literature review indicates a growing interest in integrating AI into the pathology of major CVDs, with a focus on enhancing diagnostic accuracy, prognostication, and treatment decision-making through advanced machine learning algorithms and imaging techniques.

Role of AI

The integration of AI in the pathology of major CVDs is transforming the landscape of cardiology by enhancing diagnostic accuracy, personalizing treatment plans, and improving patient outcomes [25]. AI technologies, including machine learning and deep learning, are being applied across various domains of cardiovascular care, from early diagnosis and risk prediction to treatment and management (Table 2) [26, 27]. These advancements are driven by AI's ability to process vast amounts of data from diverse sources, such as electronic health records, imaging studies, and wearable devices, providing insights that enhance clinical decision-making. However, the integration of AI in cardiovascular pathology also presents challenges, including data privacy concerns, algorithm transparency, and the need for interdisciplinary collaboration to ensure ethical and effective implementation [28, 29].

In disease prediction and risk stratification

Recent advancements in the field of AI have shown promise in disease prediction and risk stratification in the pathology of major CVDs. Kanbay et al. [30] emphasized the importance of risk stratification in patients with chronic kidney disease to prevent sudden cardiac death. Hakeem et al. [31] focused on screening and risk stratification of CAD in end-stage renal disease. Arbab-Zadeh and Fuster [32] discussed the transition from focusing on individual lesions to atherosclerotic disease burden for CAD risk assessment. Machine learning and deep learning, subfields of AI, have been increasingly applied to cardiovascular imaging for risk stratification, as highlighted by Lin et al. [33] in their review of AI applications in CAD risk quantification. AI has also been utilized in aortic disease, as discussed by Hahn et al. [34], showcasing its application in analyzing flow dynamics and computational simulation. Li et al. [35] developed a Chinese-specific AI-powered predictive model for CVD, incorporating physiological measurements, existing diseases, medications, and laboratory tests from Chinese patients. Miller et al. [36] and Razipour et al. [37] demonstrated the use of AI in improving risk stratification through cardiac anatomy analysis and quantification of cardiac chambers and myocardium from imaging data.

A study by Nurmohamed et al. [38] highlights the use of AI-guided quantitative coronary computed tomography angiography (AI-QCT) for analyzing atherosclerotic plaque burden, which offers rapid and detailed insights. AI-QCT provides significant prognostic value for predicting major adverse cardiac events (MACE) over a 10-year period, outperforming traditional methods like coronary artery calcium scoring (CACS) and manual CCTA assessments. Patients with higher plaque stages (stage 3) and noncalcified plaque volume have a significantly increased risk of MACE, indicating the importance of AI-QCT in risk stratification. Incorporating AI-QCT into predictive models enhances their accuracy, as evidenced by improved AUC metrics and net reclassification improvement. The study involved 536 patients with a mean age of 58.6 years, and 55% were male. Over a median follow-up of 10.3 years, 21% of patients experienced MACE, including nonfatal myocardial infarction, stroke, coronary revascularization, and all-cause mortality. Patients with stage 3 plaque burden had a more than threefold increased risk of MACE, while those with a percentage of noncalcified plaque volume of 7.5 had a fourfold increased risk. The addition of AI-QCT to models with clinical risk factors and CACS improved predictive accuracy, with a 10-year AUC of 0.82 compared to 0.73 without AI-QCT (Figure 2). AI-QCT showed better discriminatory value than manual CCTA and CAD-RADS 2.0, although the net reclassification improvement was modest [38].

Furthermore, Rijken et al. [39] outlined the VASCUL-AID-RETRO study protocol, aiming to develop trustworthy AI models for predicting vascular disease progression and cardiovascular events in patients with abdominal aortic aneurysm and peripheral artery disease. The predictive capabilities of AI are particularly valuable in the context of CVDs, where early detection can significantly impact patient outcomes. Alqahtani et al. [21] propose an ensemble-based approach that utilizes machine learning models to predict the likelihood of developing CVD, achieving an impressive accuracy of 88.70%. These studies collectively highlight the potential of AI in enhancing disease prediction and risk stratification in major CVDs. Furthermore, highlighting the potential of AI to assist clinicians in identifying high-risk patients and implementing timely interventions [39].

In cardiovascular imaging

AI has been increasingly utilized in cardiovascular imaging, providing tools that enhance the interpretation of complex data. Dey et al. [40] emphasizes the role of AI in cardiovascular imaging, noting its ability to analyze vast amounts of imaging data, which can lead to improved diagnostic accuracy. The application of AI in imaging modalities such as coronary computed tomography (CT) has been particularly noteworthy. Zheng and Lu [41] discussed how coronary CT can reflect coronary atherosclerosis, aiding in the early risk prediction of MACE. Machine learning algorithms have been employed to analyze imaging data, enabling the identification of patterns that may not be

Table 2: AI applications in specific CVDs.

CVD	AI application	Key benefits	Example AI techniques
Atherosclerosis	Plaque detection and characterization	Early diagnosis and risk assessment	Deep learning for CT angiography analysis
CAD	Automated coronary artery segmentation	Enhanced precision in plaque analysis	Convolutional neural network-based image processing
Heart failure	Predictive models for disease progression	Early identification of decompensation	Machine learning-based prognostic models
Arrhythmias	Automated ECG interpretation	Improved arrhythmia detection and classification	Recurrent neural networks
Valvular heart disease	AI-enhanced ECG interpretation	Accurate detection of stenosis and regurgitation	Deep learning models for valve morphology assessment
Hypertension	AI-based risk prediction models	Early detection of complications	Random forests and support vector machines

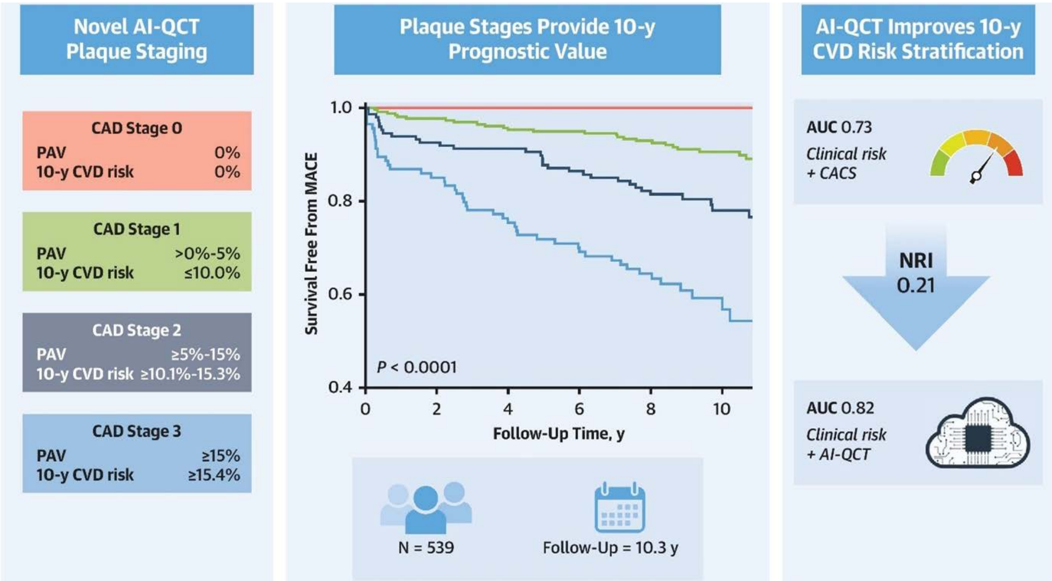

Figure 2: AI-QCT plaque staging improves long-term CVD risk stratification [38].

visible to the human eye. For instance, Slart et al. [18] highlights the integration of machine learning in multimodal imaging techniques, which enhances the diagnostic and prognostic capabilities for patients with CVDs. Furthermore, the use of AI in cardiac CT imaging has been shown to streamline workflows and improve efficiency in cardiac care [42].

AI algorithms, including supervised and unsupervised learning, have been employed for tasks such as left and right ventricular segmentation, ejection fraction measurement, and wall motion analysis. These applications improve the accuracy and efficiency of echocardiographic assessments, which are crucial for diagnosing various heart conditions [43]. Deep learning models have been instrumental in enhancing the detection of coronary artery stenosis and calcification, as well as in determining plaque characteristics. AI's ability to process large volumes of imaging data quickly and accurately aids in the early detection of CAD [44]. AI techniques, such as convolutional neural networks, are used for automatic segmentation of heart chambers and structures, tissue property determination, and perfusion analysis. These capabilities facilitate a comprehensive assessment of cardiac health and improve diagnostic precision [45]. AI applications in nuclear cardiology include the integration of anatomical, functional, and molecular data, which provides a holistic view of cardiac pathology. This integration is particularly beneficial for managing ischemic heart disease and guiding therapeutic decisions [45].

In diagnostic enhancements

AI algorithms have significantly improved the accuracy and speed of diagnosing CVDs by analyzing medical images such as CT scans, X-rays, and electrocardiographs (ECGs). By leveraging advanced algorithms and data analysis, AI can identify patterns and risk factors that may not be apparent through conventional methods, leading to earlier and more accurate diagnoses [46]. These technologies enable early detection and intervention, which are crucial for preventing adverse cardiovascular events [47, 48]. Machine learning models, including decision trees and neural networks, have demonstrated high accuracy in predicting CVD risks by analyzing large datasets from electronic health records and wearable devices. These models can detect subtle cardiac abnormalities and provide real-time risk assessments.

AI has made significant strides in enhancing the diagnosis of major CVDs, revolutionizing various aspects of cardiac imaging and ECG. These advancements have improved accuracy, efficiency, and early detection capabilities across multiple modalities. In ECG, AI algorithms have demonstrated remarkable progress. Convolutional neural networks have achieved high accuracy in detecting cardiac arrhythmia, with one study reporting an overall accuracy of 91.33% for 17 cardiac arrhythmia disorders [49]. AI-based ECG interpretation has shown comparable or superior performance to standard software and human experts, with one study reporting that only 8.2% of AI algorithm reports were deemed unacceptable compared to 13.5% of standard software reports [49]. AI has also shown promise in detecting structural heart abnormalities through ECG analysis. Researchers at the Mayo Clinic developed a deep learning model that could identify left ventricular systolic dysfunction with an area under curve (AUC) of 0.93, 85.7% accuracy, and 86.3% sensitivity [50]. Study demonstrated AI's ability to detect hypertrophic cardiomyopathy from ECGs with an AUC of 0.96, sensitivity of 87%, and specificity of 90% [50].

In drug discovery and design

AI is transforming the management of drug response in major CVDs by enabling precision-driven approaches to drug discovery, personalized treatment selection, and real-time therapeutic monitoring. These advancements address longstanding challenges in predicting individual patient responses and optimizing outcomes through data integration and predictive modeling. AI accelerates cardiovascular drug development by predicting protein structures and simulating molecular interactions. AlphaFold and related models enable precise mapping of protein targets like CDK20, facilitating the identification of novel small-molecule inhibitors for CVD therapies [51]. Generative AI further expands this capability by designing custom proteins and peptides tailored to cardiovascular targets, using diffusion models to iteratively refine molecular configurations. This approach reduces traditional drug development timelines while improving specificity for conditions such as hypertrophic cardiomyopathy and arrhythmias [51, 52].

AI integrates multimodal data-including imaging, ECGs, and clinical characteristics—to predict individual responses to therapies.

For example, machine learning models analyze 12-lead ECGs to guide safe initiation and titration of myosin inhibitors in hypertrophic cardiomyopathy [51]. BeatProfiler, a Columbia University-developed tool, automates cardiac function analysis using video data to quantify drug effects on contractility and calcium handling in heart cells [52]. These systems enable dose optimization for antiarrhythmics while minimizing risks like QTc prolongation [51, 53].

By synthesizing genomics, proteomics, and metabolomics data, AI identifies biomarkers that predict cardiovascular events and therapeutic responses. Foundation models correlate multiomic profiles with clinical outcomes to stratify patients by arrhythmic vs nonarrhythmic mortality risks, informing decisions about implantable cardioverter-defibrillators [51, 54]. This approach also enables drug repurposing by matching existing therapies to specific molecular endotypes in heart failure populations. These innovations demonstrate AI's capacity to bridge gaps between drug development, clinical application, and longitudinal care in cardiovascular medicine. By converting heterogeneous data streams into actionable insights, AI systems are redefining therapeutic precision across the CVD spectrum.

In clinical trial design and recruitment

AI streamlines trial design by optimizing protocols through predictive modeling of enrollment rates, endpoint feasibility, and cost estimation [55]. For patient recruitment, natural language processing algorithms analyze electronic health records to identify eligible candidates across healthcare systems, while federated learning preserves data privacy during multi-center collaborations [55, 56]. Decentralized trial models powered by AI enable remote participation through wearable devices and mobile apps, improving accessibility for underrepresented populations and reducing geographic barriers to diversity [51, 56]. This approach has shown promise in increasing adherence among Black patients and socioeconomically deprived groups in diabetes-related studies [57].

In disease management

The use of AI in disease management in the pathology of major CVDs has shown promising results in various studies. Campochiaro and Akhlaq [58] discussed the sustained suppression of VEGF for the treatment of retinal/choroidal vascular diseases, highlighting the potential of AI in targeting specific pathways for therapeutic interventions. Hormel et al. [59] focused on the application of AI in optical coherence tomographic angiography, demonstrating the utility of AI in analyzing complex imaging data for disease diagnosis and monitoring. Schmidt-Erfurth et al. [60] explored AI-based monitoring of retinal fluid in disease activity and under therapy, showcasing how AI can enhance the precision and efficiency of disease management strategies. Hanssen et al. [61] investigated the relationship between retinal vessel diameters and function in cardiovascular risk and disease, suggesting that AI can aid in identifying early markers of cardiovascular complications through retinal imaging.

The integration of multiomics data with AI has emerged as a promising strategy for improving CVD management. Sopic et al. [62] discuss how multiomics tools can enhance the understanding of atherosclerotic CVD, allowing for more personalized treatment approaches. By combining genomic, proteomic, and metabolomic data, AI can provide a comprehensive view of disease mechanisms, facilitating targeted therapies. Overall, the literature suggests that AI holds great potential in revolutionizing disease management in the pathology of major CVDs by enhancing diagnostic accuracy, treatment efficacy, and personalized medicine approaches.

In personalized treatment

AI systems are capable of analyzing complex medical data to provide individualized therapy recommendations, tailoring treatment plans to the specific needs and characteristics of each patient. This approach enhances the precision of medical interventions and improves patient outcomes [46, 47]. AI-driven predictive analytics facilitate the development of personalized treatment plans by integrating data from various sources, including genomic data and digital health records. This comprehensive approach allows for more accurate and efficient management of CVDs [63].

AI-driven digital twin technology represents a breakthrough in treatment personalization, with generative models simulating cardiac responses to medications and procedures. Researchers at NTT Communication Science Laboratories are developing heart-specific digital twins that predict individual responses to therapies like novel myosin inhibitors in hypertrophic cardiomyopathy, potentially reducing trial-and-error approaches [51, 64]. Multiomics integration through AI (genomics, proteomics, metabolomics) allows identification of patient subpopulations with distinct molecular signatures, enabling targeted drug development and repurposing existing medications for specific cardiovascular endotypes [51, 53, 65]. This approach has shown promise in optimizing antiarrhythmic drug selection by predicting QTc prolongation risks and safe dosing thresholds [51, 66].

Advanced imaging analytics powered by AI enhance diagnostic precision across modalities. Deep learning models automate coronary plaque quantification in CT angiography, calculate fractional flow reserve, and analyze myocardial perfusion patterns [65, 66]. In cardiac MRI, AI algorithms detect fibrosis patterns predictive of ventricular tachycardia, guiding ablation strategies [66, 67]. These tools complement wearable technologies that provide continuous physiological monitoring, creating dynamic risk profiles adjusted in real-time based on activity levels and biomarker fluctuations [53, 68]. As these technologies mature, they promise to transform cardiovascular care from reactive disease management to proactive, individualized health optimization anchored in predictive analytics and simulated treatment outcomes.

Multimodal AI

Multimodal AI systems are increasingly being recognized for their potential to revolutionize the pathology and management of major CVDs. These systems integrate diverse data types, such as images, genomics, clinical records, and biosensors, to provide a comprehensive view of cardiovascular health. The integration of multimodal data allows for more accurate diagnosis, personalized treatment strategies, and improved patient outcomes. Despite the promise, the complexity of multimodal AI systems poses challenges in their widespread adoption in clinical practice.

Multimodal AI systems leverage various data sources, including medical images, genomics, and clinical records, to enhance diagnostic accuracy and patient stratification. For instance, a study by Lee et al. [69] developed an AI model to predict CVD using multimodal data, which included clinical risk factors and fundus photographs. This model was validated using data from the Samsung Medical Center (SMC) and the United Kingdom (UK) Biobank. In the internal validation at SMC, the model achieved an area under the receiver operating characteristic curve (AUROC) of 0.781, indicating a good ability to distinguish between CVD cases and non-CVD controls. For external validation using the UK Biobank, the model performed even better, achieving an AUROC of 0.872. This suggests that the model is effective across different populations. The study included a total of 1758 images for CVD cases and 1760 images for non-CVD controls during model development. For validation, it used 1421 images for CVD cases and 1533 for non-CVD controls from SMC, and 613 images for CVD cases and 10,685 for controls from the UK Biobank. The model's performance was compared with traditional deep neural networks that used only clinical risk factors. The multimodal model showed a statistically significant improvement in AUROC compared to the deep neural network, which had an AUROC of 0.766 in internal validation. The model also demonstrated strong predictive capabilities, with a hazard ratio of 6.28 for the incidence of CVD among at-risk patients in the UK Biobank, indicating that those identified as high-risk by the model had a significantly higher likelihood of developing CVD. The results highlight the potential of using non-invasive fundus photography as a predictive marker for CVD, suggesting that it could be a valuable tool in clinical settings, especially in resource-limited environments. Overall, the findings indicate that combining fundus photographs with traditional risk factors can enhance the prediction of cardiovascular risks, which is crucial for early diagnosis and intervention [69].

The use of multi-omics data, such as RNA sequencing and whole-genome sequencing, allows for the discovery of novel biomarkers and personalized risk profiling. A study by DeGroat et al. [70] presents several significant findings regarding the use of multimodal AI techniques in understanding CVDs through multi-omics profiles. The research identified a signature of 27 transcriptomic features and single nucleotide polymorphisms that serve as effective predictors of CVD. This was achieved through a robust feature selection approach that prioritized biological relevance and efficiency in machine learning. The classification models developed in the study demonstrated high accuracy in predicting CVD. The best-performing model was an XGBoost classifier, which was optimized using Bayesian hyperparameter tuning. This model successfully classified all patients in the test dataset, showcasing its effectiveness [70].

AI-enhanced multimodality imaging, including echocardiography, MRI, and CT angiography, provides comprehensive insights into cardiac pathology. These technologies optimize image acquisition and interpretation, improving diagnostic precision and guiding therapeutic decisions. Clinical applications of multimodality imaging are supported by case studies showing improved patient outcomes. For instance, combining coronary CT angiography with myocardial perfusion imaging has been shown to enhance diagnostic accuracy and reduce the need for invasive procedures. emerging technologies like 4D flow MRI and molecular imaging, which provide detailed insights into blood flow dynamics and metabolic changes in the heart. These advancements are seen as transformative for the management of ischemic heart disease, enabling personalized treatment strategies based on individual patient profiles [45].

A study by Ding et al. [71] introduced a model called CardiacNets, which enhances the analysis of ECGs by using advanced techniques to improve the detection of CVDs and cardiomyopathy. This model was validated using large datasets, including the UK Biobank and MIMIC-IV-ECG, among others. CardiacNets was trained on two large public datasets: the UK Biobank, which included 41,519 individuals, and the MIMIC-IV-ECG dataset, which comprised 501,172 samples. The model also utilized three private datasets for further validation. The results showed that CardiacNets significantly outperformed traditional ECG-only models. For instance, in cardiomyopathy detection, CardiacNets achieved an AUC score of 87.65%, compared to 72.56% for the ECG-only model. This indicates a substantial improvement in diagnostic accuracy. In terms of predicting cardiac structural indicators, CardiacNets achieved an average Pearson correlation coefficient of 0.426, which was higher than the ECG-only models (0.351) but lower than cardiac MRI-based models (0.612). This suggests that while CardiacNets is effective, there is still room for improvement compared to cardiac MRI. The model demonstrated high label efficiency, meaning it could achieve good performance with only 10% of the training data, which is crucial for real-world applications where data may be scarce. In a reader study involving physicians, the use of AI-generated cardiac MRI images significantly improved the accuracy of cardiomyopathy screening compared to using ECG data alone. This highlights the practical utility of CardiacNets in clinical settings. Overall, the findings suggest that CardiacNets can effectively utilize ECG data to screen for various cardiovascular conditions, potentially transforming how CVDs are diagnosed and managed, especially in settings with limited access to advanced imaging technologies [71].

A study by Soenksen et al. [72] introduced a new framework called Holistic AI in Medicine (HAIM), which effectively combines various types of healthcare data to improve predictive modeling in clinical settings. This framework was tested using a large dataset known as HAIM-MIMIC-MM, which included 34,537 samples from 6485 unique patients and 7279 hospitalizations. The HAIM framework was able to train and evaluate a total of 14,324 independent models, demonstrating its capability to handle multiple data modalities, including tabular data, time-series data, text, and images. The results showed that models using multimodal input consistently outperformed those using single data sources, with improvements in predictive accuracy ranging from 6% to 33% across various tasks. Specifically, for chest pathology diagnosis, the framework achieved significant improvements in model performance. For example, the model predictions for conditions like pneumonia and lung lesions showed an increase in accuracy of 6% to 10% when using multimodal data compared to single-modal approaches. The study also highlighted the importance of different data modalities for various predictive tasks. For instance, visual data (like X-rays) was found to be most beneficial for diagnosing chest pathologies, while historical time-series data was more relevant for predicting patient length-of-stay and mortality. The researchers utilized Shapley values to analyze the contribution of each data source and modality to the model's performance. This analysis revealed that while all modalities contributed positively, there were diminishing returns when too many similar data types were included, indicating the need for careful selection of inputs. Overall, the HAIM framework demonstrated a promising approach for developing predictive models in healthcare, potentially leading to better patient outcomes and more efficient clinical operations [72].

While multimodal AI systems offer promising advancements in the pathology of CVDs, their implementation in clinical settings requires careful consideration of technical, ethical, and regulatory challenges. Collaborative efforts among clinicians, researchers, and industry stakeholders are essential to harness the full potential of these systems, ensuring enhanced diagnostics and personalized patient care.

Challenges and Future Directions

Despite the promising advancements in AI applications for cardiovascular pathology, several challenges remain. The need for large, diverse datasets to train AI models is critical, as highlighted by Wong et al. [73]. Additionally, concerns regarding the interpretability and generalizability of AI algorithms must be addressed to ensure

Table 3: Future technological advancements in AI for CVD pathology.

Technological advancement	Description	Potential benefits	Challenges to overcome
Explainable AI	Models providing interpretable outputs	Increased clinician trust and transparency	Balancing accuracy with interpretability
Real-time AI assistance	AI-powered clinical decision support systems	Faster diagnosis and more accurate treatment	Integration into existing clinical workflows
AI-powered multimodal systems	Combining imaging, genomic, and clinical data	Comprehensive and personalized disease profiling	Data interoperability and standardization
Federated learning	AI training across decentralized data sources	Improved model generalizability	Ensuring data privacy and security
Predictive analytics platforms	AI for long-term risk prediction	Enhanced preventive care and patient outcomes	Continuous model updates and validation
Digital twin technology	AI-driven virtual models of individual hearts	Precision medicine through personalized simulations	Complexity and computational demands

their successful integration into clinical practice. The American Heart Association [24] emphasizes the importance of developing AI tools that not only improve diagnostic accuracy but also address biases in clinical studies.

While AI integration in cardiovascular imaging offers numerous benefits, it also presents challenges such as data quality and interoperability, ethical concerns regarding patient privacy, and algorithm transparency. Addressing these issues is essential for the broader adoption of AI technologies in clinical practice [74, 75]. Additionally, the successful implementation of AI in healthcare requires robust infrastructure and interdisciplinary collaboration among clinicians, data scientists, and policymakers.

- AI models require high-quality, standardized data to function effectively. Variability in data quality, especially in medical imaging and electronic health records, can lead to inconsistent AI performance. This inconsistency poses a challenge in ensuring reliable diagnostic outcomes across different healthcare settings [75, 76].

- The lack of standardized algorithms for data collection and review further complicates the integration of AI into clinical workflows, as it can lead to discrepancies in AI model outputs.

- AI models, particularly deep learning algorithms, often function as "black boxes," making it difficult for clinicians to interpret their decision-making processes. This lack of transparency can hinder trust and acceptance among healthcare professionals [77].

- Algorithmic bias is another significant concern, as AI models trained on non-representative datasets may produce biased outcomes, potentially leading to disparities in care for different patient populations [77, 78].

- Ethical considerations, such as data privacy and patient consent, are critical when implementing AI in healthcare. Ensuring that AI systems comply with regulatory standards and ethical guidelines is essential to protect patient rights and maintain public trust [75].

- Regulatory challenges also include the need for extensive validation and approval processes before AI tools can be widely adopted in clinical practice [77].

- Integrating AI tools into existing clinical workflows requires robust infrastructure and interdisciplinary collaboration. Many healthcare systems face challenges related to electronic health record interoperability, which can impede the seamless integration of AI technologies [79].

- Usability issues, such as the complexity of AI interfaces and the need for specialized training, can limit the practical application of AI tools by clinicians [79].

- AI systems may struggle with certain technical limitations, such as the inability to accurately process poor-quality images or detect subtle abnormalities in complex cases. These limitations can affect the diagnostic accuracy and reliability of AI models [76, 78].

- The need for continuous monitoring and updating of AI models to adapt to new medical knowledge and practices is another technical challenge that requires ongoing resources and expertise [80].

While AI offers transformative potential in the pathology of CVDs, these limitations highlight the need for careful consideration and strategic planning in its implementation. Addressing these challenges requires collaboration among clinicians, data scientists, and policymakers to ensure that AI technologies are used ethically and effectively. Additionally, ongoing research and development are crucial to overcoming these barriers and enhancing the capabilities of AI in cardiovascular care (Table 3).

Conclusion

The integration of AI into the pathology of major CVDs represents a transformative shift in diagnostic accuracy, prognostic assessment, and personalized treatment strategies. This review highlights how AI-powered algorithms, particularly machine learning and deep learning, enhance the detection of subtle pathological changes, improve imaging interpretation, and streamline clinical workflows. AI-driven predictive models show remarkable promise in risk stratification and early disease detection, enabling more precise and timely interventions. Furthermore, AI's applications in drug discovery, clinical trials, and disease management are revolutionizing CVD care, offering greater efficiency and improved patient outcomes. Despite these advancements, challenges such as data standardization, algorithm transparency, and clinical validation remain significant barriers that must be addressed to ensure the widespread adoption of AI in cardiovascular pathology.

In the coming years, AI is expected to play an even more prominent role in CVD pathology, with multimodal systems integrating imaging, genomic, and clinical data for comprehensive disease profiling. Advances in explainable AI will enhance the interpretability of models, fostering greater trust and acceptance among clinicians. Real-time AI-based decision support tools will become standard in clinical practice, assisting physicians with rapid and accurate diagnosis, treatment planning, and outcome prediction. Additionally, AI-powered precision medicine will enable highly personalized interventions by tailoring therapies to individual patient profiles, ultimately improving long-term cardiovascular health and reducing mortality rates.

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None.

Conflict of Interest

None.

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