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A scientometrics survey of machine learning applications in cardiovascular disease research: An analysis of highly-cited literature

Seyed Jafar Sadjadi[a*]

[a]*Department of Industrial Engineering, School of Engineering, Iran University of Science and Technology, Tehran, Iran*

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A B S T R A C T

Heart disease is one of the most common causes for death among human nations for many years. There have been substantial efforts to reduce heart diseases in the world. It is essential to implement the recent advances of data science to discover any symptoms of cardiovascular disease (CVD). Machine learning (ML) has given scientists a tool to detect early causes of such disease and this survey uses the combination of ML and CVD as a search keyword to determine 200 highly cited articles from the Scopus database. The study performs a survey on the data which were published from 2018 to 2025 and present possible road-map for future studies. The results indicate that a significant number of highly cited articles are published in Open Access journals such as PlosOne, IEEE Access and Scientific Report. In addition, the study presents seven different areas of research which have been under significant progress.

1. Introduction

The joint integration of machine learning (ML) and cardiovascular disease (CVD) studies present one of the essential progress in today's medical science. There has been a rapid growth in cardiovascular data sources, such as electronic health records, medical imaging, genomic data, and wearable device outputs, which have provided fantastic tools for ML applications in CVD diagnosis, prognosis, and treatment optimization. This survey provides and analyzes 200 highly-cited papers to map the intellectual landscape of this quickly evolving field, determining key research trends, methodological innovations, and clinical applications that have changed recent advancements.

CVDs have remained the main death-cause worldwide and it is blamed for about 17.9 million deaths per year according to World Health Organization (WHO). ML approaches have been used to identify subtle patterns across diverse data modalities which could elude traditional statistical techniques. Many articles investigated in this article collectively offer the cutting edge of study at this intersection, giving insights into how ML is transforming cardiovascular medicine across different domains, including risk forecasting, diagnostic imaging, drug discovery, and objective treatment planning.

Concentrating on a subset of highly-cited articles, the study separates the most important research trajectories and methodological frameworks that have absorbed substantial scholarly engagement. Rather than conducting an exhaustive bibliometric sweep across all literature in the domain, citation frequency is used as a surrogate for relevance and influence. This

* Corresponding author.
E-mail address: sjsadjadi@iust.ac.ir (S. J. Sadjadi)

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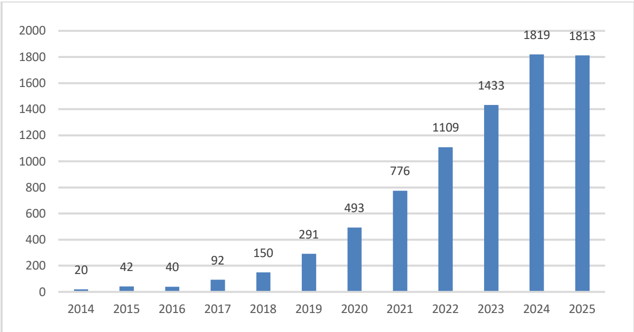
selective strategy helps a more refined mapping of productive research pathways and highlights methodological designs that have shown exceptional effectiveness in tackling cardiovascular complexities.

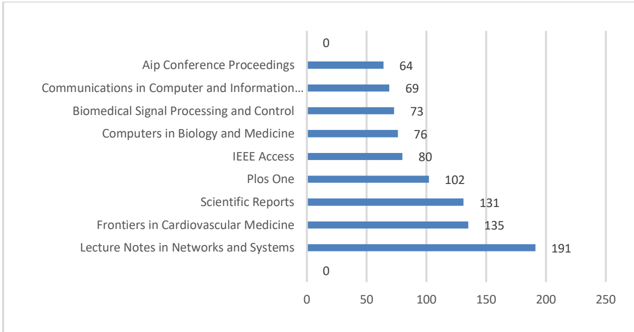
2. Methodology and Dataset Characteristics

The dataset for this scientometrics analysis comprises 200 highly-cited papers retrieved from the Scopus database using the search query "cardiovascular disease" AND "Machine Learning". These papers are the highly cited articles from the over 8,100 records determined through this search strategy. The focus of highly-cited articles in recent years shows both the rapid growth of this research domain and the accelerating pace of scientific discovery at the intersection of ML and cardiology.

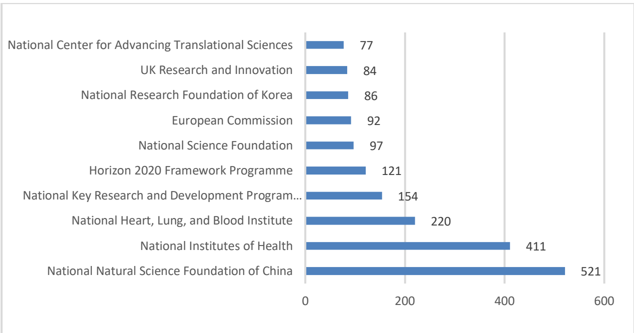
The analysis of the dataset discloses a recency bias, with approximately 75% dating from 2020 to 2024. This distribution underscores the rapidly evolving nature of ML applications in CVD studies, with substantial growth in publication output coinciding with advancements in deep learning architectures and increased availability of large-scale cardiovascular datasets. The years 2019-2021 seem specifically productive, representing for nearly 50% of the highly-cited publications in the dataset, implying a period of intensified research activity and methodological innovation. Fig. 1 shows some facts on all 8164 records that we used in our survey.



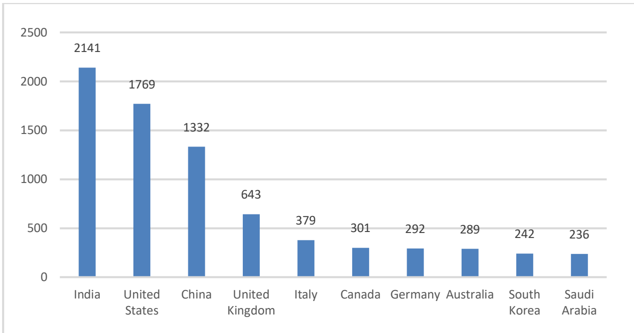
(a)The number of publications per year



(b)Diversity of the publications and journals



(c)Funding agencies



(d)Documents per country

Fig. 1. Some basic scientometric information

According to Fig. 1(a), a substantial growth is observed in terms of the number of publications in the area of CVDs and ML. Fig. 1(b) shows the diversity of the journals involved with the publications of these articles. Our survey shows that Open Access journals such as PlosOne, IEEE Access and Scientific Reports have major contributions in this survey. Fig. 1(c) shows the information of funding agencies for the published articles. In our survey, the National Natural Science Foundation of China is the number one agency for spending funds on this research. Finally, Fig. 1(d) shows the contribution of different countries in this subject area. As we can observe, researchers from India, United States and China have contributed the most in this survey.

3 Methodological Approaches in Machine Learning for CVD

3.1 Evolution of Machine Learning Techniques

The closer look at the highly-cited papers discloses a crystal-clear image in different methodologies, from conventional ML methods to complex deep learning frameworks. Early influential studies in this area utilized supervised learning methods, including logistic regression, support vector machines, random forests, and gradient boosting methods. Alaa et al. (2019) presented the application of automated machine learning (AutoML) methodologies for cardiovascular risk prediction, while

Nusinovici et al. (2020) gave comparative analyses of conventional statistical methods against ML methods for chronic disease prediction.

There is a movement from deep learning techniques, which represents a substantial trend in the dataset, with convolutional neural networks (CNNs), recurrent neural networks (RNNs), and hybrid architectures featuring prominently in recent publications. Litjens et al. (2019) presented an in-depth review on deep learning applications in cardiovascular image analysis, while Bizopoulos and Koutsouris (2019) presented systematic evaluation of deep learning applications across multiple cardiology domains. The superior performance of deep learning methods in processing complex, high-dimensional data such as medical images and physiological signals has prompted their rapid adoption for cardiovascular applications.

Ensemble techniques and hybrid methods have appeared as specifically influential methodological directions, combining multiple methods to help improve predictive performance and robustness. Mohan et al. (2019) showed the effectiveness of hybrid ML methods for heart disease prediction, while Plawiak and Acharya (2020) presented a novel deep genetic ensemble classifier for arrhythmia detection. These methods leverage the complementary strengths of various methods, often reaching performance superior to any single method alone.

3.2 Feature Engineering and Selection Strategies

Feature engineering and selection are critical components of successful ML application for cardiovascular implementation, with highly-cited articles stating diverse methods to this challenge. Conventional feature selection techniques, including filter methods (such as Relief and LASSO), wrapper methods, and embedded techniques, feature prominently in earlier publications. Ghosh et al. (2021) presented comprehensive evaluation of feature selection techniques for CVD prediction, while Srinivas and Katarya (2022) presented optimized frameworks incorporating feature selection for improved model performance.

The emergence of automated feature learning through deep architectures gives a substantial shift in methodology, particularly for image and signal processing applications. Wang et al. (2020) showed the effectiveness of multi-scale fusion neural networks for arrhythmia detection, while Lih et al. (2020) proposed comprehensive ECG diagnosis systems utilizing automated feature extraction. This transition from manual feature engineering to learned representations shows broader trends in ML and has helped effective utilization of complex cardiovascular data modalities.

Combination of multimodal features shows another essential direction, with various highly-cited papers combining clinical, imaging, genetic, and biomarker data to contribute predictive performance. Amal et al. (2022) performed an investigation on multi-modal data integration for contributing cardiovascular care, while Zhao et al. (2019) studied longitudinal data from electronic health records in conjunction with genetic information. These methods acknowledge the multifactorial nature of cardiovascular diseases and look for capturing complementary information across data types for better risk assessment and disease characterization.

4 Clinical Applications and Research Domains

4.1 Cardiovascular Risk Prediction and Stratification

Risk prediction is the vast extensively studied task of ML in cardiovascular medicine, with various highly-cited papers developing and validating techniques for different cardiovascular outcomes. Conventional risk factors combined with novel data sources have helped more precise determination of high-risk individuals. Khan et al. (2023) presented novel prediction equations by considering cardiovascular-kidney-metabolic health, while Alaa et al. (2019) presented automated ML frameworks for population-scale risk assessment.

The development of risk prediction to specific cardiovascular conditions is an essential research path. Papers concentrating on heart failure prediction, including Chicco and Jurman (2020) describing prediction of survival from serum creatinine and ejection fraction, have garnered substantial attention. Similarly, Hill et al. (2019) proposed ML methods for forecasting atrial fibrillation in primary care settings. These condition-specific methods address the unique challenges and opportunities given by various cardiovascular diseases, moving beyond uniform cardiovascular risk toward more targeted prognostic structures.

Combination of novel biomarkers and data sources has significantly advanced risk prediction capabilities. Poss et al. (2020) disclosed serum sphingolipids as cholesterol-independent biomarkers of coronary artery disease using ML techniques, while Aryal et al. (2020) proposed gut microbiome-based diagnostic screening for CVD. These papers show how ML may uncover novel risk factors and biomarkers which could not be detected through conventional statistical methods, potentially helping earlier intervention and more personalized risk modification techniques.

4.2 Diagnostic Applications and Medical Imaging

The implementations of ML in cardiovascular diagnosis includes different modalities, with specifically substantial contributions in electrocardiography (ECG) analysis, cardiac imaging, and wearable sensor data interpretation. Xie et al. (2020) reviewed computational diagnostic techniques for ECG signal analysis, while Wagner et al. (2020) presented PTB-XL, a large publicly available electrocardiography dataset that has helped many subsequent ML achievements. These basic techniques have helped more precise and automated interpretation of cardiac electrical activity.

Cardiac imaging is another basic application domain, with highly-cited articles demonstrating ML applications across echocardiography, cardiac MRI, CT angiography, and nuclear imaging. Sermesant et al. (2021) studied artificial intelligence techniques in cardiovascular imaging, while Litjens et al. (2019) provided evaluation of deep learning in cardiovascular image analysis. These methods range from automated image segmentation and quantification to disease detection and characterization, potentially affecting inter-observer variability and helping in diagnostic accuracy.

Emerging diagnostic applications are analysis of novel signal kinds and integration of multiple data modalities. Oliveira et al. (2022) presented the CirCor DigiScope Dataset for murmur detection and classification, while Taebi et al. (2019) presented a comprehensive review on advances in seismocardiography for cardiovascular assessment. These methods expand the diagnostic toolkit available to clinicians, potentially enabling earlier determination of cardiovascular abnormalities through non-invasive, readily available data sources.

4.3 Drug Discovery and Therapeutic Optimization

ML implementations in cardiovascular drug discovery and therapy optimization are also considered as a growing study direction, with various highly-cited papers exploring these applications. Minikel et al. (2024) studied the effect of genetic evidence on clinical success in drug development, while Garcia Jimenez et al. (2023) presented a comprehensive review on macrocycles in drug discovery, highlighting ML implementation in compound screening and optimization. These methods leverage the pattern recognition capabilities of ML to determine promising therapeutic candidates and forecast their efficacy and safety systems.

Personalized treatment selection and optimization are another application in this domain. Babel et al. (2021) investigated artificial intelligence solutions to improve medication adherence in patients with non-communicable diseases, including cardiovascular conditions. Moreover, Subramanian et al. (2020) investigated the precision medicine applications in chronic disease management, focusing the role of ML in tailoring interventions to individual patient characteristics.

The application of ML to clinical trial design and analysis are another emerging frontier. Although less extensively represented in the current dataset, various papers hint at the potential of ML to improve trial protocols, determine suitable patient populations, and analyze complex trial data. As cardiovascular therapeutics become increasingly targeted and personalized, ML methods are most likely to play an essential role in joining molecular mechanisms, patient characteristics, and therapeutic outcomes to optimize treatment strategies.

5 Data Types and Sources in ML-CVD Research

5.1 Electronic Health Records and Clinical Data

Electronic health records (EHRs) are considered as basic data sources for ML implementations in cardiovascular research, giving comprehensive clinical data across large patient populations. Landi et al. (2020) performed an investigation on deep representation learning methods for EHR data to help patient stratification at scale, while Zhao et al. (2019) studied learning from longitudinal data in EHRs along with genetic data. These methods show how ML may provide significant patterns from the complex, heterogeneous data with clinical records.

The challenges of working with EHR data, including missing data and information, documentation variability, and irregular sampling, have helped methodological innovations in data preprocessing and representation learning. Highly-cited papers investigating these challenges have contributed substantially to the field's development. Alaa et al. (2019) used automated machine learning methods to handle the complexity of EHR-derived features, while Dinh et al. (2019) contributed data-driven methods for forecasting diabetes and cardiovascular disease using survey data with inherent missingness and measurement variability.

Integration of EHR data with other data types is an essential research direction. Various highly-cited papers integrate clinical data with genetic data, imaging findings, or biomarker measurements to build more comprehensive patient profiles. This multimodal method confirms the multifactorial nature of cardiovascular diseases and looks for capturing complementary data across data types. The technical challenges of integrating heterogeneous data sources while considering various sampling frequencies, measurement scales, and data quality have helped development of specialized ML techniques tailored to these complex integration tasks.

5.2 Genomic and Multi-Omics Data

The combination of genomic and multi-omics data is a quickly progressing frontier in ML techniques for cardiovascular research. Folkersen et al. (2020) performed genomic and drug target evaluation of 90 cardiovascular proteins in large population cohorts, specifying the power of ML methods for analyzing high-dimensional molecular data.

Multi-omics integration, combining genomic, transcriptomic, proteomic, metabolomic, and other molecular data, are a specifically promising direction. Joshi et al. (2021) presented a comprehensive review on biology methods in cardiovascular disease based on multi-omics data, while Shen et al. (2024) studied nonlinear dynamics of multi-omics profiles during human aging. These methods look for capturing the complex interactions in biological scales, which underlie cardiovascular pathophysiology, moving beyond single-omics analyses toward more comprehensive molecular characterization.

The implementation of ML to functional genomics and causal inference are another essential research direction. Rosoff et al. (2020) used multivariable Mendelian randomization to make an assessment on the relationships between alcohol consumption, tobacco use, and cardiovascular disease, while Nicholls et al. (2020) performed a comprehensive review on machine learning methods for prioritizing complex disease loci from genome-wide association papers. These applications show how ML may enhance causal inference from observational genetic data, potentially determining novel therapeutic targets and elucidating disease mechanisms.

5.3 Wearable Devices and Physiological Monitoring

Wearable devices and continuous physiological monitoring are rapidly growing data sources for cardiovascular ML methods, helping unprecedented temporal resolution and real-time evaluation. Hughes et al. (2023) studied wearable devices in cardiovascular medicine, while Krittanawong et al. (2021) performed an investigation on the integration of novel monitoring devices with ML technology for scalable cardiovascular management. These methods leverage the continuous, longitudinal nature of wearable data to determine subtle physiological changes which could precede clinical events.

The technical challenges of executing wearable device data, including noise, artifact, and individual variability, have guided the development of specialized ML methods. Kireev et al. (2022) proposed a method for continuous cuffless monitoring of arterial blood pressure via graphene bioimpedance tattoos, while Fang et al. (2021) built machine-learning-assisted textile triboelectric sensors for ambulatory cardiovascular monitoring. These hardware innovations, coupled with advanced ML algorithms, help us for a more precise and easy physiological monitoring outside clinical settings.

The combination of wearable data with other data types are an essential research direction. Various highly-cited papers integrate physiological signals from wearables with clinical information, patient-reported outcomes, or environmental data to achieve better health assessments. This multimodal method acknowledges that cardiovascular health is affected by multiple factors executing across various timescales, from acute physiological responses to chronic lifestyle patterns. The development of ML methods helps for integrating these diverse data streams and for a significant methodological challenge with significant clinical potential.

6 Implementation Challenges and Clinical Translation

6.1 Interpretability and Explainability

The interpretability and explainability of ML techniques are critical concerns for clinical implementation, with various highly-cited papers focusing on this challenge. Petch et al. (2022) studied the promise and limitations of explainable machine learning in cardiology, while Zhang et al. (2021) performed interpretable deep learning methods for automatic diagnosis of 12-lead electrocardiogram. These efforts look for bridging the gap between model performance and clinical utility by looking for model decision-making processes.

Technical methods to model interpretability differ significantly across the literature, ranging from post-hoc explanation techniques to inherently interpretable model architectures. Wang et al. (2021) implemented SHAP (SHapley Additive exPlanations) values to build interpretable prediction techniques for all-cause mortality in patients with heart failure, while Jahmunah et al. (2022) combined Grad-CAM methods for explainable detection of myocardial infarction based on deep learning models on ECG signals. These methods give different levels of insight into model behavior, with trade-offs between explanation fidelity, comprehensibility, and computational complexity.

The clinical validation of explanation techniques is an essential study direction. Various papers specify that explanations should not only be technically sound but also clinically significant, aligning with medical understanding and helping clinical decision-making. The tension between model complexity and interpretability is still a substantial challenge, with the most precise models often being the least interpretable. Developing methods that balance these competing demands is an active area of investigation with essential implications for clinical adoption of ML technologies in cardiovascular medicine.

6.2 Generalizability and Validation

The generalizability of ML techniques across various populations, healthcare systems, and clinical settings is a fundamental challenge for clinical translation. Van Smeden et al. (2022) gave critical appraisal of artificial intelligence-based prediction models for cardiovascular disease, focusing on the attributes of rigorous validation and evaluation of generalizability. Similarly, Nusinovici et al. (2020) performed a comparison between logistic regression and machine learning techniques, giving validation considerations for prognostic modeling.

Approaches to evaluating and contributing model generalizability cover external validation across diverse datasets, domain adaptation techniques, and incorporation of population heterogeneity during model development. Various highly-cited papers present the relative importance of assessing model performance across various demographic groups, clinical settings, and geographic regions to determine potential biases and performance variations. These validation efforts are important for understanding the real-world performance of ML models and determining contexts in which they may be safely deployed.

The development of reporting standards and validation frameworks is an essential direction for the field. While not explicitly addressed in most highly-cited research papers, the necessity for standardized evaluation metrics, benchmarking datasets, and reporting guidelines has been recognized as important for advancing the field.

6.3 Integration with Clinical Workflows

The integration of ML methods into clinical workflows is a substantial challenge, with various highly-cited papers addressing different perspectives of this transition. Aminizadeh et al. (2024) performed a comprehensive study on opportunities and challenges of artificial intelligence and distributed systems for having a better healthcare service quality, while Dunn & Hazzard (2019) studied technology methods to digital health literacy. These papers show the relative importance of considering not only technical performance but also usability, workflow integration, and human factors when proposing clinical ML applications.

The development of clinical decision support systems is a promising method for combining ML methods into existing care processes. Sardar et al. (2019) studied the effect of artificial intelligence on interventional cardiology, from decision-making helps to advanced interventional procedure assistance. Similarly, Kagiyama et al. (2019) gave a practical primer for clinical study in cardiovascular disease, focusing on clinical implementation. These methods look for positioning ML methods as complementary applications that enhance rather than replace clinical expertise.

Ethical and regulatory considerations is essential aspects of clinical integration. Armoundas et al. (2024) investigated implementation of artificial intelligence in improving outcomes in heart disease in a scientific statement from the American Heart Association, addressing implementation considerations. As ML methods advance toward clinical implementation, addressing these non-technical challenges could be considered an important task for successful translation.

7 Emerging Trends and Future Directions

7.1 Digital Twins and Personalized Modeling

The advance of digital twins, virtual representations of individual patients, is an emerging frontier in cardiovascular ML applications. Coorey et al. (2022) performed a comprehensive review on the health digital twin concept for tackling cardiovascular disease, while Martinez-Velazquez et al. (2019) performed another survey named “Cardio Twin: A digital twin of the human heart running on the edge”. These methods try to build personalized computational techniques which could simulate disease progression, forecast treatment responses, and improve individual care plans.

The technical obstacles of developing digital twins are substantial, requiring integration of multiple data types, development of mechanistic techniques, and building of effective simulation frameworks. Highly-cited papers in this domain show promising progress to reach these objectives, specifically in concentrated applications such as cardiac electrophysiology and hemodynamics. As data availability happens more and computational methods get better, digital twins may help personalized cardiovascular medicine, with interventions tailored to individual pathophysiology and predicted responses.

The potential implementations of digital twins span multiple domains, such as drug development, treatment optimization, and medical education. By building in silico representations of each patient, researcher and clinician could potentially examine interventions virtually prior to implementing them in practice, reducing risks and improving outcomes. The realization of this vision may need more progress in multiple areas, including data integration, model personalization, and validation against clinical outcomes, but shows a good long-term direction for the field.

7.2 Federated Learning and Privacy-Preserving Methods

Federated learning and other privacy-preserving ML techniques are an essential new direction, specifically for cardiovascular implementation involving sensitive patient data. While less represented in the current dataset of highly-cited papers, various published papers hint the relative importance of these techniques. The development of methods which enable model training across multiple institutions without sharing raw patient data addresses essential privacy concerns and regulatory requirements while facilitating larger, more diverse datasets.

As cardiovascular ML applications increasingly depend on multi-institutional data collaborations, expanding robust federated learning methods will be necessary for advancing the field while protecting patient privacy. Early implementations in medical imaging and EHR analysis shows the feasibility of this method, with cardiovascular implementations likely to follow.

7.3 Integration with Emerging Data Types

The combination of newly available data types is another essential future direction, with several highly-cited papers exploring novel data sources for cardiovascular assessment. Gut microbiome analysis, environmental exposure data, social determinants of health, and patient-generated health data from mobile applications all give good information sources which would possibly enhance cardiovascular risk assessment and management. Aryal et al. (2020) proposed machine learning techniques for gut microbiome-based diagnostic screening of cardiovascular disease, showing the potential of integrating novel biological data types.

There are some challenges on integrating these types of data including managing various data formats, temporal scales, and measurement frequencies, as well as handling missingness and quality variability. ML techniques help us handle these heterogeneous data streams for leveraging the full potential of emerging data sources. Moreover, developing interpretable models which may provide significant insights into the relationships between these novel parameters and cardiovascular outcomes will be essential for constructing clinical understanding and trust.

8. Conclusion

The present scientometrics study of 200 highly-cited papers on "machine learning" and "cardiovascular disease" has disclosed a quickly evolving field characterized by methodological sophistication, diverse clinical applications, and growing emphasis on implementation challenges. The study has shown a clear progression from traditional machine learning methods to increasingly complex deep learning architectures, with ensemble methods and hybrid methods featuring prominently among influential publications. Clinical methods span risk prediction, diagnostic imaging, drug discovery, and therapeutic optimization, with growing integration of multimodal data sources including electronic health records, genomic information, and wearable device outputs.

The field has depicted an increasing focus on the implementation considerations such as model interpretability, generalizability, and workflow integration, reflecting the maturation of cardiovascular ML research from proof-of-concept investigations toward clinically applicable tools. Emerging trends including digital twins, federated learning, and integration of novel data types point toward future directions that may further transform cardiovascular research and clinical practice. In spite of substantial progress, essential challenges have remained in validating models across diverse populations, preserving clinical utility in randomized trials, and addressing ethical and regulatory considerations.

The highly-cited literature investigated in this survey is the collective knowledge and methodological innovations that have most substantially advanced the field in the past five years. By mapping this intellectual landscape, detecting key developments, and highlighting emerging trends, this analysis gives both a reference for understanding the current state of cardiovascular ML study and a foundation for future work in this quickly advancing domain. As methodological abilities continue to get better and cardiovascular datasets expand, machine learning methods are likely to play an increasingly central role in understanding, preventing, and treating cardiovascular diseases.

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