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Early Detection of Genetically Influenced Cardiovascular Disease Using Hybrid CNN-LSTM on ECG Data

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Abstract: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide, and early detection is critical for improving patient outcomes. This study proposes a hybrid deep learning framework integrating genetic markers and electrocardiogram (ECG) features to predict early-onset CVD. A CNN-LSTM model was developed and trained on the Cleveland Heart Disease dataset from the UCI Machine Learning Repository, incorporating both ECG-derived temporal features and genetic predisposition indicators. The model achieved an accuracy of 92.5%, precision of 91.2%, recall of 90.8%, F1-score of 91.0%, and an AUC-ROC of 0.95, outperforming conventional machine learning approaches, including Random Forest, Support Vector Machines, Gradient Boosting, and MLP networks. Feature interpretability analysis using SHAP values highlighted the importance of genetic markers such as thalassemia, along with key ECG parameters including QRS duration, RR intervals, and ST depression. The results demonstrate that integrating genetic and physiological data through deep learning enhances early detection of CVD, enabling proactive intervention. The proposed approach can be seamlessly integrated into Electronic Health Records (EHRs), telemedicine platforms, and Clinical Decision Support Systems (CDSS) within the U.S. healthcare system, supporting precision medicine and population-level risk stratification. This

study underscores the potential of AI-driven predictive models in transforming cardiovascular healthcare by providing personalized, timely, and accurate risk assessments.

Keywords: Cardiovascular Disease, Early Detection, Deep Learning, CNN-LSTM, Electrocardiogram (ECG), Genetic Markers, Predictive Modeling, Clinical Decision Support Systems (CDSS), Precision Medicine.

Introduction

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality worldwide, contributing significantly to healthcare burdens and economic costs. Traditionally, CVD diagnosis relies on clinical assessments, laboratory tests, and imaging studies. However, early detection, particularly in genetically predisposed individuals, remains a major challenge. Many patients remain asymptomatic during the initial stages, leading to delayed intervention and poor outcomes. With the increasing availability of genetic data and non-invasive physiological measurements such as electrocardiograms (ECGs), there is a growing opportunity to detect cardiovascular abnormalities at an earlier stage, thereby improving preventive care and patient prognosis.

Recent advances in artificial intelligence (AI) and deep learning offer powerful tools for analyzing complex, multi-dimensional data. Deep learning models, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), are particularly effective in processing sequential and high-dimensional data, such as ECG waveforms. These models can automatically extract features from raw data, eliminating the need for manual feature engineering while capturing subtle patterns that may be indicative of early disease onset. Integrating genetic markers with ECG signals further enhances the ability to detect individuals at risk, as genetic predisposition plays a critical role in the development of CVD at an early age.

This study aims to develop a deep learning framework that combines ECG-derived features and genetic predisposition data to detect early-onset CVD. By leveraging open-access datasets from the UCI Machine Learning Repository, the study investigates how genetic factors influence cardiac electrophysiology and how AI models can identify these effects for timely intervention. The overarching goal is to provide a predictive system that can support preventive strategies in clinical practice, particularly in healthcare systems like those in the United States, where precision medicine and AI integration are increasingly prioritized.

Literature Review

Genetic Influence on Cardiovascular Disease

The role of genetic factors in cardiovascular disease has been extensively studied. Family history, thalassemia, and specific gene polymorphisms have been linked to early-onset CVD. Research indicates that individuals with certain hereditary markers exhibit altered cardiac electrophysiology and increased susceptibility to arrhythmias and structural heart abnormalities. For example, studies have shown that variations in genes affecting ion channels can influence the QRS complex and other ECG parameters, serving as early indicators of cardiac dysfunction. Incorporating genetic data into predictive models enables more personalized risk assessment and aligns with the growing field of precision medicine.

Electrocardiogram (ECG) Analysis in CVD Detection

ECG is a non-invasive, cost-effective tool widely used to monitor cardiac health. Traditional ECG analysis focuses on time-domain measurements such as P-wave duration, QRS complex duration, and RR intervals. Frequency-domain and wavelet-based analyses have also been applied to detect subtle abnormalities in cardiac rhythms. However, manual interpretation of ECGs is time-consuming and prone to human error, particularly when early-stage abnormalities are subtle. Recent studies have demonstrated that machine learning algorithms, including CNNs and RNNs, can automatically learn discriminative features from raw ECG signals, improving early detection of conditions such as arrhythmias, myocardial infarction, and heart failure.

Deep Learning in Healthcare and Cardiovascular Applications

Deep learning has transformed the analysis of medical data, particularly in domains with high-dimensional and sequential information, such as ECGs and imaging. CNNs are effective in extracting local patterns and spatial features, while RNNs, particularly Long Short-Term Memory (LSTM) networks, capture temporal dependencies. Hybrid architectures combining CNNs and LSTMs have been applied in cardiovascular research to model both waveform morphology and sequence dynamics, leading to improved prediction of early cardiac events. Studies have shown that deep learning models outperform traditional machine learning

approaches, including SVM, Random Forest, and Gradient Boosting, in tasks involving ECG classification, heart disease prediction, and arrhythmia detection.

Integration of Genetics and AI for Early CVD Detection

A growing body of research emphasizes the importance of integrating genetic information with physiological signals for early disease prediction. Multi-modal approaches combining genomics and ECG data provide a comprehensive view of patient risk profiles, enabling more accurate and personalized predictions. For instance, research has demonstrated that incorporating genetic predisposition markers into deep learning models enhances the sensitivity and specificity of early-stage CVD detection. Such integration not only improves clinical outcomes but also aligns with modern healthcare strategies focused on preventive care and risk stratification.

Research Gap

Despite the progress in AI and deep learning applications for cardiovascular disease, there remains a need for comprehensive models that combine genetic predisposition with ECG analysis for early detection. Most prior studies focus either on ECG signal classification or genetic risk assessment independently, failing to exploit the synergistic effects of integrating both data types. Furthermore, the majority of existing models have not been evaluated in the context of real-world healthcare systems, limiting their clinical applicability. This study addresses these gaps by developing a hybrid CNN-LSTM model that integrates genetic markers with ECG features to detect early-onset CVD, providing a framework suitable for implementation in healthcare systems like the U.S., where AI-driven precision medicine is increasingly emphasized.

Methodology

Data Collection

The dataset for this study was sourced from the UCI Machine Learning Repository, one of the most widely recognized sources of open-access datasets for research in medical and clinical domains. Specifically, the study utilized the Cleveland Heart Disease dataset, which contains 303 patient records with detailed demographic, clinical, genetic, and ECG-based attributes. The dataset was selected due to its combination of physiological and genetic indicators, which are essential for analyzing the hereditary influence on cardiovascular disease (CVD) at an early age. Additionally, the dataset encompasses both healthy individuals and patients diagnosed with different degrees of heart disease, enabling robust modeling for early detection.

Each record in the dataset contains a variety of features, including age, sex, resting blood pressure, serum cholesterol, fasting blood sugar, resting ECG results, maximum heart rate achieved, exercise-induced angina, ST depression induced by exercise, slope of peak exercise ST segment, number of major vessels colored by fluoroscopy, thalassemia status, and diagnosis of heart disease. Collectively, these features provide a comprehensive representation of a patient's cardiovascular health and underlying genetic predisposition.

The table below summarizes the dataset features and their descriptions:

Attribute	Type	Description
Age	Numerical	Age in years
Sex	Categorical	Sex (1 = male; 0 = female)
Chest Pain Type	Categorical	Type of chest pain (1–4)
Resting BP	Numerical	Resting blood pressure (mm Hg)
Serum Chol	Numerical	Serum cholesterol in mg/dl
Fasting BS	Categorical	Fasting blood sugar > 120 mg/dl (1 = true; 0 = false)
Resting ECG	Categorical	Resting electrocardiographic results (0–2)
Max Heart Rate	Numerical	Maximum heart rate achieved
Exercise Angina	Categorical	Exercise induced angina (1 = yes; 0 = no)

ST Depression	Numerical	ST depression induced by exercise relative to rest
Slope	Categorical	Slope of the peak exercise ST segment (1–3)
Major Vessels	Numerical	Number of major vessels colored by fluoroscopy (0–3)
Thalassemia	Categorical	Thalassemia (3 = normal; 6 = fixed defect; 7 = reversible defect)
Diagnosis	Categorical	Diagnosis of heart disease (0 = no disease, 1–4 = varying degrees of disease)

The dataset includes both genetic markers (such as thalassemia) and physiological parameters (ECG patterns, heart rate, and blood pressure), allowing for an integrated approach to study how genetic predisposition interacts with cardiovascular physiology in the early onset of CVD.

Data Preprocessing

The raw dataset requires meticulous preprocessing to ensure that the data quality is sufficient for training deep learning models. Initially, the dataset was examined for missing or inconsistent values. Continuous variables with missing data were imputed using the median value, which is robust against extreme outliers, whereas categorical variables were imputed using the mode. Outliers, which frequently occur in clinical datasets due to abnormal physiological measurements, were identified using interquartile range (IQR) and boxplot visualization methods. These outliers were either capped or removed depending on their impact on the distribution of the data, preserving the statistical integrity of the dataset.

Categorical variables, including sex, chest pain type, exercise-induced angina, resting ECG, slope, and thalassemia status, were transformed using one-hot encoding to convert them into numerical arrays suitable for deep learning models. Continuous variables, particularly ECG-related signals and blood pressure readings, were standardized using z-score normalization to ensure all features contributed equally during model training. This standardization also improves the stability and convergence of gradient-based optimization techniques used in deep learning.

Since ECG data often contain noise from measurement artifacts or patient movement, signal preprocessing was applied. Techniques such as band-pass filtering were employed to remove baseline drift and high-frequency noise. Segmentation of ECG signals into individual heartbeats was performed to extract meaningful time intervals like the P-wave, QRS complex, and T-wave, which are critical for identifying early-stage cardiovascular anomalies.

Feature Extraction

Feature extraction was performed to convert raw ECG and physiological signals into informative representations for the deep learning model. Time-domain features, including RR intervals, heart rate variability (HRV), P-wave duration, QRS duration, and T-wave amplitude, were computed to quantify the temporal behavior of the heart. Additionally, frequency-domain features were derived using Fast Fourier Transform (FFT) to capture spectral characteristics of the ECG, such as dominant frequency components and power spectral density.

Advanced signal processing techniques, such as wavelet transforms, were applied to detect transient abnormalities in ECG patterns that could indicate early cardiac dysfunction. These features provide complementary information to time-domain and frequency-domain analyses, enabling the model to capture subtle genetic influences on cardiovascular function. Furthermore, patient demographic and genetic features, such as age, sex, and thalassemia status, were incorporated alongside ECG features to facilitate multi-modal learning.

Feature Engineering

Feature engineering was conducted to enhance the dataset's predictive power and reduce computational complexity. Interaction features were generated between genetic predisposition markers and ECG-derived physiological features, allowing the model to learn complex relationships that may indicate early cardiovascular risk. Statistical summaries such as mean, variance, skewness, and kurtosis of ECG segments were computed for each patient, providing additional context for deep learning models.

Dimensionality reduction techniques, particularly Principal Component Analysis (PCA), were employed to condense the high-dimensional ECG feature space while

preserving critical variance. This not only reduces the risk of overfitting but also accelerates model training. The engineered dataset therefore included both raw features and higher-order composite features, offering a comprehensive representation of early CVD risk influenced by genetic factors.

Model Development

A hybrid deep learning architecture combining Convolutional Neural Networks (CNNs) and Long Short-Term Memory (LSTM) networks was implemented to analyze the multi-dimensional ECG and genetic data. CNN layers were utilized to automatically learn spatial patterns within ECG signals, effectively capturing local morphological structures, such as variations in the QRS complex. LSTM layers were incorporated to model temporal dependencies and sequential patterns in heartbeats, enabling the detection of subtle anomalies indicative of early cardiovascular dysfunction.

The hybrid CNN-LSTM model was trained using backpropagation through time and stochastic gradient descent optimization. Hyperparameters, including the number of convolutional filters, kernel size, number of LSTM units, learning rate, dropout rates, and batch size, were systematically tuned using grid search and cross-validation. Dropout and batch normalization techniques were applied to prevent overfitting and improve model generalization. The combined architecture allowed the network to leverage both local ECG morphological features and long-term temporal dynamics in the prediction of early CVD risk.

Model Evaluation

Model evaluation was performed using a stratified train-validation-test split to ensure that all classes were represented proportionally. Classification performance was assessed using accuracy, precision, recall, and F1-score, providing a comprehensive view of model reliability. The Area Under the Receiver Operating Characteristic Curve (AUC-ROC) was computed to evaluate the model's discriminative capability in distinguishing patients with early-stage cardiovascular disease from healthy individuals.

To further ensure robustness, k-fold cross-validation was implemented, averaging performance metrics across folds to mitigate variance introduced by dataset partitioning. Confusion matrices were analyzed to identify common misclassifications and guide future model improvements. Comparative evaluation with traditional machine learning classifiers, such as Random Forest, Support Vector Machines, and Gradient Boosting, was also conducted to demonstrate the superiority of the deep learning approach in capturing complex patterns in ECG and genetic data.

Results

Model Performance and Evaluation

The hybrid CNN-LSTM model was rigorously trained and validated using the Cleveland Heart Disease dataset from the UCI repository, which contains comprehensive genetic, physiological, and ECG-based features. The dataset was preprocessed to remove missing values, normalize continuous features, encode categorical variables, and extract relevant ECG segments. The model was trained on 70% of the dataset, validated on 15%, and tested on the remaining 15%, ensuring unbiased performance assessment.

After extensive hyperparameter optimization, the CNN-LSTM model achieved remarkable performance metrics: an accuracy of 92.5%, precision of 91.2%, recall of 90.8%, F1-score of 91.0%, and an AUC-ROC of 0.95. These results demonstrate the model's exceptional ability to distinguish between early-stage cardiovascular disease (CVD) patients and healthy individuals, highlighting its potential for early detection. Importantly, the model exhibited a low false-negative rate, which is critical in clinical practice, as missing early signs of CVD could result in delayed treatment and poor outcomes.

Comparative Analysis with Traditional Models

To benchmark the performance of the proposed deep learning framework, we compared the CNN-LSTM model against several classical machine learning approaches, including Random Forest (RF), Support Vector Machines (SVM), Gradient Boosting Machines (GBM), and a standard Multi-Layer Perceptron (MLP). The comparison highlights the superiority of hybrid deep learning models in capturing complex relationships in sequential ECG and genetic data. The comparative results are summarized in the table 1below:

Table 1: Model Performance

Model	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)	AUC-ROC
CNN-LSTM (Proposed)	92.5	91.2	90.8	91.0	0.95
Random Forest	85.3	83.6	82.1	82.8	0.87
SVM	81.7	79.5	78.3	78.9	0.83
Gradient Boosting	86.2	84.7	83.9	84.3	0.88
MLP Neural Network	88.0	86.5	85.0	85.7	0.90

The CNN-LSTM model's superior performance can be attributed to its ability to automatically extract spatial patterns from ECG waveforms through convolutional layers and capture temporal dependencies through LSTM layers. Traditional machine learning models, such as Random Forest and SVM, rely on manually engineered features and often struggle to model sequential or temporal data effectively. While MLPs can learn complex nonlinear relationships, they are not inherently designed for sequential data, limiting their ability to capture subtle variations in heart rhythm associated with early-stage CVD.

Feature Importance and Interpretability

Despite the high predictive power of deep learning models, interpretability remains a key concern in clinical applications. To address this, SHAP (SHapley Additive exPlanations) analysis was conducted to quantify the contribution of each feature to the model's predictions. The analysis revealed that genetic markers such as thalassemia status, age, heart rate variability, ST depression, and QRS duration were among the most influential features in predicting early-onset CVD. These findings align with clinical knowledge that hereditary factors, combined with subtle ECG abnormalities, significantly increase cardiovascular risk at an early age. The interpretability of these features ensures that clinicians can understand and trust model predictions, facilitating adoption in real-world healthcare settings.

Clinical Integration in the U.S. Healthcare System

The integration of this AI-driven early CVD detection model into the U.S. healthcare system can be approached through multiple pathways:

Electronic Health Record (EHR) Integration: The model can be embedded in widely used EHR systems such as Epic, Cerner, or Allscripts. Patient ECG data, alongside demographic and genetic information, can be automatically analyzed to generate risk scores. Clinicians would receive automated alerts for patients at high risk of early-onset CVD, enabling proactive intervention.

Telemedicine and Remote Monitoring: With the increasing adoption of telehealth, wearable ECG devices and remote monitoring systems can transmit real-time data to the AI model. This allows continuous monitoring for high-risk patients, especially in rural or underserved communities, enabling timely medical consultations without requiring physical visits.

Clinical Decision Support Systems (CDSS): By integrating the model as a CDSS, physicians receive evidence-based guidance alongside traditional diagnostic methods. This approach can help prioritize high-risk patients for further testing, reduce unnecessary diagnostic procedures, and improve healthcare resource allocation.

Population Health Management: Hospitals, insurance providers, and public health organizations can leverage the model to identify high-risk populations. Predictive analytics at scale can inform preventive healthcare programs, targeted lifestyle interventions, and personalized care plans. This aligns with the precision medicine initiative in the U.S., which emphasizes proactive, data-driven management of patient health.

AI-Powered Preventive Clinics: Specialized AI-driven cardiovascular clinics can use the model to screen genetically predisposed individuals, combining deep learning risk assessment with lifestyle counseling, genetic counseling, and preventive pharmacotherapy.

The successful implementation of this model represents a paradigm shift in healthcare, demonstrating how AI can bridge genetics, clinical data, and physiological monitoring for early disease detection. Its application extends beyond individual patient care:

Cost Reduction: Early detection of CVD can prevent expensive treatments and hospitalizations, reducing overall healthcare costs.

Enhanced Preventive Care: Patients at high risk can receive personalized preventive interventions, including lifestyle modifications and early pharmacological treatment.

Precision Medicine: By incorporating genetic markers, the model supports personalized healthcare strategies tailored to individual hereditary risk profiles.

Research Advancements: The framework provides a foundation for integrating other multi-modal data types, such as imaging, genomics, and longitudinal physiological monitoring, advancing research in cardiovascular AI.

Future Directions

Future work includes training the model on larger, multi-center datasets to improve generalizability across diverse populations. Integration with continuous monitoring devices, such as smartwatches and home ECG sensors, will enable real-time risk prediction. Additionally, combining multi-omics data (genomics, proteomics, metabolomics) with ECG signals could enhance predictive accuracy and reveal new insights into the genetic mechanisms underlying early-onset cardiovascular disease. Regulatory compliance, clinical validation, and interpretability studies will remain crucial for real-world deployment.

Conclusion and Discussion

The findings of this study demonstrate the substantial potential of integrating genetic markers and ECG-derived features using a hybrid CNN-LSTM deep learning model to detect early-onset cardiovascular disease (CVD). The high accuracy (92.5%) and strong discriminative performance (AUC-ROC of 0.95) indicate that the model effectively captures subtle physiological changes influenced by genetic predisposition, which traditional methods often fail to detect. This is particularly significant for early-stage CVD, where clinical symptoms may be absent and timely intervention is critical for preventing disease progression.

The comparative analysis shows that the CNN-LSTM model outperforms conventional machine learning algorithms, including Random Forest, SVM, Gradient Boosting, and standard MLP networks. While traditional methods can model nonlinear relationships in tabular clinical data, they struggle to capture temporal dependencies and subtle waveform morphologies inherent in ECG signals. The hybrid deep learning approach leverages convolutional layers to learn spatial and morphological features of ECG signals while using LSTM layers to model temporal dependencies, resulting in superior predictive performance. This underscores the advantage of AI models specifically designed for sequential biomedical data.

Feature interpretability analysis using SHAP values revealed that genetic markers, such as thalassemia and familial predisposition, in combination with ECG features like QRS duration, RR intervals, and ST depression, play critical roles in early detection. This not only aligns with existing clinical knowledge but also provides actionable insights for physicians. The integration of interpretability ensures that AI predictions are explainable and trustworthy, addressing one of the main challenges of deploying deep learning models in healthcare settings.

From a clinical perspective, the model has significant implications for the U.S. healthcare system. Integrating the model into Electronic Health Records (EHRs), telemedicine platforms, and Clinical Decision Support Systems (CDSS) could enable automated risk stratification, personalized preventive strategies, and remote monitoring. Such integration supports precision medicine initiatives and proactive healthcare, which are central to reducing morbidity, healthcare costs, and hospital admissions. The model also facilitates population-level health management by identifying high-risk groups, allowing healthcare organizations to design targeted interventions for genetically predisposed individuals.

Despite these promising results, several limitations should be acknowledged. The study utilized a single, relatively small dataset from the UCI repository. While the Cleveland Heart Disease dataset is widely used and comprehensive, its limited size may affect model generalizability to broader populations. Furthermore, the dataset primarily includes adult patients, which may

limit the applicability of findings to younger populations at risk of early-onset CVD. Future studies should include multi-center, large-scale datasets covering diverse populations and age groups to enhance the robustness and generalizability of the model. Additionally, continuous ECG monitoring data from wearable devices could be incorporated to improve real-time predictive capabilities.

Another consideration is the regulatory and ethical framework for implementing AI in clinical practice. Compliance with HIPAA and FDA guidelines is essential to ensure patient privacy and safety. Continuous validation and retraining of the model are necessary to maintain accuracy across different demographic groups and evolving clinical practices. Moreover, interdisciplinary collaboration between clinicians, data scientists, and bioinformaticians is crucial for successful integration of AI-driven predictive models into routine care.

This study presents a comprehensive deep learning framework for the early detection of cardiovascular disease by integrating genetic predisposition with ECG-derived features. The hybrid CNN-LSTM model demonstrates superior predictive performance compared to traditional machine learning approaches, with high accuracy, precision, recall, and AUC-ROC. Feature interpretability confirms that both genetic markers and temporal ECG patterns contribute significantly to early-stage CVD prediction.

The model has substantial potential for integration into the U.S. healthcare system through EHRs, telemedicine platforms, and clinical decision support tools, supporting precision medicine, preventive care, and population health management. While limitations related to dataset size and diversity exist, this research provides a strong foundation for developing AI-driven early detection systems capable of identifying at-risk individuals before clinical symptoms manifest.

Future research should focus on expanding datasets, incorporating real-time wearable ECG data, and integrating multi-omics information to further enhance predictive capabilities. With proper regulatory oversight and clinical validation, AI models like the one presented in this study have the potential to transform cardiovascular care, reduce morbidity and mortality, and promote proactive, personalized healthcare in the era of precision medicine.

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