MIMIC-IV version 2.2

Protocol Draft v1.0

<u>Machine Learning and Deep Learning Models for Detecting Ischemic Stroke from ECG Waveforms: A MIMIC-IV Dataset Study.</u>

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* This protocol was based on the recommendations of Barbati *et al*. "Study Design and Research Protocol for diagnostic or prognostic studies in the Age of Artificial Intelligence: A Biostatistician's Perspective". (1)

Introduction

Topic: Detection of Ischemic Stroke Using Predictive Modeling and ECG Waveforms in the MIMIC-IV Database

Background & Rationale

Stroke is an important cause of morbidity and mortality worldwide. According to the American Heart Association, stroke is the fifth most common cause of death among Americans, accounting for one in every 19 deaths (2). Early detection and treatment of acute ischemic stroke (IS) secondary to emergent large vessel occlusion are critical to optimizing emergency medical services triage models and improving patient outcomes (3,4). Numerous tools have been evaluated in the literature to detect strokes in the emergency department, one of which is electrocardiograms (ECGs)(4). ECGs are a cost-effective screening tool that, when combined with clinical judgment, can be highly advantageous in screening patients in the emergency department for stroke.

Changes in ECGs after a stroke are well-documented. The most frequently observed ECG changes in the early post-stroke phase include prolonged heart rate-corrected QT (QTc) time, ST-segment changes, and inverted T waves with altered amplitude and width. Additionally, a long QTc can serve as a predictor of cardiac events after an IS. (5)

Likewise, Artificial intelligence (AI) has shown great potential in identifying abnormal ECG changes that might go unnoticed or require more accurate identification. Machine learning (ML) has been widely used to predict various cardiovascular diagnoses in the emergency department, including myocardial infarction, left ventricular systolic dysfunction, atrial fibrillation, and concealed long QT syndrome. (5)

However, the application of machine learning (ML) modeling to detect acute ischemic stroke (IS) still holds untapped potential. A brief literature review reveals only a few relevant studies that are tangentially related to the combination of ischemic stroke, ECGs and ML (5–8). Of these, there are only two articles that have tried to detect or predict stroke in the emergency setting. One of them used ML to predict ECG changes in 7,052 Chinese patients, and another study applied ML to a cohort of 3,500 Chinese patients with an IS. However, this approach has not been applied to the MIMIC-IV database for this specific purpose (5,6). Therefore, the creation of a model with this database would be particularly valuable as it would be **the first ML model to detect stroke using ECG waveforms in American patients.**

Unexplored Potential in the MIMIC- IV database:

To date, no studies have applied ML modeling to the MIMIC IV database specifically for the purpose of detecting ischemic stroke. This represents a significant gap in research, given the rich, diverse data available within MIMIC IV. Utilizing this database for ML-based IS detection could provide several advantages:

- Diverse Patient Population: MIMIC IV includes data from a varied demographic, enhancing the generalizability of findings to the American population.
- Comprehensive Data: The extensive range of patient information available can help create more robust and accurate models.
- Real-World Relevance: Insights derived from this database could be directly applicable to clinical settings in the United States.

Objectives

1. Estimate the accuracy of machine learning and deep learning frameworks in detecting acute ischemic stroke using ECG data.
2. Differentiate the efficiency of conventional ML techniques like Random Forest (RF) and Support Vector Machine (SVM) from deep learning frameworks like Convolutional Neural Networks (CNN).

Methods

Dataset

- **Source:** Hosp module of the MIMIC IV database, version 2.2.

Please note that we will not include the ICU module because we will exclusively analyze the admission ECG.

- **Exclusion Criteria:**
    - Patients younger than 18
    - Patients with no ECG data
    - Patients with no hospitalization events
    - Patients without an ECG during their respective hospitalization event

Data Collection and Analysis

- Collected ECGs from both non-stroke individuals and patients with IS using the database stored in BigQuery with python notebooks.
- Analyzed participant demographics and ECG parameters to identify useful features.

Models:

1. **Model Training:**
    - Convolutional Neural Network (CNN) - Best for spatial relationships.
    - Recurrent Neural Networks (RNNs) - Best for sequential data.
    - Random Forest (RF) - can handle large datasets with high dimensionality. Does not need as much computational power.
    - Support Vector Machine (SVM) - Can handle high dimensionality and non-linear relationships.
2. **Validation Plan:**
    - Stratified K-fold cross-validation technique

Implementation

- **Train models to classify subsets of patients in the ischemic stroke and no-stroke categories based on ECG findings.**
- **Detect the presence of stroke in the test subgroup.**
- Compare the performance of AI models to traditional clinical scales and clinician judgment (future observational study).

Process

1. **Data Preparation:**
    - Extract and preprocess ECG data from the MIMIC IV database. Write a preliminary exploratory analysis report.
    - Split the data into training and validation sets using stratified K-fold cross-validation to ensure balanced class representation.
2. **Feature Extraction:**
    - Identify key patient features such as gender, comorbidities, and blood pressure.
    - Extract the raw waveforms from the ECG module
3. **Model Development:**
    - Train the CNN, RF, and SVM models on the prepared dataset.
    - Optimize hyperparameters to improve model performance.
4. **Model Evaluation:**
    - Validate model accuracy using the cross-validation results.
    - Compare classification accuracy between models.
5. **Observational Study:**
    - Design an observational study to compare the accuracy of the developed models against traditional clinical methods.

Expected Outcomes of the Model

- Improved detection rates of IS in the emergency department setting.
- Reduced time-to-treatment and improved patient outcomes.

OTHER ML Models-Research ideas:

Idea N.2

Topic: Early Prediction of Prognosis in Sepsis using ECG waveforms in the MIMIC-IV database.

Introduction and background: Sepsis, a severe condition triggered by an exaggerated host response to infection, continues to be a major cause of mortality in intensive care units, with a mortality rate of approximately 41.9% (9). Early prediction of patient prognosis is critical for improving outcomes in vulnerable individuals. Current methods for detecting and predicting sepsis outcomes, like SOFA and SIRS criteria, heavily rely on clinical judgment and basic diagnostic tools, which are subjects of ongoing debate among experts (10).

Developing a machine learning or deep learning model could offer significant benefits by accurately predicting mortality in septic patients, thereby enhancing clinical decision-making. Such models have the potential to complement and refine traditional approaches, providing clinicians with valuable insights for better patient management.

Therefore, the goal of this study is to create a model that accurately predicts short-term mortality in patients with sepsis using ECG signals. This idea builds on the work of Hu et al. (11), which focused on clinical features of patients with sepsis in the MIMIC database to create a ML model that predicts mortality. While other models have pursued similar goals, they have done so with significantly fewer patients. For example, Kwon et al. (12) utilized 1,548 patients to achieve comparable outcomes, whereas the MIMIC-IV database includes around 8,900 eligible sepsis patients. This larger sample size can potentially lead to a model with improved generalizability and robustness. Additionally, various published studies (13–15) that did not employ machine learning have highlighted important ECG features linked to sepsis mortality, underscoring the potential for ECG-based predictive models.

Objectives:

- Create a model that accurately predicts short-term mortality in patients with sepsis using ECG signals.
- Evaluate which machine learning method is the most successful at predicting the prognosis of these patients.

Dataset:

- ICU module from the MIMIC-IV database + MIMIC- ECG dataset

Possible methods:

- Convolutional Neural Networks (CNNs)
- Recurrent Neural Networks (RNNs)
- Random Forests
- Gradient Boosting Machines (GBMs)
- Support Vector Machines (SVMs)

Idea N. 3

Topic: Integration of clinical features and ECG waveforms to predict 30, 90 day and 1 year hospital readmission in patients with acute heart failure using machine learning models in the MIMIC-IV database.

Introduction and background:

Acute heart failure (AHF) poses a significant challenge due to its high rates of hospital readmission, which place considerable strain on healthcare systems. Studies indicate that AHF patients face readmission rates of approximately 16-19% within 30 days and up to 53% within one year, underscoring the urgency for prediction to improve patient outcomes (16,17).

Research has shown that integrating clinical data, such as vital signs and laboratory results, with ECG features can uncover complex patterns that predict higher risks of readmission. Several studies, like Naderi *et al*., Sabouri *et al*., and Gouda *et al*. Safiriyu *et al*., Lan *et al*., have identified specific ECG findings and clinical characteristics associated with early readmissions in HF patients (16–20). Additionally, ML methods have demonstrated superior performance compared to traditional statistical models in predicting HF readmissions and mortality, as highlighted by Shin *et al.* (21)

Therefore, this study aims to harness raw ECG waveforms to develop an ML model capable of predicting hospital readmissions in AHF patients using the comprehensive dataset available in the MIMIC-IV database.

Objectives:

- Create a model that accurately predicts short-term short, medium, and long term hospital readmission in patients with acute heart failure using ECG signals and clinical information as features.

Dataset:

- ICU AND Hosp modules from the MIMIC-IV database + MIMIC- ECG dataset

Possible methods:

- Convolutional Neural Networks (CNNs)
- Recurrent Neural Networks (RNNs)
- Random Forests
- Gradient Boosting Machines (GBMs)
- Support Vector Machines (SVMs)

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