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LLM Machine Learning for Predicting Cardiovascular Mortality in Patients

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ABSTRACT
Patients with chronic kidney disease (CKD) face a high risk of cardiovascular death, yet accurately predicting this risk remains challenging. This study aims to develop an interpretable machine learning (ML) model to predict 10-year cardiovascular mortality in CKD patients using SHAP explainers. [1]Six ML models were created and tested, with the best model selected for prediction and patient categorization. Survival rates were analyzed using log-rank tests on Kaplan-Meier curves, and Cox regression was employed to explore the relationship between ML-predicted risk scores and mortality. The chosen autoencoder (AE) model demonstrated superior performance, with higher ML scores[2] significantly correlating with increased cardiovascular mortality risk. Key determinants such as age, high blood pressure, C-reactive protein, and serum creatinine were identified. The ML-driven tool showcased high accuracy in determining the 10-year cardiovascular mortality risk for CKD patients, offering valuable insights for individual risk assessments.

Keywords: cardiovascular mortality, chronic kidney disease, machine learning, interpretable model, shap

I. INTRODUCTION

Machine learning (ML) has seen extensive adoption in the medical domain, revolutionizing healthcare technologies (12).[3] Within ML for the medical field, cardiovascular risk prediction remains a popular research area, where ML models have emerged as prominent tools, often surpassing traditional methods in risk assessment and stratification. In particular, recent studies report ML outperforming conventional methods in tasks such as atherosclerotic plaque tissue characterization[4,5,6,7,8,9], stratification of CVD risk [10,11,12,13,14,15], prediction of stroke risk, and forecasting of cardiac events (6). However, a significant gap persists in applying these advancements to understand cardiovascular implications in CKD patients. Given the continued increase in CKD prevalence and incidence it is essential to provide more focus on cardiovascular Specifically, this study integrated an advanced ML model with a framework based on SHAP. This approach not only enhances the accuracy of predicting 10-year cardiac mortality risk in CKD patients. Additionally, it assists clinicians in daily routine associated with the assessment of disease severity, thereby optimizing the potential for early intervention. Such developments represent a significant advancement for ML in medicine (16,17,20) and contribute to establishing interpretable and individualized models for risk prediction.

Related work

The global rise in CVD incidence and mortality remains a major obstacle to healthy ageing [19]. Current research prioritizes early detection, management, and treatment of CVD [20]. Advanced statistical and machine learning techniques have improved predictive health models [21]. More researchers utilize machine learning for cardiac mortality risk prediction, leveraging diverse models to assess mortality causes by CVD, from individual to composite risk factors [22]. While numerous studies have employed ML to predict and analyze cardiovascular mortality, reports on CVD within the context of CKD remain hardly explored. It is noteworthy that CKD induces a systemic, chronic proinflammatory state [23]. This state plays a pivotal role in vascular and myocardial remodeling, contributing to accelerated atherosclerotic lesion development, vascular calcification and senescence, as well as myocardial fibrosis and cardiac valve calcification. Consequently, CKD can be perceived as causing an expedited aging of the cardiovascular system. Given this, research on risk prediction of cardiac death within CKD is of paramount importance [16]. To this end, several common ML algorithms include Naive Bayesian, Support Vector Machine, KNN, and Multilayer perceptron etc. in our report. Yet, the "curse of dimensionality" in biological CVD data remains. Dimensionality reduction methods like Principal Component Analysis and Autoencoders[24] have become essential. In practical terms, achieving a balance between model precision and clarity is challenging, and making model outcomes more intuitive for medical professionals is necessary [25].

II. METHODS

2.1 Study Population

The study analyzed the data from the combination of five continuous survey circles of the National Health and Nutrition Examination Survey (NHANES), spanning from 2001 to 2010. The inclusion criteria for the current research were as follows: (1) age ≥20 years; (2) diagnosed with CKD (defined as an estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m2[using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation (26) and/or a urinary albumin-Cr ratio [ACR] >30 mg/g); (3) possessing complete baseline, and follow-up data. Ultimately, date from a cohort of 2,935 individuals were used in the present research (Figure 1).

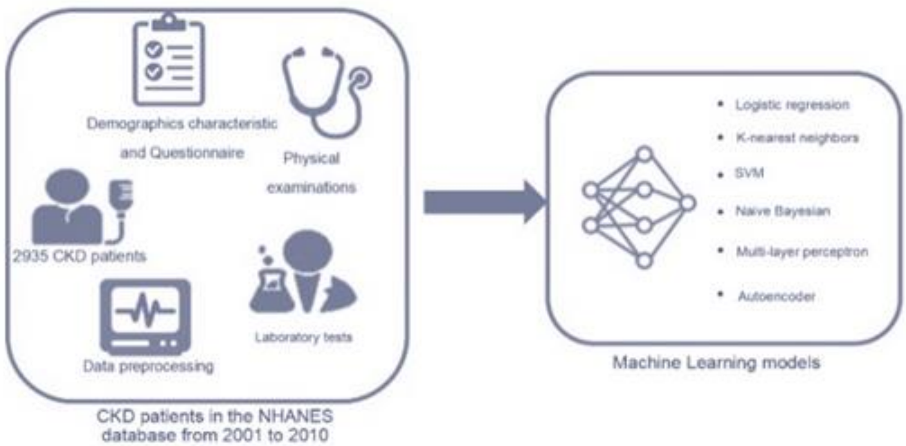
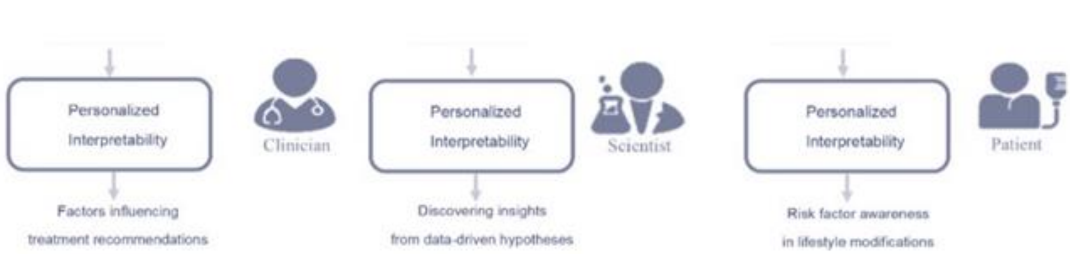


Figure 1: Framework for predicting cardiovascular mortality in patients with chronic kidney disease. SVM: support vector machines, SHAP: SHapley Additive exPlanations.

2.2 Data Source

All data utilized in this research were sourced from NHANES, an ongoing cross-sectional survey designed to capture nationally representative samples of the non-institutionalized population in the United States. Data were collected through the official website of the Centers for Disease Control and Prevention [https://wwwn.cdc.gov/Nchs/Nhanes]. The NHANES sampling frame is established on a complex, stratified, and multi-stage probability sample design. Data were extracted from various files, each encompassing a specific set of variables for a given year. Integration of these files was performed to construct a consolidated database containing the entirety of available data for each individual (with the SEQN identifier serving as the linkage across all datasets). This approach facilitated the generation of a unique and comprehensive database encompassing the entire cohort of examined subjects, along with their related data. The Ethics Review Board of the National Center for Health Statistics granted approval for all NHANES protocols, and all participants provided written informed consent.



2.3 Feature Selection

Our structured database encompassed 33 variables, often referred to as “features” in ML, which were selected to be associated with the cause or progression of CKD based on domain knowledge and literature search. Features exhibiting a missing data rate not exceeding 30% were retained and subjected to multivariate feature imputation to in the final

Sensitivity	0.7444	0.7218	0.5639	0.4812	0.7594	0.8095
	(0.7091,0.7797)	(0.6856,0.7581)	(0.5238,0.6040)	(0.4408,0.5216)	(0.7248,0.7940)	(0.7765,0.8425)
Specificity	0.9758	0.9824	0.9846	0.9868	0.9251	0.9634
	(0.9633,0.9882)	(0.9717,0.9930)	(0.9746,0.9945)	(0.9775,0.9960)	(0.9038,0.9464)	(0.9357,0.9912)
F1-score	0.8148	0.8101	0.6977	0.6305	0.7537	0.7000
	(0.7834,0.8462)	(0.7784,0.8419)	(0.6605,0.7348)	(0.5915,0.6696)	(0.7189,0.7886)	(0.6629,0.7371)
	0.0627	0.0628	0.0930	0.0949	0.0909	0.1206
	(0.0431,0.0823)	(0.0432,0.0825)	(0.0695,0.1165)	(0.0712,0.1186)	(0.0676,0.1141)	(0.0943,0.1469)

2.4 Model Development

Six ML models were formulated to predict 10-year cardiovascular mortality leveraging follow-up data. In addition to the five common models sourced from Scikit-learn (28), namely, logistic regression (LR), k-nearest neighbors (KNN), multi-layer perceptron (MLP), support vector machines (SVM), Naive Bayesian (NB), and k-nearest neighbors (KNN), we incorporated autoencoders (AE) [29]. AE emerges as an innovative learning technique capable of ensuring data-driven dimensionality reduction with minimal prior the endpoint of cardiac mortality we employed stratified random sampling to partition 2,935 patients into training and test sets, maintaining a 7: 3 ratio. The training dataset was preprocessed via the Adaptive Synthetic Sampling Approach (ADASYN) (30), assuring a balanced distribution between the minority and majority classes. The optimization of ML model parameters was achieved through ten-fold cross-validation.

2.5 Model Interpretation for Healthcare

In healthcare, the interpretability of machine learning models influences clinical decision-making. Understanding prediction drivers is important for patient outcomes, but machine learning models, dubbed 'black boxes' can cloud their logic in fields like healthcare[30] To bridge this chasm, we introduced the SHAP values into our research, presented by Lundberg and Lee (31), SHAP offers a consolidated structure tailored to elucidate the predictions of ML models, presenting an easy to grasp approach to various intricate ML algorithms in an e.g. routine clinical setting. Its prowess in enhancing interpretability, a pivotal asset in healthcare, has been corroborated in prior research [32-35]. Notably, SHAP facilitates both fine- and coarse-grained model interpretability, setting it apart with a more theoretical foundation than many of its previous published the endpoint of cardiac mortality we employed stratified random sampling to partition 2,935 patients into training and test sets, maintaining a 7: 3 ratio. The training dataset was preprocessed via the Adaptive Synthetic Sampling Approach (ADASYN) (30), assuring a balanced distribution between the minority and majority classes. The optimization of ML model parameters was achieved through ten-fold cross-validation.

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2.7 Experimental Implementation and Statistical Analysis

Analyses were conducted utilizing Python (Version 3.9) with the integration of several libraries including Imblearn, Sklearn, Matplotlib, Lifelines, Shap, and Tensorflow. Additionally, R (Version 4.2.1) was employed, specifically leveraging the survival and survminer packages. To fully assess the capability of the ML models, various evaluation metrics were adopted, as described in [37], encompassing specificity, sensitivity, F1-score, and the area under the receiver operating characteristic curve (AUC). For comparative analysis, the evaluation metrics across the six models by one-way ANOVA, followed by post-hoc pair wise comparisons using the least-significant difference method. The optimal cut-off, as determined by maximizing the Youden's index, enabled the stratification of patients into low and high ML risk groups. Differences in survival outcomes were assessed via the log-rank test on the Kaplan–Meier curves. Furthermore, multivariable Cox regression was employed to evaluate the relationship between ML risk and 10-year cardiovascular death. All statistical inferences were made with a threshold for significance set at a two-tailed P value ≤ 0.05.[45,46,47,48,49,50]

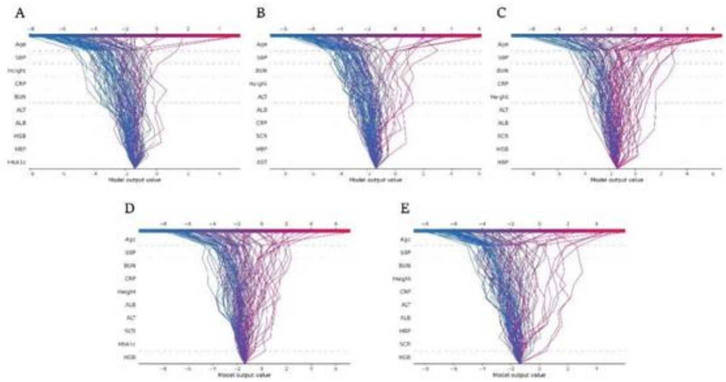

Figure 3: Variable importance in ML classification for race. (A) Mexican American, (B) of these influences resulted in the final SHAP value, corresponding to the prediction score.

III. CONCLUSION

In summary, the tested ML models have demonstrated satisfying performance in predicting 10-year cardiovascular mortality among patients with CKD. Our ML model effectively incorporates important clinical and demographic features to accurately discern cardiovascular mortality in CKD stage 3-5 population, thus facilitating personalized preventive strategies in clinic practice. The combination of ML and SHAP holds promise in delivering precise and transparent individualized risk predictions. This integration helps doctors understand key features in the model, improving their insight into the decision-making related to disease severity assessment.

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