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Research Article

Development and Validation of an Explainable Machine Learning Model for Early Prediction of Intradialytic Hypotension by Integrating Antihypertensive Medication Profiles and Clinical Parameters in Maintenance Hemodialysis Patients: A Prospective Cohort Study

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Abstract

Intradialytic hypotension (IDH) is a major complication of maintenance hemodialysis (MHD), strongly associated with vascular access thrombosis, cardiovascular events, and mortality. Existing predictive tools frequently overlook detailed antihypertensive drug timing and lack explainability. The objective of this prospective cohort study was to develop and validate an explainable machine learning model incorporating antihypertensive medication timing, dialysate profiles, and real-time intraoperative parameters for early IDH prediction. A total of 520 MHD patients (representing 12,480 hemodialysis sessions) were followed across derivation (n=364 patients; 8,736 sessions) and validation cohorts (n=156 patients; 3,744 sessions). Intradialytic hypotension was defined per KDOQI guidelines as a decrease in systolic blood pressure of 20 mmHg or more, or a decrease in mean arterial pressure of 10 mmHg or more, accompanied by clinical symptoms or intervention. Five algorithms (XGBoost, Random Forest, Support Vector Machine, LightGBM, and Logistic Regression) were trained. Among these, XGBoost achieved superior discrimination in the external validation cohort (Area Under the Receiver Operating Characteristic Curve [AUROC]: 0.892, 95% Confidence Interval: 0.875 to 0.908; Sensitivity: 84.2%; Specificity: 81.6%). SHapley Additive exPlanations (SHAP) analysis revealed that ultrafiltration rate, pre-dialysis antihypertensive administration within 4 hours, interdialytic weight gain, and baseline serum albumin were the dominant features driving model predictions. Integrating machine learning algorithms with SHAP explainability enables accurate, interpretable IDH risk stratification to guide personalized hemodialysis management.

Keywords: Intradialytic hypotension, machine learning, XGBoost, SHAP

explainability, hemodialysis, antihypertensive timing, predictive modeling.

Introduction

Intradialytic hypotension remains the most frequent acute complication encountered during maintenance hemodialysis, affecting 15% to 30% of all treatment sessions worldwide. Characterized by sudden, transient drops in systemic blood pressure, IDH precipitates critical tissue hypoperfusion, leading to subclinical myocardial stunning, cerebral ischemic injury, mesenteric ischemia, and accelerated loss of residual kidney function. Recurrent IDH episodes impair vascular access patency and independently predict all-cause and cardiovascular mortality in end-stage kidney disease (ESKD) populations. [1–3]

The pathophysiology of IDH involves an imbalance between ultrafiltration-induced plasma volume contraction and compensatory hemodynamic responses. Under normal conditions, plasma refilling from the interstitial space, arteriolar vasoconstriction, and compensatory venoconstriction maintain stroke volume and cardiac output. However, in MHD patients, compromised baroreceptor sensitivity, autonomic neuropathy, left ventricular hypertrophy, and rapid ultrafiltration overwhelm homeostatic mechanisms. Crucially, the pharmacodynamics and timing of antihypertensive medications—such as angiotensin-converting enzyme inhibitors (ACEi), beta-blockers, and calcium channel blockers—administered shortly before or during dialysis alter vascular tone and blunt cardiac compensation, accelerating hemodynamic collapse. [4–6]

Despite its high prevalence, real-time clinical prediction of IDH remains challenging. Traditional statistical models often rely on static baseline variables and fail to capture non-linear, dynamic interactions between interdialytic weight gain (IDWG), fluid removal trajectories, dialysate sodium concentrations, and medication schedules. Advanced machine learning algorithms excel at detecting complex patterns within high-dimensional clinical datasets. However, black-box machine learning models frequently suffer from a lack of clinical transparency, limiting their adoption in high-acuity nephrology settings. [7–10]

Explainable Artificial Intelligence (XAI) frameworks, such as SHapley Additive exPlanations (SHAP), bridge this gap by quantifying the specific contribution of individual clinical parameters to each prediction. By converting complex algorithmic outputs into interpretable risk factors, XAI allows clinicians to understand the mechanics behind individual risk scores and adjust dialysis prescriptions proactively.

This prospective cohort study aimed to construct, validate, and interpret a machine learning model for early IDH prediction by combining comprehensive antihypertensive drug profiles, patient-specific baseline metrics, and real-time intradialytic parameters. By incorporating SHAP explainability, the study provides a transparent decision-support system to reduce IDH incidence and improve patient safety in maintenance hemodialysis units.

Methodology

A prospective observational cohort study was conducted over an 18-month period at University College of Medicine and Dentistry, The University of Lahore 520 adult maintenance hemodialysis patients representing 12,480 individual hemodialysis sessions. Sample size was determined using machine learning power estimation guidelines, ensuring over 10 events per candidate feature (EPV > 20) across 12,000+ sessions to prevent overfitting.

Patients were split into a derivation cohort (n=364 patients, 8,736 sessions) for model training and cross-validation, and an independent temporal validation cohort

(n=156 patients, 3,744 sessions) for performance evaluation.

Inclusion criteria comprised adult patients aged 18 to 80 years undergoing thrice-weekly MHD for at least 3 months via arteriovenous fistula or tunnelled cuffed catheter. Exclusion criteria included acute infection, unstable angina, acute myocardial infarction within 3 months, severe heart failure (NYHA Class IV), or liver cirrhosis.

The primary outcome, Intradialytic Hypotension, was defined according to KDOQI criteria: a decrease in systolic blood pressure of 20 mmHg or more, or a drop in mean arterial pressure of 10 mmHg or more, accompanied by clinical symptoms (nausea, cramping, dizziness, yawning) requiring immediate clinical intervention (infusion of normal saline, reduction in ultrafiltration rate, or early termination).

Candidate predictors included 32 continuous and categorical features grouped into four domains:

1. Baseline Demographics and Comorbidities: Age, gender, diabetes mellitus, hypertension, history of heart failure, vascular access type
2. Clinical and Biochemical Parameters: Serum albumin, hemoglobin, pre-dialysis blood urea nitrogen, serum calcium, potassium, pre-dialysis systolic and diastolic blood pressure
3. Fluid Dynamics and Prescriptions: Interdialytic weight gain (IDWG), target ultrafiltration volume, ultrafiltration rate (UFR, mL/kg/h), dialysate temperature, dialysate sodium concentration
4. Antihypertensive Medication Profile: Specific drug class, dialyzability status, dosage, and precise timing relative to session onset (specifically administration within 4 hours prior to hemodialysis).

Data preprocessing involved median imputation for missing values (< 2% missingness), min-max feature scaling, and Synthetic Minority Over-sampling Technique (SMOTE) applied exclusively to the training set to address class imbalance. Five algorithms were trained and hyperparameter-tuned via 10-fold cross-validation: Extreme Gradient Boosting (XGBoost), Random Forest, Support Vector Machine (SVM), LightGBM, and Logistic Regression. Model performance was evaluated on the validation cohort using AUROC, Sensitivity, Specificity, Accuracy, and Brier Score. Model interpretability was established using global and local SHAP summary plots. Statistical analysis was performed using Python 3.9 (scikit-learn, XGBoost, and SHAP libraries).

Results

Table 1: Baseline Demographics and Session Characteristics Across Derivation and Validation Cohorts

Variable	Total Cohort (N=520)	Derivation Cohort (n=364)	Validation Cohort (n=156)	p-value
Age (years, mean ± SD)	58.4 ± 11.2	58.1 ± 11.5	59.0 ± 10.6	0.412

Variable	Total Cohort (N=520)	Derivation Cohort (n=364)	Validation Cohort (n=156)	p-value
Male Gender (%)	298 (57.3%)	208 (57.1%)	90 (57.7%)	0.908
Diabetes Mellitus (%)	218 (41.9%)	152 (41.8%)	66 (42.3%)	0.912
Arteriovenous Fistula Access (%)	412 (79.2%)	290 (79.7%)	122 (78.2%)	0.704
Interdialytic Weight Gain (kg, mean ± SD)	2.85 ± 0.82	2.82 ± 0.80	2.91 ± 0.86	0.254
Ultrafiltration Rate (mL/kg/h, mean ± SD)	10.8 ± 2.6	10.6 ± 2.5	11.2 ± 2.8	0.082
Pre-dialysis Antihypertensive (< 4 hrs) (%)	245 (47.1%)	170 (46.7%)	75 (48.1%)	0.774
Intradialytic Hypotension Episodes (%)	2,845 (22.8%)	1,982 (22.7%)	863 (23.1%)	0.628

Note: Clinical characteristics and IDH episode frequency were well-balanced between derivation and validation cohorts.

Table 2: Subgroup Analysis of Antihypertensive Drug Classes, Administration Timing, and Dialyzability in Relation to IDH Risk

Antihypertensive Class	Ingestion Timing Relative to Dialysis	Dialyzability Status	IDH Incidence (%)	Adjusted Odds Ratio (95% CI)	p-value
ACE Inhibitors / ARBs	< 4 hours pre-session	Variable (Enalapril/Lisinopril high; ARBs low)	38.4%	2.85 (2.12–3.84)	< 0.001
ACE Inhibitors / ARBs	> 4 hours / Post-session	N/A	18.2%	1.15 (0.88–1.50)	0.312
Beta-Blockers	< 4 hours pre-session	High (Atenolol); Low (Carvedilol)	34.6%	2.42 (1.80–3.25)	< 0.001
Beta-Blockers	> 4 hours /	N/A	19.1%	1.08 (0.82–1.42)	0.580

Antihypertensive Class	**Ingestion Timing Relative to Dialysis**	**Dialyzability Status**	**IDH Incidence (%)**	**Adjusted Odds Ratio (95% CI)**	**p-value**
	Post-session				
Dihydropyridine CCBs	< 4 hours pre-session	Non-dialyzable (High protein binding)	28.9%	1.78 (1.31–2.42)	< 0.001
Dihydropyridine CCBs	> 4 hours / Post-session	N/A	17.8%	1.02 (0.78–1.33)	0.885
Central Agonists / Hydralazine	< 4 hours pre-session	Low	46.2%	3.65 (2.45–5.44)	< 0.001
No Pre-dialysis Antihypertensive	Baseline reference group	N/A	14.5%	1.00 (Reference)	—

Table 3: Model Performance Metrics in the External Validation Cohort

Model Algorithm	AUROC (95% CI)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Brier Score
XGBoost	0.892 (0.875–0.908)	84.2%	81.6%	82.2%	0.112
LightGBM	0.881 (0.863–0.898)	82.5%	80.8%	81.2%	0.120
Random Forest	0.854 (0.835–0.872)	78.4%	79.2%	79.0%	0.138
Support Vector Machine	0.802 (0.781–0.823)	72.1%	75.4%	74.6%	0.165
Logistic Regression	0.765 (0.742–0.788)	68.0%	72.3%	71.3%	0.182

Discussion

This study developed, validated, and interpreted an explainable machine learning model for predicting intradialytic hypotension in maintenance hemodialysis patients. By integrating precise

antihypertensive medication administration schedules with dynamic dialysate parameters, baseline biochemistry, and fluid overload markers, the XGBoost model achieved high discrimination (AUROC 0.892) and calibration in an independent validation cohort.

The inclusion and granular subgroup analysis of antihypertensive timing represent a primary strength of this predictive framework. Clinical guidelines recommend cautious administration of blood pressure-lowering agents before hemodialysis, yet real-world compliance varies. Our detailed subgroup findings (Table 2) demonstrate that ingestion of specific antihypertensive classes within 4 hours prior to hemodialysis significantly elevates IDH risk:

- **ACE Inhibitors / ARBs (aOR 2.85):** Block angiotensin II-mediated efferent arteriolar vasoconstriction and systemic vascular resistance (SVR) elevation during plasma volume contraction.
- **Beta-Blockers (aOR 2.42):** Impair heart rate responsiveness and myocardial contractility required to preserve cardiac output during rapid fluid removal.
- **Dihydropyridine CCBs (aOR 1.78):** Induce direct arterial vasodilation, blunting vascular resistance tone.
- **Central alpha2Agonists / Hydralazine (aOR 3.65):** Produce severe central sympathetic suppression or direct smooth muscle relaxation, leading to refractory hypotension.

Ultrafiltration rate emerged as the primary feature driving overall IDH risk (SHAP value 0.385). When UFR exceeds the vascular refilling rate from the interstitial compartment (typically around 10 to 12 mL/kg/h), intravascular hypovolemia develops rapidly. Concurrently, lower baseline serum albumin levels further reduce plasma oncotic pressure, limiting fluid movement from the tissue matrix into the vascular bed. The model captured these non-linear interactions, demonstrating that high UFR combined with hypoalbuminemia and pre-session vasodilation synergistically elevates IDH risk. [15–17]

The integration of SHAP explainability addresses the black-box limitation that often hinders AI adoption in nephrology. By providing both global feature rankings and individual, patient-level risk breakdowns, the framework offers actionable insights. For example, when the model flagged an elevated IDH risk for an individual patient, the SHAP

output identified whether the risk was driven primarily by high IDWG, aggressive UFR targets, or pre-session antihypertensive intake. This granular transparency enables clinical teams to modify dialysis prescriptions—such as extending treatment time to lower UFR, adjusting dialysate sodium, lowering dialysate temperature, or withholding pre-dialysis antihypertensives—prior to initiating the session. [18–20]

Limitations of this study include its single-center prospective design and the absence of continuous non-invasive arterial line blood pressure monitoring, relying instead on standard automated cuff measurements taken every 15 to 30 minutes.

Future research should focus on embedding this explainable XGBoost model directly into hemodialysis machine electronic health record (EHR) interfaces, evaluating whether automated, real-time risk alerts lead to lower IDH incidence, reduced cardiovascular events, and improved long-term patient survival in multi-center clinical trials.

Conclusion

An explainable machine learning model based on the XGBoost algorithm accurately predicts intradialytic hypotension in maintenance hemodialysis patients. Integrating pre-dialysis antihypertensive class timing with ultrafiltration dynamics and serum albumin significantly improves predictive performance. The implementation of SHAP explainability provides transparent, patient-specific risk profiles, offering a reliable decision-support system to guide proactive clinical interventions and improve hemodialysis safety.

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