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Predicting mortality and short-term outcomes of continuous kidney replacement therapies in neonates and infants

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ABSTRACT

Background. Continuous kidney replacement therapy (CKRT) has emerged as a valuable treatment option in critically ill neonates and infants with acute kidney injury (AKI) requiring dialysis. In this population, we apply artificial intelligence (AI) to identify factors influencing mortality and short-term adverse kidney outcomes.

Methods. The study involved neonates and infants included in the EurAKId Registry (NCT 02960867), who underwent CKRT treatment. Using the AI XGBoost models, we identified key clinical factors associated with short-term outcomes: mortality before hospital discharge, as well as proteinuria at discharge. We considered the patients' clinical characteristics, anthropometric features, and CKRT technical settings.

Results. The study comprised 95 patients: 31.6% neonates and 68.4% infants with a median age at hospital admission of 1 month (interquartile range, IQR 0–7 months). Ten children were born prematurely. The overall mortality rate was 47.3% and did not differ significantly between neonates and infants (53.3% vs 44.4%, respectively, $P = .422$). The XGBoost model for predicting mortality had the accuracy of 59.53% ± 0.96% and AUC of 0.64 ± 0.11. Lower urine output at CKRT initiation, a greater rise in serum creatinine (SCr), longer time to dialysis initiation, and lower blood pressure were associated with increased risk of mortality. Proteinuria at hospital discharge was present in 30.6% of survivors. The XGBoost model for predicting proteinuria had the accuracy of 79.11% ± 2.46% and AUC (0.74 ± 0.04). Higher SCr concentrations at hospital admission and at CKRT start, as well as primary kidney disease were the most important risk factors for proteinuria.

Conclusion. We propose the XGBoost models for identifying factors associated with short-term outcomes of CKRT in neonates and infants. Lower urine output at CKRT start, more severe AKI progression and longer time to CKRT initiation might be important risk factors for mortality in infants and neonates. Primary kidney disease and related biochemical parameters are strong predictors of proteinuria at hospital discharge.

Keywords: acute kidney injury, artificial intelligence, continuous kidney replacement therapies, neonates and infants, outcomes

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KEY LEARNING POINTS

What was known:

- AKI in critically ill neonates and infants is a common complication associated with difficult dialysis management, as well as increased mortality and adverse kidney outcomes.
- Recently, artificial intelligence (AI) models have been developed to improve prediction of AKI occurrence in different settings. Application of AI in neonatal AKI my increase the likelihood of precocious diagnosis and successful management.

This study adds:

- The present study proposes the implementation of AI models to identify predictive factors influencing mortality and short-term outcomes of CKRT in neonates and infants.
- In neonates and infants, more severe AKI progression between admission and CKRT initiation, together with longer time since dialysis initiation and longer dialysis duration were associated with increased risk of mortality.
- More than a quarter of patients who survived CKRT presented proteinuria. Proteinuria at hospital discharge was associated with and higher SCr at admission and dialysis start and with primary kidney disease.

Potential impact:

- In this study, the AI XGBoost identify potential predictive factors for mortality and development of proteinuria in survivors.
- Although larger studies are required to provide definitive results, paying attention to these factors might be clinically relevant in this vulnerable population.

INTRODUCTION

Acute kidney injury (AKI) occurs in around a quarter of hospitalized children [1] and the need for acute kidney replacement therapy (KRT) is increasing in all pediatric population age groups [2]. In the youngest children, peritoneal dialysis (PD) remains a long-established KRT of choice [3–5]. In recent decades, continuous kidney replacement therapy (CKRT) has emerged as an important treatment modality in critically ill neonates and infants requiring dialysis in the acute setting [6]. In this vulnerable population, where physiological reserves are minimal, managing kidney dysfunction requires careful consideration of both the patient's unique developmental physiology and the technical challenges associated with extracorporeal therapies [7].

Neonates and infants present distinct challenges in CKRT due to their small body size, immaturity, and increased sensitivity to fluid and electrolyte imbalances. The hemodynamic instability, commonly seen in critically ill infants, demands especially precise fluid management, making CKRT particularly beneficial for this population.

Recent advances in CKRT technology, tailored specifically for pediatric and neonatal use, have improved the safety and efficacy of this therapy [8–10]. Although the survival rate for children receiving CKRT has improved in recent decades, mortality remains considerably high [11]. The patients surviving CKRT procedures are at risk of developing adverse kidney outcomes both in short- and long-term observation [12, 13].

Artificial Intelligence (AI) methods revolutionize the analysis of scientific data in different fields including nephrology [14]. Recent studies show that AI-based models employing tree-based algorithms (e.g. random forest or XGBoost), neural networks, or support vector machines, can be used to predict the occurrence of AKI post-surgery [15–18], severe burn injuries [19], or in critical care setting [20, 21].

The objective of this study is to identify factors influencing mortality and the occurrence of adverse kidney outcomes in short-term observation in neonates and infants with AKI using the AI XGBoost models.

MATERIALS AND METHODS

EurAKId Registry (European Registry of Pediatric Acute Kidney Injury Dialysis Treatment)

The EurAKId Registry (ClinicalTrials.gov NCT 02960867) is a prospective, international study gathering data on acute pediatric KRT from 14 European pediatric nephrology centers. It was established in September 2016 by the ESCAPE Network (European Study Consortium for Chronic Kidney Disorders Affecting Pediatric Patients) based on the results of a survey conducted earlier that year. Each participating center has obtained and presented a local bioethics committee approval.

The registry is based on an online case-report questionnaire and collects data on patients 0–18 years of age, who require acute KRT. It includes three KRT modalities—PD, intermittent hemodialysis (iHD), and CKRT—chosen in accordance with regional standards of care) conducted both in intensive care and ward settings, due to AKI and other indications, for example inborn errors of metabolism, sepsis, or fluid overload (FO). Pre-existing chronic kidney disease (by KDIGO definition) is an exclusion criterion. AKI diagnosis, AKI staging, and CKD exclusion are defined by the on-site investigators in accordance with current guidelines. Data are collected in seven domains: demographic and admission data, clinical parameters at dialysis start, data at pediatric intensive care unit admission, modality-specific (PD, iHD, and CKRT) data, and data on the occurrence short-term outcomes (mortality, proteinuria, hypertension, and requirement for chronic dialysis at hospital discharge, all assessed by regional investigators). All definitions are available in previous publications [22].

Study group

The present study comprises children up to 12 months of age included in the EurAKId Registry who underwent CKRT between September 2016 and September 2023. During this period, 450 patients were enrolled in the registry, of whom 136 met the age criteria for this study. We excluded 41 children (37 patients treated with PD, two patients treated with iHD and two with significant missing data). In total, 95 patients were included in the present

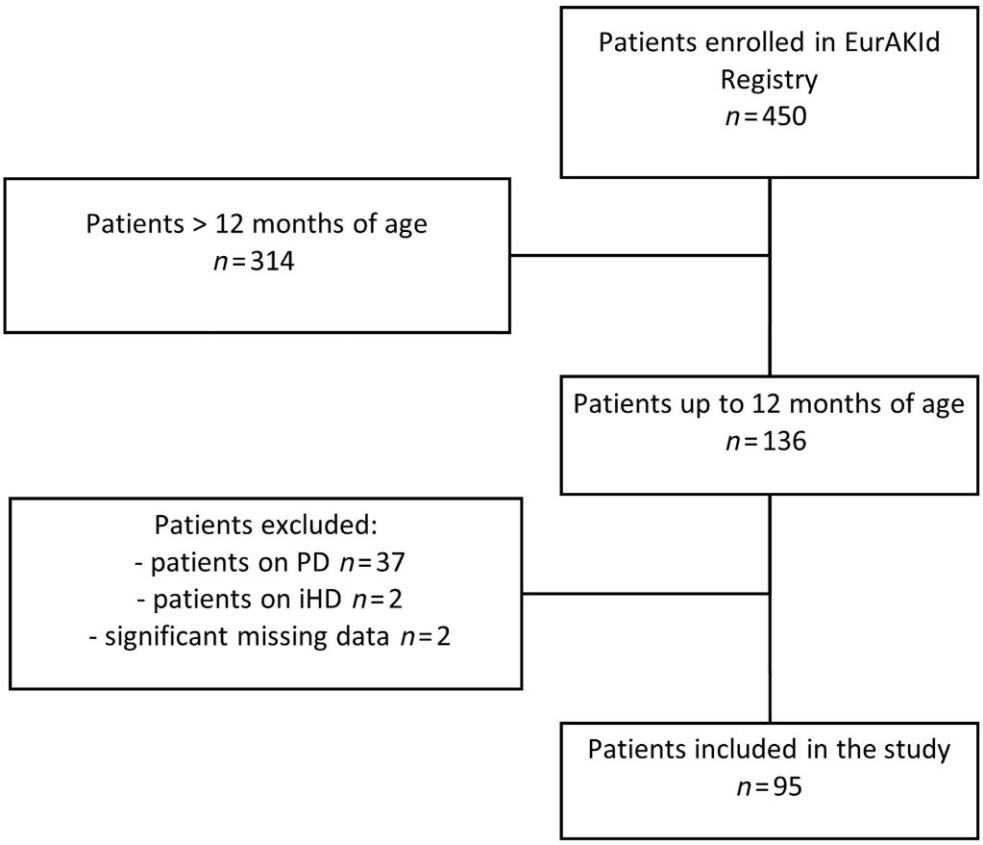

Figure 1: Patient selection for the study.

analysis (Fig. 1). The study focuses on CKRT because it presents specific technical and clinical challenges in neonates and infants; among children up to 12 months, CKRT was the most representative and homogeneous group.

Baseline characteristics

Based on patient characteristics reported in the registry, we defined the study population. We included basic anthropometric parameters and demographic data, baseline clinical characteristics, and serum creatinine (SCr) concentrations. The full list of variables considered in this study is available in the Supplementary Material (Supplementary Table 2). The cohort was divided by age into two groups: neonates aged <1 month and infants (1–12 months). For the patients admitted to the pediatric intensive care unit, the illness severity was assessed using the PRISM III score. Urine output decline (calculated as the difference between urine output at admission and at dialysis initiation) and SCr rise (calculated as the difference between SCr at dialysis start and at hospital admission) were used as indicators of AKI trajectory. We identified seven categories of primary disease: cardiac disease, shock, acute kidney disease, inborn error of metabolism (IEM), malignancy/hematologic disease, liver disease, and pulmonary disease.

CKRT technical aspects and settings

We analyzed the technical aspects and settings of performed CKRT procedures. They are available in the Supplementary Material (Supplementary Table 2). Due to significant technical distinctive features, the analyzed population was divided by the use of standard CKRT, and ECMO-related CKRT. Depending on the CKRT modality, the prescribed dialysis dose was calculated as dialysate flow rate in CVVHD, replacement flow rate in CVVH, or the sum of both for CVVHDF.

Primary and secondary outcome measures

The primary endpoint was mortality before hospital discharge. Secondary endpoints were assessed at hospital discharge and included: need for chronic dialysis, presence of proteinuria, and presence of hypertension.

Basic statistical analyses

Depending on the distribution (assessed with the Shapiro–Wilk test), data were expressed as mean ± standard deviation (SD) for variables with normal distribution or median (interquartile range, IQR) for variables with distribution other than normal. The following statistical tests were applied: Mann–Whitney *U*-test, Kruskal–Wallis ANOVA test, and chi-squared test. The results were considered significant with $P < .05$. Basic statistical analyses were performed using Dell Statistica v.13.3 software.

Machine learning-based analyses

We used a machine learning (ML) method, specifically XGBoost gradient-based decision trees to analyze nonlinear relations between observed variables and the outcome measures: mortality, proteinuria, and hypertension. Independent binary classifiers were used to predict the outcomes given the set of observations by minimizing the negative log-likelihood of the Bernoulli distribution defined by the target variable XGBoost was chosen due to

its high performance proven by numerous applications, natural way of managing missing data, and simple explainability. However, for clarity, we also compared the performance of the XGBoost model with other approaches including: Cox model, random forest, decision tree, linear regression, *K*-nearest neighbors, and naive Bayes.

Explanation of the classifiers' decisions

In this study, we put special attention to the explanations of models decisions, as our goal was to explore the predictors of short-term AKI outcomes. Therefore, we investigated the structure of the trained classifiers with the SHAP technique, which measures the contribution of each feature to the final prediction of the model based on all splits in trained decision trees. SHAP values were calculated for each attribute in each case from our dataset. We report (i) the mean absolute SHAP value for each attribute and (ii) the actual contribution (positive/negative) of a given attribute for a particular range of values. For readability, we present only important features that exceed 0.1 mean absolute SHAP value. The full list of variables is provided in the Supplementary Material.

Experiment methodology

Cross-validation was used to assess the performance of the trained classifier. We randomly divided the dataset into 10 separate pieces and trained XGBoost models using different combinations of 9 out of 10 available parts, while evaluating it on the hold-out 10th piece. To ensure the consistency of final results, we additionally reran the same analyses five times using different random splits. We then averaged the results over all runs and all splits. For metrics, we used accuracy, specificity, sensitivity, positive predictive value (PPV), and area under the receiver-operating characteristic (ROC) curve (AUC). We report the average value with its SD. For explainability, we average SHAP values over individual models. However, since our goal was to assess the main risk factors, we extracted the SHAP values only from the models that achieved satisfactory AUC score >0.6 on a given cross-validation test split. To avoid overfitting of the data we did not use any automatic fine-tuning of the XGBoost parameters relying on the default values while limiting the number of decision trees to 40 for the mortality and 20 for the proteinuria model.

In the following we discuss the predictors for mortality and proteinuria, focusing on the XGBoost due to its superior performance. The comparison of the factors identified by XGBoost and simple Cox models is presented in the Supplementary Material (Appendix 2).

RESULTS

Study group characteristics

The anthropometric, demographic, and basic clinical features of analyzed patients are displayed in Table 1. The study group comprised 30 neonates and 65 infants. On admission, the median SCr level was 0.6 mg/dl (IQR 0.2–1.2) and median urine output was 2.3 ml/kg/h (IQR 0.8–4.1). At CKRT initiation, SCr level was significantly higher comparing to baseline (0.9 mg/dl, IQR 0.5–1.4, $P < .001$). In the entire cohort, urine output decrease was statistically insignificant (−1.5 ml/kg/h, IQR −3.9–0.0, $P = .145$), and urine output at CKRT start did not differ significantly between survivors and non-survivors (1.1 ml/kg/h, IQR 0.2–3.5 vs 2.1 ml/kg/h, IQR 0.0–4.1 respectively; $P = .880$). FO at dialysis initiation was 3.6% (IQR 0.0–10.6%) and was equal in the two groups (survivors 4.0%, IQR 0.0–9.1%; non-survivors 3.7%, IQR 0.0–14.8%). Median time from hospital admission to CKRT initiation was 4 days (IQR 1–15) and was significantly shorter in survivors than non-survivors (2 days, IQR 0–8.5 vs 10 days, IQR 2.0–32.0 respectively, $P < .001$). In 29.5% of patients CKRT was initiated within 1 day after admission.

CKRT management

In the analyzed group, the median CKRT duration was 116 hours (IQR 56–219) per patient, with the mean circuit lifetime of 29 hours (IQR 18–46). In most patients (84.2%, $n = 80$), CKRT was performed using the Prismaflex/Prismax devices. Five infants (body weight 3.8–8.6 kg, none of them premature) underwent procedures on CARPEDIEM device, three children on Aquarius device, and in seven patients the system was not specified. The most commonly applied anticoagulation was heparin (57.9%), followed by procedures with no anticoagulation (20%), and regional citrate anticoagulation (16.8%), no data on anticoagulation in five patients. CVVHDF was the leading CKRT modality (46.3%). CVVHD and CVVH were applied in 9.5% and 8.4% of patients, respectively. ECMO-related CKRT procedures were conducted in 33 (34.7%) patients. Among the remaining 62 patients, the most common vascular access site was right internal jugular vein (56.5%), followed by femoral (21.0%), left internal jugular (12.9%), and subclavian veins (8.1%). One patient (1.1%) required a CKRT-therapeutic plasma exchange tandem therapy. The technical aspects of CKRT procedures by ECMO and non-ECMO groups are displayed in Supplementary Table 1.

In the entire analyzed population, the median prescribed dialysis dose was 3187 ml/h/1.73 m^2 (IQR 2359–3844) and differed significantly regarding the patient's primary disease ($P = .020$). The highest dialysis dose was prescribed in the IEM group (6513 ml/h/1.73 m^2, IQR 3077–17 281).

Mortality

The overall mortality rate was 47.3% ($n = 44$) and did not differ significantly between neonates and infants (53.3% vs 44.4% respectively, $P = .422$, chi-squared test). Using the XGBoost model, we identified factors influencing the occurrence of the mortality endpoint, of which the most important predictors were urine output at dialysis start and SCr rise. The feature importance of the variables included in the model is displayed in Fig. 2a. The mean accuracy of the model was 59.53% ± 0.96% (sensitivity 54.90 ± 1.54, specificity 63.90 ± 1.72, PPV 60.84 ± 1.43), and the AUC was 0.64 ± 0.11 (Fig. 4a). Lower urine output at dialysis start as well as a larger rise in SCr, longer time from admission to dialysis initiation, lower blood pressure at admission, lower body weight at admission, CKRT modality other than CVVHDF, longer dialysis duration, and larger urine output decline were associated with increased risk of mortality (Fig. 2b). ECMO use was included in the model but did not surpass the SHAP importance threshold (>0.1).

Proteinuria

Proteinuria at hospital discharge was present in 30.6% ($n = 15$) of survivors.

Higher serum creatinine concentration at hospital admission and primary kidney disease were the most important predictors identified in the XGBoost model. Figure 3 displays the importance scores (Fig. 3a) and influence of parameter values on the occurrence of proteinuria (Fig. 3b) for the remaining variables. The mean model accuracy was 79.11 ± 2.46 (sensitivity 54.67 ± 5.40,

Table 1: Demographic, anthropometric, and clinical characteristics of the study group.

Parameter	Entire cohort ($n = 95$)	Survivors ($n = 49$)	Non-survivors ($n = 44$)
Sex (n, boys/girls)	58/37	27/22	29/15
Born prematurely (n, %)	10 (10.5%)	7 (14.3%)	3 (6.8%)
Age (months)	1 (0–7)	5 (0–8)	1 (0–6.5)
Race (n, %)			
Caucasian	90 (94.7%)	47 (96.0%)	42 (95.4%)
Asian	2 (2.1%)	1 (2.0%)	1 (2.3%)
Black	1 (1.1%)	0	0
Unknown	2 (2.1%)	1 (2.0%)	1 (2.3%)
Body length at admission (cm)	55.0 (50.0–65.0)	59.0 (50.0–68.0)	52.0 (50.0–60.0)
Weight at admission (kg)	4.0 (3.2–7.0)	4.6 (3.5–7.6)	3.8 (3.0–6.1)
BSA (m^2)	0.25 (0.21–0.36)	0.29 (0.22–0.37)	0.22 (0.20–0.31)
Primary disease (n, %)			
Pulmonary	23 (24.2%)	12 (24.5%)	11 (25.6%)
Cardiac	12 (12.6%)	5 (10.2%)	7 (16.3%)
Liver	12 (12.6%)	6 (12.3%)	5 (11.6%)
IEM	12 (12.6%)	8 (16.3%)	4 (9.3%)
Kidney	11 (11.6%)	10 (20.4%)	1 (2.3%)
Malignancy/hematologic	10 (10.5%)	3 (6.1%)	6 (14.0%)
Shock	10 (10.5%)	5 (10.2%)	5 (11.6%)
Other[a]	5 (5.4%)	0 (0.0%)	4 (9.3%)
Nephrotoxic drugs (n, %)	43 (45.3%)	18 (36.7%)	23 (52.3%)
1	32 (74.4%)	13 (72.2%)	17 (74.0%)
2	6 (14.0%)	3 (16.7%)	3 (13.0%)
3	5 (11.6%)	2 (11.1%)	3 (13.0%)
AKI (n, %)	65 (68.4%)	33 (67.4%)	32 (72.7%)
Stage			
1	11 (16.9%)	3 (9.1%)	8 (25%)
2	19 (29.2%)	9 (27.3%)	10 (31.3%)
3	34 (52.3%)	21 (63.6%)	13 (40.6%)
No data	1 (1.6%)	0 (0%)	1 (3.1%)
PICU admission (n, %)	93 (97.9%)	48 (97.9%)	44 (100.0%)
MODS (n, %)	69 (72.6%)	30 (61.2%)	37 (84.1%)
Number of organs involved (n, % of MODS)			
2	11 (15.9%)	6 (20.0%)	4 (10.8%)
3	38 (55.1%)	19 (63.3%)	19 (51.4%)
4	17 (24.6%)	5 (16.7%)	12 (32.4%)
>4	3 (4.4%)	0 (0.0%)	2 (5.4%)
Vasopressor use (n, %)	69 (72.6%)	32 (65.3%)	35 (79.5%)
Total PRISM III score	14.0 (10.0–19.0)	13.0 (8.0–22.0)	14.0 (10.0–17.0)

[a]Including three immunologic disorders, one neurologic disorder; missing data in one patient
No data on survival in two patients.
BSA, body surface area; MODS, multiorgan dysfunction syndrome; PICU, pediatric intensive care unit.

specificity 90.67 ± 3.34, PPV 76.38 ± 6.46). The AUC was 0.74 ± 0.04 (Fig. 4b).

Other outcome measures

We found no significant predictors for the remaining outcome measures set for this study. Hypertension was present in 24.5% ($n = 12$) of survivors, and the XGBoost model had predictive accuracy comparable to random. Only one patient required chronic KRT at hospital discharge.

DISCUSSION

In this analysis of prospectively collected data, we propose XGBoost models to identify factors influencing mortality and proteinuria in neonates and infants requiring CKRT. Compared to the traditional Cox models, the performance of XGBoost was superior, particularly in predicting proteinuria at discharge (Supplementary material, Appendix 2). We believe this improvement in performance by the XGBoost model may be partially attributed to its native ability to handle missing and correlated data. Meanwhile, Cox models prioritize categorical variables with well-defined effects, which it can represent efficiently.

In our cohort of CKRT-treated neonates and infants, the overall mortality rate was 47.3%. This is consistent with the recent WE-ROCK study report [11], and lower than the rates from the ppCRRT study conducted previously [24]. Our XGBoost model identified low urine output at CKRT initiation as the most important mortality predictor. Interestingly, it was not associated with FO rate and had an importance of 0.14. In literature, FO is the most well-established predictor, contributing to increased risk of mortality in CKRT-treated children [25] as well as in critically ill neonates [26]. Of note, the median FO rate in the presented group was relatively low (3.6%) and did not differ significantly between survivors and non-survivors. As this study represents a recent cohort, our results suggest that CKRT may have been initiated earlier, which may enable the new prognostic factors for mortality to emerge.

We found that more severe AKI progression (defined as larger urine output decline and SCr rise) between admission and CKRT initiation was also a factor predicting mortality. Although all

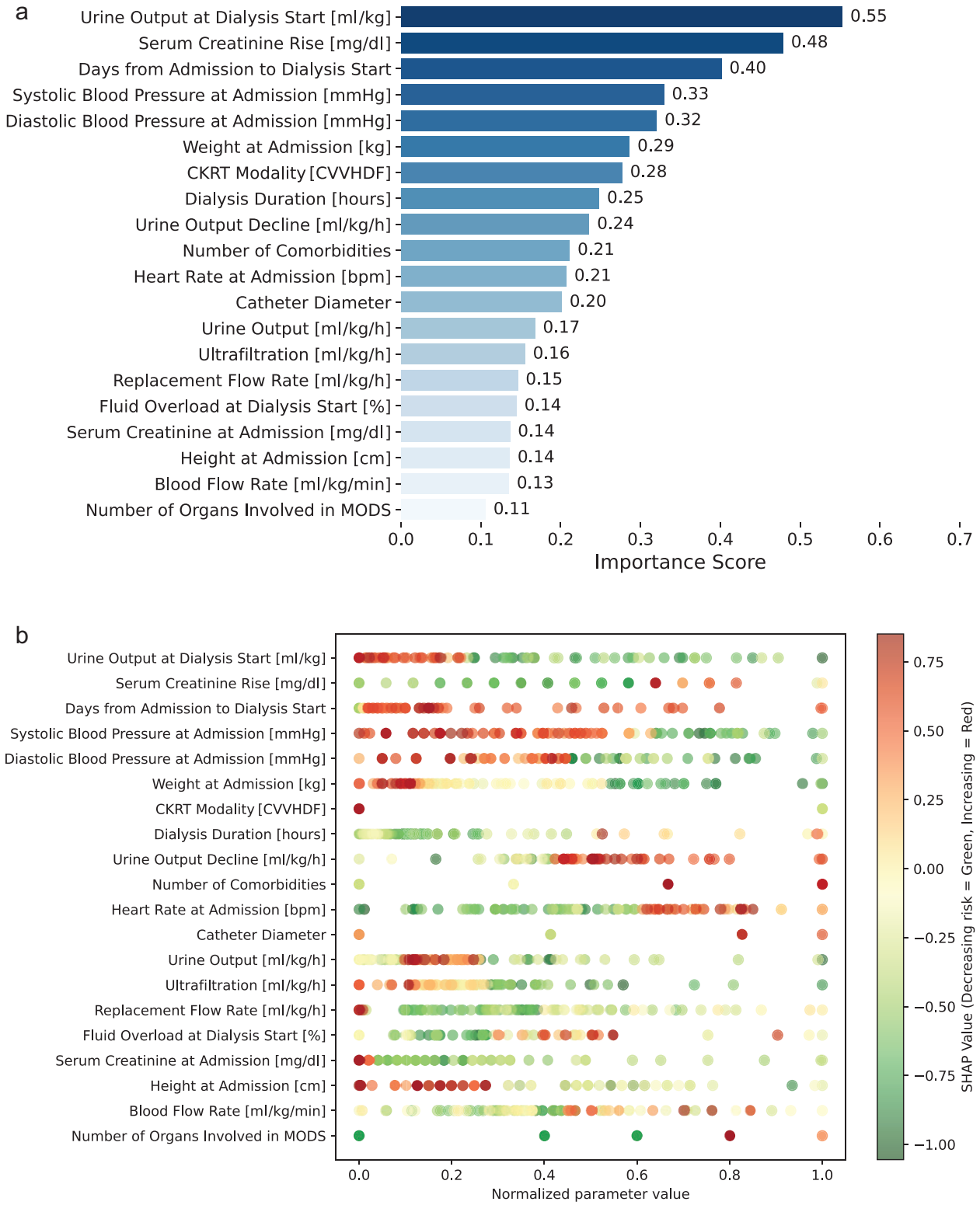

Figure 2: (**a**) Importance of factors influencing mortality identified in the XGBoost model. (**b**) Influence of the identified factors on mortality. Green, decreasing risk; red, increasing risk.

children met the criteria for severe AKI (KDIGO stage 3) at CKRT initiation, their functional deterioration varied in rate and magnitude, affecting outcomes. Longer time from admission to dialysis initiation and longer dialysis duration were also associated with higher mortality (importance scores 0.40 and 0.25, respectively). As the registry lacks exact AKI diagnosis times, we used the interval from hospital admission to CKRT initiation as a proxy. This provides a consistent metric for both early AKI at ICU admission and AKI developing later due to secondary insults such as nephrotoxicity or sepsis. Randomized controlled trials in adults have reported contradicting results regarding the impact of early CKRT initiation on outcomes [27, 28], but a metanalysis [29] showed

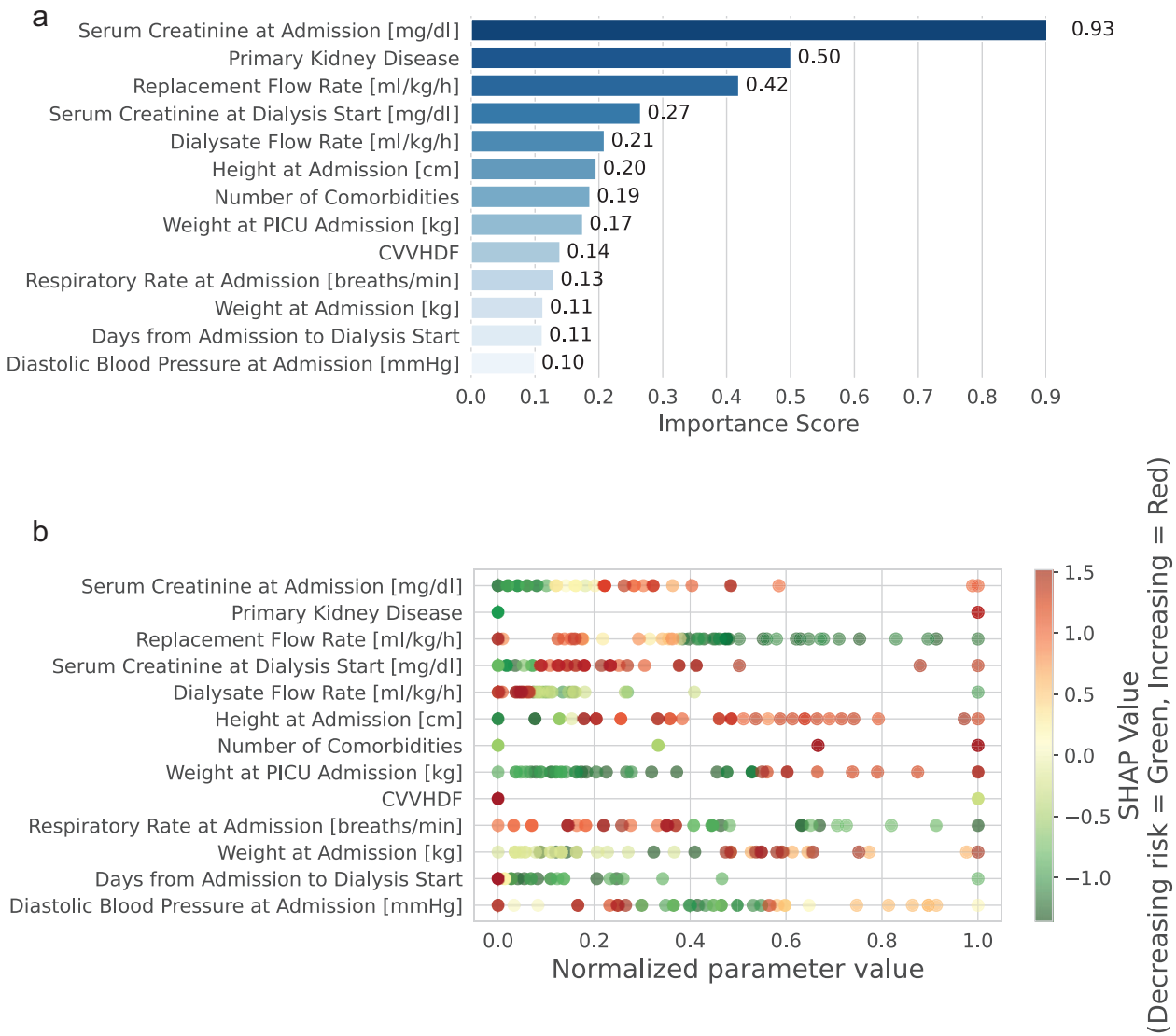

Figure 3: (**a**) Importance of factors influencing proteinuria at hospital discharge, identified in the XGBoost model. (**b**) Influence of the identified factors on proteinuria at hospital discharge. Green, decreasing risk; red, increasing risk.

reduced mortality and dialysis-dependency with early CKRT initiation. Retrospective pediatric studies [30, 31] also found reduced mortality rate with earlier start. The recent WE-ROCK study [32] linked delayed CKRT initiation to higher mortality and major adverse kidney events on 90 days (MAKE-90) in children and young adults. The influence of CKRT duration on mortality is not thoroughly studied. One pediatric study [33] showed slightly higher mortality in children with longer CKRT duration, but with no statistical significance. Prolonged CKRT was also associated with lower chances of kidney function recovery [34].

An important factor in the XGBoost model was low blood pressure at admission, which together with high heart rate might be attributed to hemodynamic instability. Lower body weight was also associated with increased mortality. Although not statistically significant, the mortality tended to be higher in neonates than infants. Most of the cohort underwent CKRT on adult equipment adapted for pediatric use. Only five patients received treatment with the dedicated, miniaturized machine (CARPEDIEM). Adult machines have been adapted and used successfully even in the smallest children for decades now [24, 35, 36]. However, recent reports provide new evidence on CARPEDIEM's safety and efficacy [8]. A comparison between the ppCRRT study and the Italian CARPEDIEM registry [37] covering two different eras, showed better survival to CKRT discontinuation in the dedicated infant machine group.

Interestingly, CVVHDF was identified as a factor improving the outcome with modest importance (0.28). This stands in contrast to the previously conducted studies. A recent adult network meta-analysis showed that no single CKRT modality was superior to others [38]. Moreover, a pediatric study showed no difference in CKRT modality between survivors and non-survivors [39]. Our findings suggest that combined convective–diffusive clearance might be beneficial for the youngest critically ill patients. This, however, requires further, preferably prospective studies on larger cohorts, and should be interpreted with caution.

The other XGBoost model proposed in the present study identified several factors predictive of proteinuria in CKRT survivors. This model had satisfactory accuracy (79.11% ± 2.46%) and AUC (0.74 ± 0.04). In our cohort of neonates and infants, proteinuria at hospital discharge was associated with higher serum creatinine levels at admission and at CKRT start, and primary kidney disease. These factors likely reflect more extensive kidney

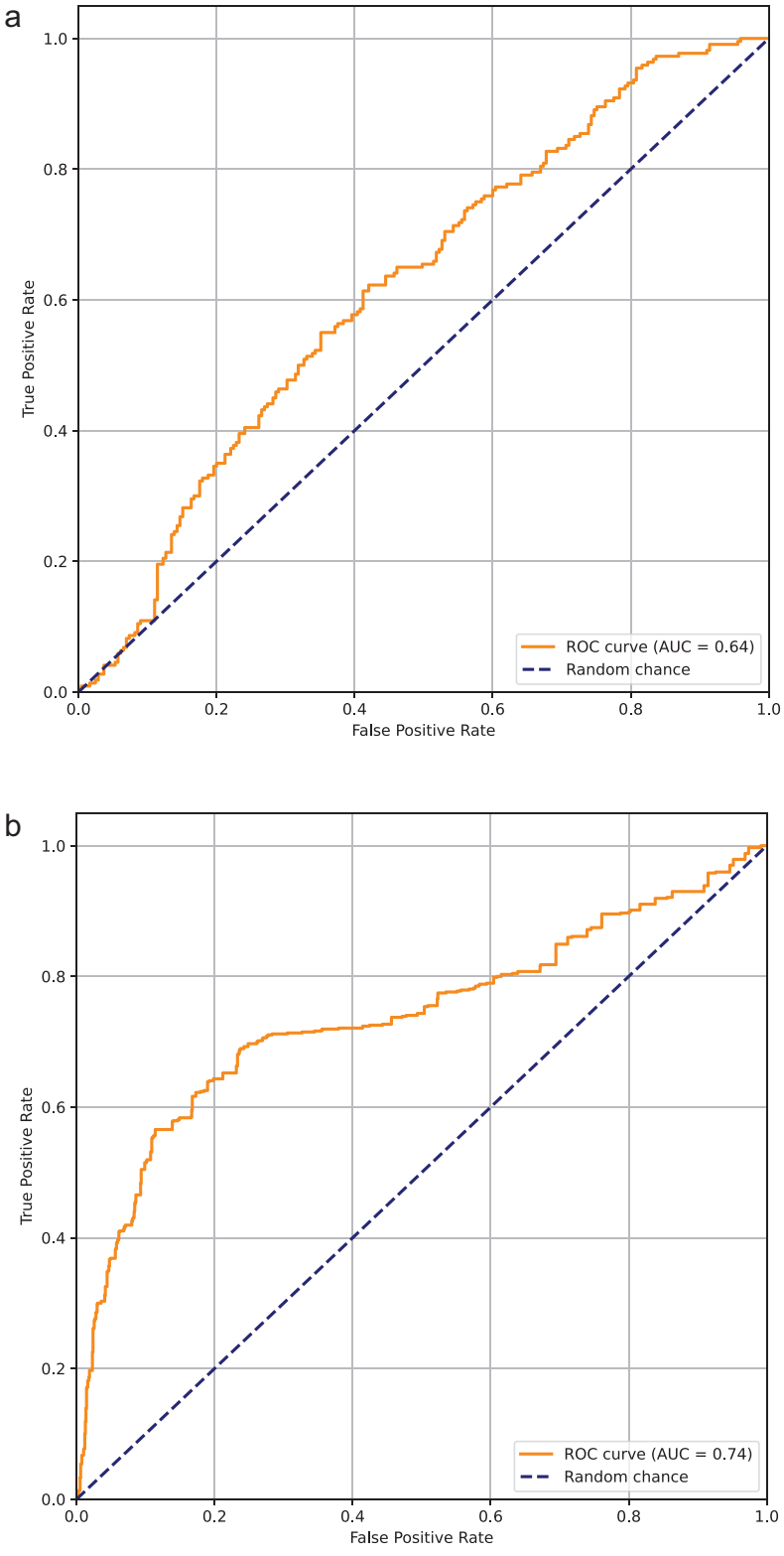

Figure 4: (**a**) ROC curve for predicting mortality. (**b**) ROC curve for predicting proteinuria at hospital discharge.

impairment, contributing to the need for CKRT. Interestingly, lower replacement and dialysate flow rates emerged as predictive factors, which once again might suggest potential benefits of the combined diffusive-convective clearance for kidney outcomes. However, it is important to note that predictors identified using AI tools do not necessarily equate to causal risk factors.

We were not able to develop a model predicting the occurrence of hypertension at hospital discharge with accuracy significantly higher than random, probably due to a low number of patients. Although the numbers of patients with proteinuria and hypertension at discharge were relatively low, they account for a significant percentage of survivors. This underlines

the need for periodical nephrological follow-up after the AKI episode.

The primary goal of our AI model was to identify the potential predictive factors for mortality and proteinuria in CKRT survivors. Among the methods tested, the XGBoost algorithm demonstrated superior performance compared to alternatives like decision trees and random forest models, as well as the Cox model (Supplementary material, Appendices 1 and 2). This finding aligns with recent research that underscores its effectiveness [40]. Future efforts to develop computer-aided diagnostic systems could benefit from integrating more advanced ML techniques, such as deep learning or multi-modal approaches. However, the success of these methods will largely depend on the size and quality of the available dataset [14].

This study presents a European, multicenter cohort of neonates and infants receiving CKRT in Europe. We analyzed data on CKRT management in these patients and, for the first time, we applied advanced AI to identify factors influencing outcomes and propose the models predicting selected outcome measures. However, we acknowledge that this study has several limitations. The multicenter character of the study limited our access to further data not collected in the EurAKId Registry that might have been useful. Moreover, as the AKI diagnosis and grading was performed by on-site investigators, the results might have been influenced by the varying severity of the patients' conditions. Notably, the initial AKI stage had low importance score in the XGBoost model (0.04). A relatively high mortality rate significantly reduced the number of patients for assessing the secondary outcomes (proteinuria, hypertension, need for chronic KRT), making it impossible to build a satisfactory XGBoost model for two of them. In this study, we build our XGBoost models to automatically find the combinations of high-risk factors for mortality and proteinuria. However, given the limited performance of the final models, further studies are needed to consider them as a direct tool supporting the decisions of the medical team. As our analysis was based on internal cross-validation within a single dataset, external validation with additional data is necessary for the accurate evaluation of models performance. Notably, our study focuses on neonates and infants receiving CKRT, excluding patients on PD, which remains a commonly chosen modality in this population. Therefore, the results do not reflect the outcomes of overall neonatal and infantile AKI requiring dialysis.

CONCLUSION

Based on the proposed XGBoost models, we conclude that more severe AKI progression and longer time to CKRT initiation might be important risk factors for mortality in children up to 12 months of age. Primary kidney disease and related biochemical parameters are strong predictors of proteinuria at hospital discharge. Although some findings align with existing knowledge, our AI approach allowed us to quantify and rank their predictive contribution using SHAP analysis, which we believe adds interpretability and methodological value. Moreover, the validation of this model might lead to analyzing even more numerous and complex variables for a more personalized risk stratification. While the predictive performance in our study is modest, the XGBoost models help prioritize key risk factors and may support early risk stratification in clinical settings. Future prospective validation and model refinement are warranted before clinical implementation. Larger studies are needed to provide definitive results and develop models applicable in clinical routine.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

SUPPLEMENTARY DATA

Supplementary data are available at *Nephrology Dialysis Transplantation* online.

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AUTHORS' CONTRIBUTIONS

A.D. and I.G. conceptualized and designed the study, and drafted and revised the paper. A.D. and K.D. analyzed data. A.C., R.L., A.K.B., G.L., S.M., I.K.B., M.T., M.C., M.K., G.M., E.V., E.Y., and A.P. collected data and revised the paper. R.B.B., Z.A., J.O., D.Y., C.P.S., F.P., A.J., L.C.C., E.V., A.T., and F.S. collected data and critically reviewed the paper for important intellectual content. All authors approved the final paper as submitted and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST STATEMENT

C.P.S declares receiving research grants from Baxter and Invizius, consulting fees from Chiesi, Bioporto, Baxter and Stada Pharma, and payment for lectures from Fresenius. M.T. declares receiving consulting fees and payment for lectures from Baxter. R.B.B declares receiving meetings and travel support from BIAL-Portela & Ca, S.A., and Kyoa Kirin Unipessonal Farmaceutica, Lda.

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