BMJ Open

Development and validation of a nomogram for predicting in-hospital mortality of elderly patients with persistent sepsis-associated acute kidney injury in intensive care units: a retrospective cohort study using the MIMIC-IV database

Wei Jiang ,[1,2] Chuanqing Zhang,[1,2] Jiangquan Yu,[1,2] Jun Shao,[1,2] Ruiqiang Zheng[1,2]

To cite: Jiang W, Zhang C, Yu J, *et al*. Development and validation of a nomogram for predicting in-hospital mortality of elderly patients with persistent sepsis-associated acute kidney injury in intensive care units: a retrospective cohort study using the MIMIC-IV database. *BMJ Open* 2023;**13**:e069824. doi:10.1136/bmjopen-2022-069824

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-069824).

WJ and CZ contributed equally.

Received 05 November 2022
Accepted 15 March 2023

[1]Medical College, Yangzhou University, Yangzhou, China
[2]Intensive Care Unit, Northern Jiangsu People's Hospital, Yangzhou, China

Correspondence to
Professor Ruiqiang Zheng;
zhengruiqiang2021@163.com

ABSTRACT

Objectives To identify the clinical risk factors that influence in-hospital mortality in elderly patients with persistent sepsis-associated acute kidney injury (S-AKI) and to establish and validate a nomogram to predict in-hospital mortality.

Design Retrospective cohort analysis.

Setting Data from critically ill patients at a US centre between 2008 and 2021 were extracted from the Medical Information Mart for Intensive Care (MIMIC)-IV database (V.1.0).

Participants Data from 1519 patients with persistent S-AKI were extracted from the MIMIC-IV database.

Primary outcome All-cause in-hospital death from persistent S-AKI.

Results Multiple logistic regression revealed that gender (OR 0.63, 95% CI 0.45–0.88), cancer (2.5, 1.69–3.71), respiratory rate (1.06, 1.01–1.12), AKI stage (2.01, 1.24–3.24), blood urea nitrogen (1.01, 1.01–1.02), Glasgow Coma Scale score (0.75, 0.70–0.81), mechanical ventilation (1.57, 1.01–2.46) and continuous renal replacement therapy within 48 hours (9.97, 3.39–33.9) were independent risk factors for mortality from persistent S-AKI. The consistency indices of the prediction and the validation cohorts were 0.780 (95% CI: 0.75–0.82) and 0.80 (95% CI: 0.75–0.85), respectively. The model's calibration plot suggested excellent consistency between the predicted and actual probabilities.

Conclusions This study's prediction model demonstrated good discrimination and calibration abilities to predict in-hospital mortality of elderly patients with persistent S-AKI, although it warrants further external validation to verify its accuracy and applicability.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study developed and validated a nomogram for predicting in-hospital mortality of elderly patients with persistent sepsis-associated acute kidney injury (AKI) in intensive care units.
⇒ Logistic regression was applied to analyse the clinical data, and the predictive models' diagnostic efficacy was assessed using the consistency index, receiver operating characteristic curve and calibration plots.
⇒ Multiple imputation was used to handle the covariates with <20% missing to minimise the bias resulting from missing values.
⇒ This investigation solely used serum creatinine criteria to define AKI; oliguria may have led to the overlooking of some acute renal damage in patients.
⇒ The model was only internally validated, warranting further external validation to verify its accuracy and applicability.

INTRODUCTION

The world's population is estimated to be >7.3 billion. Of this estimate, individuals aged ≥65 years would constitute approximately 9% of the population, which is expected to expand to 17% by 2050.[1] Ageing has been associated with a decline in renal functions. Clinical studies have demonstrated that elderly patients have a higher risk of acute kidney injury (AKI) with a worsening prognosis.[2–5] According to the US Renal Data System data from 2018, the in-hospital mortality for patients aged >66 years who were hospitalised for the first time with AKI was 8.2%, while that for inpatients without AKI was only 1.8%. On including the patients discharged to a hospice in the mortality calculation, the mortality of elderly inpatients with AKI and those without AKI increased by 13.2% and 3.8%, respectively.[6] In addition, the mortality of elderly patients with AKI receiving dialysis treatment

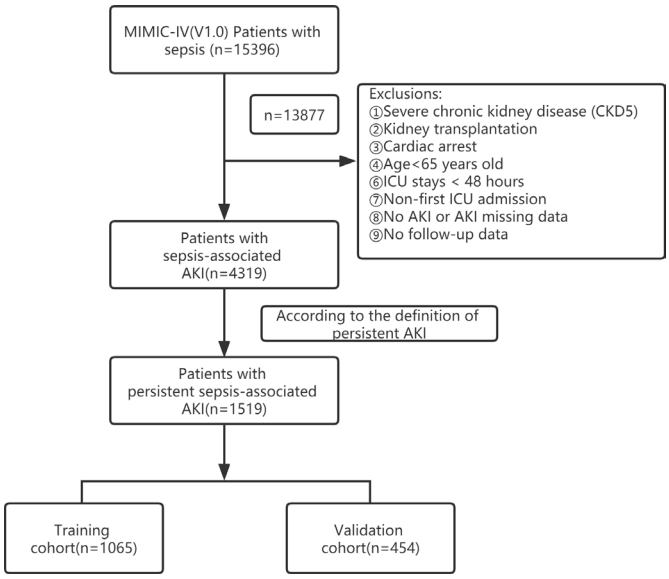

Figure 1 Study flow chart. AKI, acute kidney injury; ICU; intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care IV.

was higher, increasing from 31% to 80%.[7] These statistics emphasise that elderly patients may encounter significant risks during AKI.

The duration of AKI significantly influences an elderly patient's prognosis. According to past studies, persistent acute renal damage, rather than transitory acute renal injury, is an independent risk factor for in-hospital mortality.[8–11] In this study, the fatality of geriatric patients with persistent AKI was found to be as high as 53.1%, while the mortality of transient AKI was only 5.9%. Li *et al*[12] conducted a retrospective analysis of elderly patients with AKI aged >75 years and found that elderly patients with persistent AKI were independently associated with a significantly higher 90-day mortality.

Elderly patients with persistent sepsis-associated AKI (S-AKI) should therefore be paid special attention to in clinical management practices. Early and precise assessment of these patients' mortality risk would facilitate early medical intervention and rational allocation of nursing resources, which, in turn, would improve patient survival through improved prognosis. The nomogram was deemed a robust tool for building a simplistic and intuitive prediction model for quantifying the perceived risk of clinical events.[13 14] In order to investigate the risk factors for the poor short-term outcome and to provide a reference for the prevention and treatment of geriatric patients with persistent S-AKI, we developed a prediction model based on this nomogram for predicting in-hospital fatality among geriatric patients with persistent S-AKI.

METHODS

Data source and preprocessing

All data used in this study were obtained from the Medical Information Mart for Intensive Care IV (MIMIC-IV V.1.0) database—a public-access database supported by the Department of Medicine at Beth Israel Deaconess Medical Center and the Computational Physiology Laboratory at MIT, which included full information of all patients admitted to the Beth Israel Deaconess Medical Center from 2008 to 2019 (last updated in March 2021).[15] This database is freely accessible to any qualified PhysioNet user. The database consists of details of more than 500 000 hospital admissions and 70 000 intensive care unit (ICU) admissions.

Study population

In this analysis, all patients with S-AKI meeting Sepsis-3.0 and the Kidney Disease Improving Global Outcomes (KDIGO) creatinine criteria were included, in accordance with the ICD-9 (The International Statistical Classification of Diseases and Related Health Problems 9th Revision) diagnostic code of the database. The following were considered the inclusion criteria: sepsis diagnosed as an infection and Sequential Organ Failure Assessment score of ≥2.[16] The diagnosis of AKI was serum creatinine (Scr) ≥0.3 mg/dL within 48 hours or Scr ≥50% within 7 days.[17] Patients were excluded from the study if they had the following diseases: severe chronic kidney disease (defined as glomerular filtration rate <15 mL/min/1.73 m^2), pregnancy, cardiac arrest, life expectancy <48 hours after the admission to the ICU and kidney transplantation.

Clinical variables and definitions

Several variables were extracted from the database, which comprised patient demographics, vital signs, medical history, laboratory tests and scoring systems. All data were collected within 24 hours of admission to the ICU. Other data collected included the requirement for mechanical ventilation and renal replacement therapy. The outcome measurements were the length of stay in the ICU, ICU mortality, the length of hospital stay and in-hospital mortality. The mean values of laboratory variables within 24 hours of ICU admission were used for analyses and included in the predictive model while considering that several variables were measured more than once. In the case of missing data, multiple imputation was employed for missing data on the biochemical parameters. For the missing data on height and weight, age and gender were used to layer the linear relationship for interpolation. For other classification variables, 'null' was used as the default value.

According to the consensus report of the Acute Dialysis Quality Initiative 16 working group, persistent AKI was defined as duration of >48 hours, which meets the KDIGO standard.[18] Transient AKI is defined as AKI with duration of <48 hours.

Statistical analyses

Qualitative variables were displayed by median (IQR) and categorical variables by frequency (n) in absolute numbers and percentage (%). Mann-Whitney U test, Fisher's exact test or X^2 test were employed for intergroup comparison, as deemed appropriate. First, univariate analyses were performed on all variables to determine the statistically

Table 1 Analysis of the risk factors for in-hospital mortality in the training cohort (univariate and multivariate logistic regression analyses)

	Univariate		Multivariate	
Variables	OR (95% CI)	P value	OR (95% CI)	P value
Gender	0.73 (0.55–0.96)	0.02	0.63 (0.45–0.88)	0.008
Chronic heart disease	2.14 (1.46–3.13)	<0.001		
Cancer	2.17 (1.54–3.06)	<0.001	2.50 (1.69–3.71)	<0.001
Heart rate	1.02 (1.01–1.03)	<0.001		
Respiratory rate	1.11 (1.07–1.15)	<0.001	1.06 (1.01–1.12)	0.013
SBP	0.98 (0.97–0.99)	0.001		
MAP	0.98 (0.97–1.00)	0.02		
SpO_2	0.90 (0.84–0.96)	<0.001		
Basal creatinine level	1.13 (1.02–1.24)	0.02		
Creatinine	1.14 (1.05–1.24)	<0.001		
Creatinine_48 hours	1.08 (1.00–1.16)	0.04		
AKI KDIGO stage	1.79 (1.19–2.68)	0.01	2.01 (1.24–3.24)	0.004
Creatinine_24 hours	1.08 (1.00–1.17)	0.04		
BUN	1.01 (1.01–1.02)	<0.001	1.01 (1.01–1.02)	0.001
Lactate	1.22 (1.14–1.31)	<0.001		
pH	0.04 (0.01–0.23)	<0.001		
SOFA score	1.07 (1.01–1.13)	0.02		
GCS score	0.77 (0.72–0.82)	<0.001	0.75 (0.70–0.81)	<0.001
Dopamine use	2.09 (1.11–3.94)	0.02		
Norepinephrine use	2.24 (1.69–2.99)	0.001		
Mechanical ventilation	1.48 (1.05–2.08)	0.02	1.57 (1.01–2.46)	0.047
CRRT within 48 hours	19.8 (8.23–47.66)	<0.001	9.97 (3.39–33.9)	<0.001
Length of ICU stay	1.03 (1.01–1.05)	<0.001		

AKI, acute kidney injury; BUN, blood urea nitrogen; CRRT, continuous renal replacement therapy; GCS, Glasgow Coma Scale; ICU, intensive care unit; KDIGO, Kidney Disease Improving Global Outcomes; MAP, mean arterial pressure; pH, potential of hydrogen; SBP, systolic blood pressure; SOFA, Sequential Organ Failure Assessment; SpO_2, peripheral oxygen saturation.

significant factors affecting mortality. When using the logistic regression method for multivariate analyses, only variables with significant differences between the groups were used. Data were described by OR and CI of 95%, and p<0.05 was considered to indicate statistical significance. A clinical prediction model for predicting in-hospital mortality of persistent S-AKI was established through logistic regression, and the nomogram was evaluated by C statistics and operation area under the curve (AUC). All statistical analyses were conducted with the R V.4.2.1 software.

Patient and public involvement

None.

RESULTS

Patient characteristics of the training and validation cohorts

A total of 15 396 patients with sepsis in MIMIC-IV were screened sequentially with reference to the inclusion and exclusion criteria. A total of 4319 elderly patients with S-AKI were assessed, of which 1519 patients met the definition of persistent AKI and were accordingly assigned to either the training cohort (n=1065) or the validation cohort (n=454) (figure 1). No statistically significant difference was noted between the training and validation cohorts (online supplemental table 1).

Predictors and nomogram for in-hospital mortality

Univariate logistic analysis was initially conducted for all variables to assess the independent risk factors for in-hospital mortality among geriatric patients with persistent S-AKI in the ICU (table 1). Univariately determined significant values (p<0.05) were then subjected to multiple logistic regression analyses, with the results presented as OR (95% CI). As presented in table 1, gender (0.63 (0.45–0.88)), cancer (2.50 (1.69–3.71)), respiratory rate (1.06 (1.01–1.12)), AKI stage (2.01 (1.24–3.24)), blood urea nitrogen (BUN) (1.01 (1.01–1.02)), Glasgow Coma

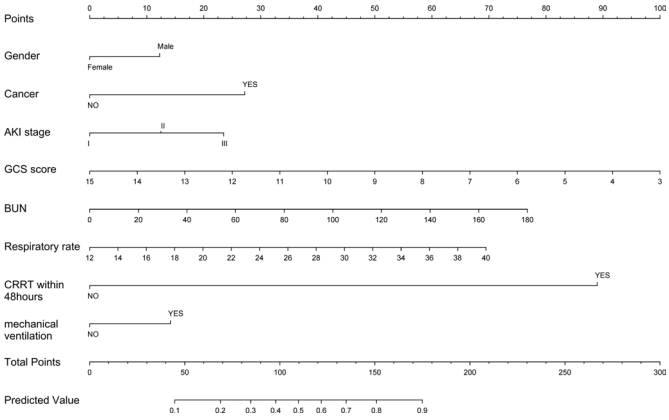

Figure 2 Nomogram for predicting in-hospital death of patients with persistent sepsis-associated AKI. AKI, acute kidney injury; BUN, blood urea nitrogen; CRRT, continuous renal replacement therapy; GCS, Glasgow Coma Scale.

Scale (GCS) score (0.75 (0.70–0.81)), mechanical ventilation (1.57 (1.01–2.46)) and continuous renal replacement therapy (CRRT) within 48 hours (9.97 (3.39–33.9)) were independently correlated with in-hospital death. Finally, we created a nomogram including the previously published predictive variables to predict the incidence of in-hospital death among geriatric individuals with persistent S-AKI (figure 2).

Evaluation and validation of the nomogram

The consistency indices for the training and validation cohorts were applied for assessing the probability of in-hospital mortality for elderly patients with persistent S-AKI of 0.78 (95% CI: 0.75–0.81) and 0.80 (95% CI: 0.75–0.85), respectively. In the training cohort, the AUC of the nomogram predicting the in-hospital risk of death was 0.78 (95% CI: 0.75–0.82) (figure 3A) in the training cohort and 0.82 (95% CI: 0.77–0.87) in the validation cohort (figure 3B). The calibration curve indicated that the nomogram model's predicted results were in excellent accordance with the actual observations (figure 4).

DISCUSSION

Based on the current findings, obtained through both univariate and multivariate regression analyses, the risks of in-hospital death among geriatric patients with persistent S-AKI were associated with gender, AKI stage, BUN, GCS score, cancer, respiratory rate, CRRT within 48 hours and mechanical ventilation. In addition, we developed a nomogram to predict the near-term outcomes in patients with persistent S-AKI, and it performed well on both the training and external validation datasets. This is the first research to develop and validate an in-hospital mortality risk prediction model for geriatric patients with persistent S-AKI that allows a simple, but relatively accurate risk-identifying tool for early detection and response.

Clinical research demonstrated that geriatric individuals were more likely to develop AKI and demonstrated a poorer prognosis following an episode of AKI.[2–5] Sepsis

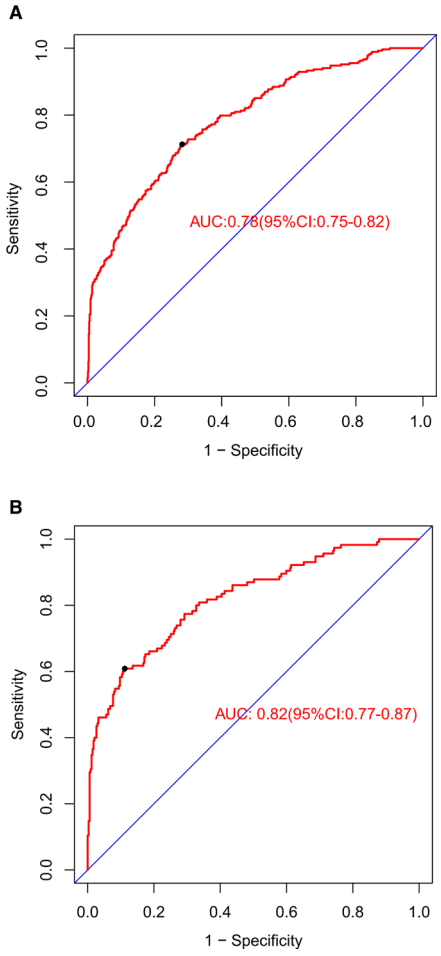

Figure 3 ROC of nomogram in training cohort (A) and validation cohort (B). AUC, area under the curve; ROC, receiver operating characteristic.

and prolonged AKI duration significantly increased all-cause mortality in elderly patients during hospitalisation.[12 19 20] Geriatric individuals with persistent S-AKI had a significantly higher frequency of in-hospital mortality and ICU mortality when compared with patients with AKI with shorter duration of renal impairment or without sepsis.[11 20] Emphasising sepsis management or renal support therapy alone does not significantly reduce mortality in elderly patients with persistent S-AKI.[21] Therefore, we focused on elderly patients with persistent S-AKI, analysed the risk factors correlated with in-hospital mortality in this segment of patients and developed a nomogram to predict persistent S-AKI, which has the potential to improve the short-term outcomes of persistent S-AKI.

The present results demonstrated that the severity of AKI is a significant risk factor for increased all-cause mortality in geriatric individuals with persistent S-AKI (OR=2.01). Our study is supported by data from past studies suggesting that the overall in-hospital mortality rate without AKI was only 0.6%, while that in patients with AKI was significantly higher; the higher the stage of AKI, the greater the mortality rate (5.3% for stage I AKI, 13.4% for stage III AKI and 35.4% for stage III AKI).[22 23]

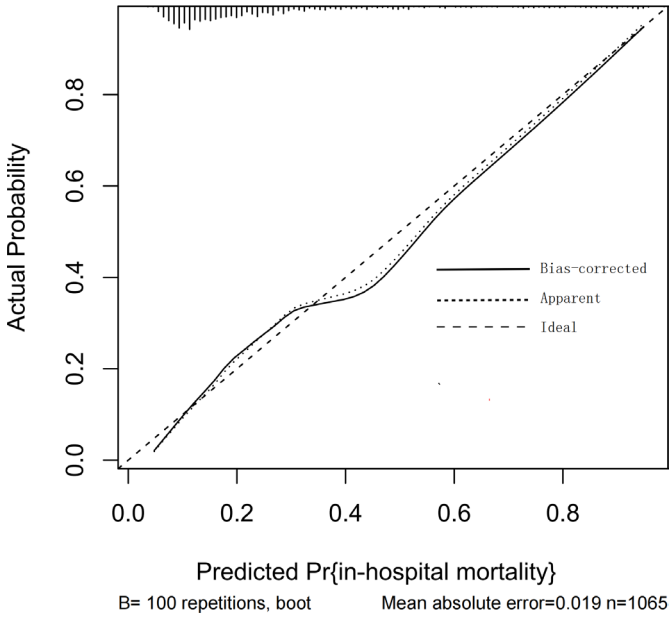

Figure 4 Calibration curve for patients with persistent sepsis-associated acute kidney injury is based on a nomogram.

Therefore, the near-term prognosis of elderly patients with persistent S-AKI may be assessed and predicted in clinical practice based on the stage of AKI.

The metric GCS score is commonly used to evaluate the degree of consciousness in patients with sepsis.[24] A previous meta-analysis revealed that patients with AKI following trauma often exhibited low GCS scores.[25] In addition, a correlation was noted between the GCS scores and in-hospital mortality in elderly patients with sepsis.[26] A higher GCS score was also recorded as a risk factor for in-hospital mortality in elderly patients with persistent S-AKI.

The role of gender in kidney diseases remains a topic of widespread interest. Gender differences in chronic disease and mortality persist with population-based studies, suggesting that women have a higher overall prevalence of chronic kidney diseases.[27–29] However, men are twice as likely as women to develop kidney cancer, with a higher mortality rate.[30] In addition, exogenous hormone therapy has been associated with an increase in the incidence of AKI in patients with prostate cancer.[31] Although our study only included patients with acute diseases, our findings implied that sex-related effects may play a role in the clinical course of S-AKI, which must be considered clinically.

Indeed, the risk of AKI increases in the first year following cancer diagnosis among elderly patients with cancer; this composite harms their survival, with a significant increase in their potential mortality rate.[32] Past studies have demonstrated that BUN predicts both short-term and long-term mortality independently of the Scr levels.[33] Pre-dialysis BUN levels predicted 60-day mortality in individuals with severe AKI requiring dialysis.[34] We found that the BUN levels acted as an independent predictor of short-term mortality.

In our study, mechanical ventilation and CRRT within 48 hours acted as independent predictors of in-hospital mortality in older adults with S-AKI. In a recent meta-analysis, van den Akker *et al* recorded an association between invasive mechanical ventilation and a three-fold higher risk of AKI.[35] Clinical studies have demonstrated that hypoxaemia, hypercapnia, high positive end-expiratory pressure values and high tidal volume are the risk predictors for AKI in people on mechanical ventilation.[35] Past evidence indicates that mechanical ventilation is related to the incidence rate, risk factors, all-cause mortality and renal prognosis of AKI in elderly patients.[36 37]CRRT is an important treatment modality for AKI in critically ill patients, with an increasing number of patients having received CRRT.[38 39] In recent studies, CRRT has been reported to significantly increase all-cause death rates.[38 39]

Finally, the in-hospital mortality prediction model proposed in this report displayed good discriminative power in training and external test sets. Owing to its simplicity, it lends itself well to generalisation and application in clinical care and treatment. This study, however, has some limitations. First, we only internally verified the model, and the result warrants external confirmation. Second, because this investigation solely used Scr criteria to define AKI, oliguria may have led to overlooking some acute renal damage in patients. Third, the current study may have missed some potential risk factors, such as the Renal Resistance Index and new biomarkers of CCL14. Thus, the prediction model requires further clinical data for assessment as well as external validation to verify its accuracy and applicability.

CONCLUSION

Our study showed that CRRT within 48 hours, mechanical ventilation, cancer, respiratory rate, gender, AKI stage, BUN and GCS score acted as independent predictors of in-hospital mortality among elderly patients with persistent S-AKI. We also showed that the resulting nomogram had good predictive performance, although it warrants further external validation to verify its accuracy and applicability.

Acknowledgements We would like to thank the participants, developers and investigators associated with the Medical Information Mart for Intensive Care (MIMIC)-IV database.

Contributors All the authors participated in literature retrieval and viewpoint discussion in this article. WJ and CZ are the main contributors to data extraction, data analysis and writing. RZ, JY, and JS revised this article. All authors have read and approved the final manuscript. RZ is responsible for all the study work as the guarantor.

Funding This work was supported by Jiangsu Province's '333 Projects' (BRA2020183), Top-notch Talents of 'Six-one Projects' of Jiangsu Commission of Health (LGY2019036), scientific research project of Jiangsu Commission of Health (Z2020055) and Yangzhou Social Development Project (YZ2021059).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Considering that this study was based on the analysis of an anonymous third-party public database with prior approval from the Institutional Review Board, no ethical review was required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iD

Wei Jiang http://orcid.org/0000-0002-5278-3057

REFERENCES

1 Coca SG. Acute kidney injury in elderly persons. *Am J Kidney Dis* 2010;56:122–31.
2 Ishani A, Xue JL, Himmelfarb J, *et al*. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol* 2009;20:223–8.
3 Fabbian F, Savriè C, De Giorgi A, *et al*. Acute kidney injury and in-hospital mortality: a retrospective analysis of a nationwide administrative database of elderly subjects in Italy. *J Clin Med* 2019;8:1371.
4 Rhee H, Jang KS, Park JM, *et al*. Short- and long-term mortality rates of elderly acute kidney injury patients who underwent continuous renal replacement therapy. *PLoS One* 2016;11:e0167067.
5 Chao C-T, Tsai H-B, Wu C-Y, *et al*. The severity of initial acute kidney injury at admission of geriatric patients significantly correlates with subsequent in-hospital complications. *Sci Rep* 2015;5:13925.
6 Saran R, Robinson B, Abbott KC, *et al*. US renal data system 2018 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney Dis* 2019;73:A7–8.
7 Rosner MH. Acute kidney injury in the elderly. *Clin Geriatr Med* 2013;29:565–78.
8 Gameiro J, Duarte I, Marques F, *et al*. Transient and persistent AKI and outcomes in patients undergoing major abdominal surgery. *Nephron* 2020;144:236–44.
9 Perinel S, Vincent F, Lautrette A, *et al*. Transient and persistent acute kidney injury and the risk of hospital mortality in critically ill patients: results of a multicenter cohort study. *Crit Care Med* 2015;43:e269–75.
10 Sood MM, Shafer LA, Ho J, *et al*. Early reversible acute kidney injury is associated with improved survival in septic shock. *J Crit Care* 2014;29:711–7.
11 Coca SG, King JT Jr, Rosenthal RA, *et al*. The duration of postoperative acute kidney injury is an additional parameter predicting long-term survival in diabetic veterans. *Kidney Int* 2010;78:926–33.
12 Li Q, Zhao M, Wang X. The impact of transient and persistent acute kidney injury on short-term outcomes in very elderly patients. *Clin Interv Aging* 2017;12:1013–20.
13 Jiang S, Fang J, Yu T, *et al*. Novel model predicts diabetic nephropathy in type 2 diabetes. *Am J Nephrol* 2020;51:130–8.
14 Guan C, Li C, Xu L, *et al*. Risk factors of cardiac surgery-associated acute kidney injury: development and validation of a perioperative predictive nomogram. *J Nephrol* 2019;32:937–45.
15 Zhao X, Lu Y, Li S, *et al*. Predicting renal function recovery and short-term reversibility among acute kidney injury patients in the ICU: comparison of machine learning methods and conventional regression. *Ren Fail* 2022;44:1326–37.
16 Singer M, Deutschman CS, Seymour CW, *et al*. The third International consensus definitions for sepsis and septic shock (sepsis-3). *JAMA* 2016;315:801–10.
17 Kellum JA, Lameire N, KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Crit Care* 2013;17:204.
18 Chawla LS, Bellomo R, Bihorac A, *et al*. Acute kidney disease and renal recovery: consensus report of the acute disease quality initiative (ADQI) 16 Workgroup. *Nat Rev Nephrol* 2017;13:241–57.
19 Yan P, Duan X-J, Liu Y, *et al*. Acute kidney disease in hospitalized acute kidney injury patients. *PeerJ* 2021;9:e11400.
20 Forni LG, Darmon M, Ostermann M, *et al*. Renal recovery after acute kidney injury. *Intensive Care Med* 2017;43:855–66.
21 Rhodes A, Evans LE, Alhazzani W, *et al*. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med* 2017;45:486–552.
22 Zeng X, McMahon GM, Brunelli SM, *et al*. Incidence, outcomes, and comparisons across definitions of AKI in hospitalized individuals. *Clin J Am Soc Nephrol* 2014;9:12–20.
23 Duan S, Liu Q, Pan P, *et al*. Rifle and akin criteria for mortality and risk factors of acute kidney injury in hospitalized patients. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2013;38:1243–52.
24 Angus DC, van der Poll T. Severe sepsis and septic shock. *N Engl J Med* 2013;369:840–51.
25 Søvik S, Isachsen MS, Nordhuus KM, *et al*. Acute kidney injury in trauma patients admitted to the ICU: a systematic review and meta-analysis. *Intensive Care Med* 2019;45:407–19.
26 Boonmee P, Ruangsomboon O, Limsuwat C, *et al*. Predictors of mortality in elderly and very elderly emergency patients with sepsis: a retrospective study. *West J Emerg Med* 2020;21:210–8.
27 Swartling O, Rydell H, Stendahl M, *et al*. CKD progression and mortality among men and women: a nationwide study in sweden. *Am J Kidney Dis* 2021;78:190–9.
28 Jung C-Y, Heo GY, Park JT, *et al*. Sex disparities and adverse cardiovascular and kidney outcomes in patients with chronic kidney disease: results from the KNOW-CKD. *Clin Res Cardiol* 2021;110:1116–27.
29 Carrero JJ, Hecking M, Chesnaye NC, *et al*. Sex and gender disparities in the epidemiology and outcomes of chronic kidney disease. *Nat Rev Nephrol* 2018;14:151–64.
30 Peired AJ, Campi R, Angelotti ML, *et al*. Sex and gender differences in kidney cancer: clinical and experimental evidence. *Cancers (Basel)* 2021;13:4588.
31 Lapi F, Azoulay L, Niazi MT, *et al*. Androgen deprivation therapy and risk of acute kidney injury in patients with prostate cancer. *JAMA* 2013;310:289–96.
32 Christiansen CF, Johansen MB, Langeberg WJ, *et al*. Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. *Eur J Intern Med* 2011;22:399–406.
33 Beier K, Eppanapally S, Bazick HS, *et al*. Elevation of blood urea nitrogen is predictive of long-term mortality in critically ill patients independent of normal creatinine. *Crit Care Med* 2011;39:305–13.
34 Liu KD, Himmelfarb J, Paganini E, *et al*. Timing of initiation of dialysis in critically ill patients with acute kidney injury. *Clin J Am Soc Nephrol* 2006;1:915–9.
35 van den Akker JPC, Egal M, Groeneveld ABJ. Invasive mechanical ventilation as a risk factor for acute kidney injury in the critically ill: a systematic review and meta-analysis. *Crit Care* 2013;17:R98.
36 Li Q, Zhao M, Zhou F. Hospital-Acquired acute kidney injury in very elderly men: clinical characteristics and short-term outcomes. *Aging Clin Exp Res* 2020;32:1121–8.
37 Li Q, Zhao M, Du J, *et al*. Outcomes of renal function in elderly patients with acute kidney injury. *Clin Interv Aging* 2017;12:153–60.
38 Park S, Lee S, Jo HA, *et al*. Epidemiology of continuous renal replacement therapy in Korea: results from the National health insurance service claims database from 2005 to 2016. *Kidney Res Clin Pract* 2018;37:119–29.
39 Wald R, McArthur E, Adhikari NKJ, *et al*. Changing incidence and outcomes following dialysis-requiring acute kidney injury among critically ill adults: a population-based cohort study. *Am J Kidney Dis* 2015;65:870–7.

Supplemental Table 1

Differences between the training cohort and the validation cohort in terms of demographic characteristics and laboratory values

Variable	Validation cohort	Training cohort	p.overall
	N=454	***N=1065***	
Age (years)	76.0 [71.0;82.0]	76.0 [71.0;83.0]	0.736
Male (n%)	261 (57.5%)	615 (57.7%)	0.971
Weight, kg	78.0 [67.8;93.1]	80.0 [67.7;95.1]	0.540
Height, cm	168 [163;175]	168 [160;175]	0.940
Comorbidities, n%			
Hypertension	188 (41.4%)	434 (40.8%)	0.856
Diabetes	178 (39.2%)	447 (42.0%)	0.344
Chronic heart disease	61 (13.4%)	130 (12.2%)	0.564
Cerebrovascular disease	68 (15.0%)	168 (15.8%)	0.753
COPD	29 (6.39%)	100 (9.39%)	0.069
Chronic kidney disease	210 (46.3%)	505 (47.4%)	0.719
Cancer	73 (16.1%)	173 (16.2%)	0.997
Source of infection, n%			
Lung	146 (32.2%)	341 (32.0%)	1.000
Urine	110 (24.2%)	278 (26.1%)	0.482
Blood	190 (41.9%)	427 (40.1%)	0.561
Other(n)	8 (1.76%)	19 (1.78%)	1.000
Vital signs			
Heart rate, bpm	84.5 [74.9;94.7]	82.9 [74.1;94.0]	0.336
Respiratory rate, bpm	19.2 [17.0;22.1]	19.2 [17.1;22.2]	0.979
Temperature, ℃	36.8 [36.5;37.1]	36.7 [36.5;37.0]	0.07
Map, mmHg	74.0 [68.0;80.0]	73.2 [68.5;79.8]	0.667

SpO_2	97.3 [95.6;98.6]	97.3 [95.8;98.6]	0.398
Basal creatinine level, mg/dL	1.35 [0.90;2.40]	1.40 [0.90;2.30]	0.980
Creatinine, mg/dL	1.80 [1.30;3.00]	1.90 [1.30;2.90]	0.829
AKI KIDGO stage			0.766
1	354 (78.0%)	812 (76.2%)	
2	49 (10.8%)	124 (11.6%)	
3	51 (11.2%)	129 (12.1%)	
Creatinine_48 h	2.10 [1.30;3.60]	2.20 [1.50;3.60]	0.383
Laboratory results within 24 h			
Creatinine, mg/dL	2.00 [1.20;3.50]	2.10 [1.30;3.30]	0.480
BUN, mg/dL	29.0 [19.0;49.5]	29.5 [20.0;48.0]	0.621
Lactate, mmol/L	1.90 [1.35;2.90]	1.85 [1.35;2.85]	0.933
PH	7.37 [7.32;7.42]	7.37 [7.32;7.42]	0.700
Hematocrit, g/dL	30.8 [27.4;35.7]	31.1 [27.1;35.5]	0.731
Hemoglobin, g/dL	10.2 [9.00;11.8]	10.2 [8.95;11.8]	0.647
Platelets, ×10^9	172 [124;230]	174 [124;246]	0.580
WBC, ×10^9	12.3 [8.42;16.4]	12.2 [8.75;16.5]	0.872
Albumin, g/dL	3.00 [2.60;3.50]	3.00 [2.60;3.50]	0.595
Sodium, mmol/L	138 [136;141]	138 [135;140]	0.291
Potassium, mmol/L	4.35 [3.95;4.80]	4.30 [3.95;4.75]	0.687
Interventions, n%			
Furosemide use	97 (21.4%)	235 (22.1%)	0.815
Dopamine use	29 (6.39%)	42 (3.94%)	0.053
Norepinephrine use	151 (33.3%)	345 (32.4%)	0.788
Mechvent use (n%)	343 (75.6%)	799 (75.0%)	0.879
CRRT use within 48hours	17 (3.74%)	41 (3.85%)	1.000
Score			

SOFA score	4.00 [2.00;5.00]	4.00 [2.00;5.00]	0.899
GCS score	15.0 [14.0;15.0]	15.0 [14.0;15.0]	0.515
APSIII score	64.0 [48.0;85.0]	65.0 [48.0;86.0]	0.718
Outcomes			
Length of ICU Stay, days	5.38 [3.00;10.3]	5.43 [2.86;10.4]	0.979
Length of Hospital Stay, days	12.8 [8.09;20.2]	13.2 [8.61;21.6]	0.381
ICU mortality (n%)	89 (19.6%)	174 (16.3%)	0.143
Hospital mortality (n%)	115 (25.3%)	268 (25.2%)	0.997

COPD, chronic obstructive pulmonary disease; Map, mean arterial pressure; SpO2, peripheral oxygen saturation; AKI, acute kidney injury; KIDGO, Kidney Disease Improving Global Outcomes; BUN, Blood Urea Nitrogen; PH, potential of hydrogen; WBC, white blood cell; CRRT, continual renal replacement therapy; SOFA, sequential organ failure assessment; GCS, Glasgow Coma Scale; APSIII, Acute Physiology Score III; ICU, Intensive Care Unit.