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Non-linear associations between renal perfusion pressure indexes and AKI incidence and recovery rate

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Abstract

Background Renal perfusion pressure plays a crucial role in the pathophysiology of acute kidney injury (AKI). While multiple methods are available for calculating renal perfusion pressure, the optimal calculation approach and its true correlation with AKI remain uncertain. This study aims to investigate the nonlinear relationship between various perfusion pressure indices and AKI, clarifying the connection between perfusion pressure, AKI onset, and recovery.

Methods Three renal perfusion pressure indices were calculated: MAP–CVP, MAP–Plateau pressure, and MAP–CVP–Plateau pressure. Restricted cubic spline (RCS) analysis was used to examine the association between these perfusion indices and AKI incidence. The relationship between MAP–CVP–Plateau pressure and both AKI occurrence and recovery rate was further assessed through linear spline function and categorical analysis.

Results A total of 8,848 ICU patients were included in the study, with an overall AKI incidence of 40%. RCS analysis revealed nonlinear relationships between the three perfusion indices and AKI incidence, each demonstrating different thresholds. ROC analysis indicated that MAP–CVP–Plateau pressure (cutoff value of 55) had the highest predictive value and was thus selected as the primary perfusion index. In the linear spline analysis, a high MAP–CVP–Plateau pressure was significantly associated with a reduced AKI risk when MAP–CVP–Plateau pressure was < 55 (OR 0.95, 95% CI 0.94–0.96, $p < 0.01$), while this association reversed when MAP–CVP–Plateau pressure exceeded 55 (OR 1.02, 95% CI 1.01–1.03, $p < 0.01$). For AKI recovery, a high MAP–CVP–Plateau pressure was significantly associated with a higher recovery rate when MAP–CVP–Plateau pressure was < 55 (OR 1.02, 95% CI 1.01–1.04, $p < 0.01$). However, when MAP–CVP–Plateau pressure was > 55, an elevated MAP–CVP–Plateau pressure was associated with a lower AKI recovery rate (OR 0.96, 95% CI 0.94–0.98, $p < 0.01$). The categorical analysis results for AKI incidence and recovery were consistent with the nonlinear relationship identified in the RCS analysis.

Conclusions This study underscores the critical role of perfusion pressure, particularly MAP–CVP–Plateau pressure, in AKI pathophysiology. Both low and high MAP–CVP–Plateau pressure levels were associated with increased AKI incidence and decreased recovery rates in critically ill patients.

Keywords Platform pressure, Renal perfusion, AKI, Acute kidney injury, Recovery rate

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Introduction

Acute kidney injury (AKI) is a common complication in critically ill patients, and its incidence significantly impacts patient outcomes, including increased mortality, prolonged hospital stays, and a higher risk of developing chronic kidney disease [1]. An important factor influencing the development of AKI in this patient population is the adequacy of perfusion pressure [2–4]. However, the most appropriate perfusion pressure in critically ill patients remains a matter of debate, which is essential for ensuring renal blood flow and preventing kidney injury [5].

A variety of concepts have been proposed for the calculation of perfusion pressure [6], including the use of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and derived renal perfusion pressure indicators, such as the difference between SBP, DBP, MAP, and central venous pressure (CVP) [7–9]. Although most researchers believe that the difference between MAP and CVP can serve as a net organ perfusion pressure [10], uncertainties remain, especially in the context of the unique anatomical location of the kidney. The most effective calculation approach for renal perfusion has yet to be determined.

Furthermore, most previous studies have used generalized linear models to examine the correlation between renal perfusion pressure and AKI, potentially overlooking nonlinear relationships, which is inconsistent with the actual situation as the kidney has a limited range of self-regulation ability [9, 11]. It remains unclear whether higher perfusion pressures are consistently associated with a reduced incidence of AKI. Moreover, existing studies primarily focus on the incidence of AKI, with limited attention given to the potential impact of perfusion pressure on AKI recovery.

The purpose of this study is to solve the existing research gaps by comprehensively investigating the nonlinear relationship between renal perfusion pressure and AKI incidence and recovery rate.

Materials and methods

Data source

This study used data from the MIMIC-IV (Medical Information Mart for Intensive Care IV) database at the Massachusetts Institute of Technology (MIT). The database contains medical records of over 70,000 adult patients who were admitted to the intensive care unit (ICU) at the Beth Israel Deaconess Medical Center in Boston from 2008 to 2019 [12]. The corresponding author, Yanfei Shen, passed the Protecting Human Research Participants exam and obtained access to the database. Since the data were obtained from an anonymized public database, informed consent and ethical approval were waived. Raw data was extracted from the MIMIC-IV database using a structure query language (SQL) in PgAdmin4.

Ethics

Above all, the study was exempt from our institutional review board approval, because the databases used deidentified data and also carried preexisting institutional review board approval.

Inclusion and exclusion criteria

This study aimed to explore the association between different pressure indexes and AKI incidence/recovery in critically ill patients. All patients receiving mechanical ventilation on ICU admission were initially screened. The general exclusion criteria were as follows: (1) patients with missing data of MAP or CVP or plateau pressure on the first day of ICU admission; (2) patients with missing data of > 20% variables; and (3) age less than 18 years. When exploring the association between perfusion indexes and AKI recovery rate, only patients with AKI were included. In patients with multiple ICU admissions, only the first ICU admission was included in the analysis.

Perfusion indexes

Three perfusion indexes were used in the current study: MAP–CVP; MAP–Plateau pressure; and MAP–CVP–plateau pressure. The mean values of these pressure indexes during the first 24 h after ICU admission were used for perfusion index calculation to minimize the potential bias introduced by transient measurements (e.g., default ventilator settings) and provides a more representative baseline value. All units for MAP, CVP, and Plateau Pressure were unified as mmHg.

Data transformation

All perfusion indexes including MAP–CVP; MAP–Plateau pressure; MAP–CVP–plateau pressure were included in the restricted cubic spline regression and the linear spline regression as continuous variables to verify the non-linear relationship between the recovery and incidence of AKI and these perfusion indexes, which were further transformed into category variables using the quartile method.

Outcome definition

The primary outcome was AKI, which was defined according to the creatinine-based kidney disease improving global outcome criteria and without urine output [13]. The lowest serum creatinine level in the past 7 days before ICU admission was defined as the baseline value. AKI was defined as a 1.5-fold increase in the serum creatinine level after ICU admission relative to baseline.

Urine output was not used in the definition of AKI due to a lack of hourly urine volume data. The severity of AKI was graded in accordance with the above guidelines. AKI recovery was defined based on the last serum creatinine value. Hypotension duration within the first 48 h after ICU admission was defined as the total time during which the mean arterial pressure (MAP) was below 65 mmHg. For example, if a patient had three consecutive MAP recordings at 8:00 (80 mmHg), 9:00 (60 mmHg), and 10:00 (75 mmHg), the duration of hypotension would be recorded as 1 h (from 9:00 to 10:00).

Data extraction

Demographics, including age, sex, ethnicity, weight, and SOFA score, as well as comorbidities, such as hypertension, were recorded. Laboratory data, including hemoglobin, white blood cell (WBC) count, platelet (PLT) count, blood urea nitrogen (BUN), creatinine, sodium, potassium, chloride, albumin, and lactate, were also collected. Vasopressor agent usage, including norepinephrine, epinephrine, dopamine, and dobutamine, was recorded within 48 h after ICU admission.

Sensitivity analysis

Chronic kidney disease (CKD) may influence the association between perfusion indexes and AKI prognosis. To ensure robustness, we performed a sensitivity analysis by excluding patients with CKD.

To ensure robust findings, we conducted sensitivity analyses using both urine output (UO) and serum creatinine-based KDIGO criteria for AKI definition. These analyses evaluated the association between perfusion indices and AKI incidence when defined by both parameters. However, the potential relationship between perfusion indexes and AKI recovery could not be assessed due to limited data availability.

Subgroup analysis

Subgroup analysis was also performed according to sepsis, which was defined as the presence of infection in patients with a sequential organ failure assessment (SOFA) score ≥ 2, according to the latest sepsis guideline [14].

Missing data management

For continuous variables with missing values less than 5%, these missing values were imputed using the random forest imputation method. Variables with more than 5% of values missing were excluded.

Statistical analysis

Continuous data were expressed as the means ± standard deviations or the medians and interquartile ranges. The t test, analysis of variance, rank-sum test, or Kruskal–Wallis test was used, as appropriate. Categorical data were expressed as frequencies and percentages and compared using Pearson's chi-squared test. The association between the perfusion indexes and the AKI incidence was explored using restricted cubic spline (RCS) analysis. If the association exhibited nonlinearity, the threshold value was estimated by trying all possible values, choosing the threshold point with the highest likelihood. In the current study, non-linear associations were detected between all perfusion indexes (MAP–CVP 65; MAP–Plateau pressure 55; MAP–CVP–plateau pressure 50.) and the AKI incidence. Furthermore, all perfusion indexes would be divided into two segments according to their respective thresholds and added into the linear spline regression model to evaluate the coefficients for robustness. In the category analysis, all perfusion indexes were transformed into quartile variables and were included in the logistic regression models. In the multivariable logistic regression, a stepwise backward elimination method was used with a significance level of $P \leq 0.10$ to establish the final models. Multi-collinearity was tested by the variance inflation factor method. Then the receiver operating characteristic (ROC) analysis was performed to compare the predictive value of these indexes by calculating the area under ROC (AUC). The statistical significance of the difference between the two AUROCs was assessed using the Delong test.

Two-tailed $P < 0.05$ were considered statistically significant. All statistical analyses were performed using the using R version 4.2.2.

Results

Baseline characteristics

A total of 8848 patients were included in the analysis. The overall AKI rate was 40.9%. The demographic characteristics between AKI and non-AKI groups are shown in Table 1. Patients in the AKI group were older, had significantly higher SOFA scores (5.0 [3.0, 7.0] vs. 8.0 [5.0, 10.7], $p < 0.01$) and hospital mortality rate (202 (3.8) vs. 619 (17.1), $p < 0.01$). The mean MAP–CVP (65.1 (7.3) vs. 62.1 (8.7), $p < 0.01$), MAP–Plateau (57.2 (7.2) vs. 54.4 (8.6), $p < 0.001$), MAP–CVP–Plateau (47.7 (8.7) vs. 42.8 (10.6), $p < 0.001$) were significantly higher in the non-AKI group than those in the AKI group.

The potential non-linear relationships between the perfusion indexes and AKI incidence were explored using RCS analysis (Fig. 1) and linear spline function analysis.

Table 1 Comparisons of baseline characteristics between AKI and non-AKI groups

Variables	Non-AKI ($n=5226$)	AKI ($n=3622$)	*p*
Demographics			
Age [years, mean (SD)]	66.2 (12.5)	68.7 (13.7)	< 0.01
Male (%)	3639 (69.6)	2310 (63.7)	< 0.01
Weight [kg, mean (SD)]	84.9 (19.6)	85.0 (22.6)	0.83
Comorbidities			
Hypertension (%)	3111 (59.5)	1647 (45.4)	0.28
Diabetes (%)	1613 (30.8)	1323 (36.5)	< 0.01
Coronary [mean (SD)]	3310 (63.3)	1930 (53.2)	< 0.01
COPD (%)	167 (3.1)	176 (4.8)	< 0.01
Sepsis3 (%)	3089 (59.1)	2692 (74.3)	< 0.01
Laboratory indexes			
Initial sodium [mmol/L, mean (SD)]	136.4 (3.5)	136.6 (4.6)	0.02
Initial chlorine [mmol/L, mean (SD)]	106.2 (4.5)	105.6 (5.7)	< 0.01
Initial creatinine [mg/dL, mean (SD)]	0.9 (0.6)	1.5 (1.3)	< 0.01
Maximum creatinine [mg/dL, mean (SD)]	1.1 (0.7)	2.5 (2.0)	< 0.01
Initial hemoglobin [g/dL, mean (SD)]	10.4 (2.1)	10.2 (2.4)	< 0.01
Initial UREA [mean (SD)]	18.2 (11.1)	26.3 (18.4)	< 0.01
Initial white blood cell [10^9/L, mean (SD)]	13.0 (5.6)	13.5 (7.0)	0.01
Initial platelet [10^9/L, mean (SD)]	164.1 (68.9)	167.2 (84.0)	0.06
Vasopressor use within 48 h (%)	1451 (27.7)	1942 (53.6)	< 0.01
Severity score			
Initial SOFA score (median [IQR])	5.0 [3.0, 7.0]	8.0 [5.0, 10.7]	< 0.01
Initial SAPSII (median [IQR])	36.0 [30.0, 43.0]	44.0 [37.0, 56.0]	< 0.01
Pressure indexes			
Initial CVP [mmHg, mean (SD)]	9.4 (3.5)	11.6 (4.3)	< 0.01
Initial MAP [mmHg, mean (SD)]	74.6 (6.3)	73.8 (7.5)	< 0.01
Initial plateau pressure [cmH2O, mean (SD)]	17.4 (3.5)	19.3 (4.4)	< 0.01
Initial plateau pressure [mmHg, mean (SD)]			
MAP–CVP [mean (SD)]	65.1 (7.3)	62.1 (8.7)	< 0.01
MAP–Plateau [mean (SD)]	57.2 (7.2)	54.4 (8.6)	< 0.01
MAP–CVP–Plateau [mean (SD)]	47.7 (8.7)	42.8 (10.6)	< 0.01
Duration of hypotension (hours)	3 (0–5.5)	5 (1–8.6)	< 0.01
Urine output within 24 h	1.0 (0.5)	0.7 (0.7)	< 0.01
Clinical outcomes			
Hospital death (%)	202 (3.8)	619 (17.1)	< 0.01
ICU length of stay [mean (SD)]	2.3 (2.4)	6.8 (8.1)	< 0.01
AKI severity (%)			< 0.01
AKI-I	0 (0.00)	2381 (65.72)	
AKI-II	0 (0.00)	596 (16.44)	
AKI-III	0 (0.00)	645 (17.84)	

AKI acute kidney injury, *COPD* chronic obstructive pulmonary disease, *CVP* central venous pressure, *ICU* intensive care unit, *MAP* mean arterial pressure, *SOFA* sequential organ failure assessment, *SAPS II* simplified acute physiology score II, *SD* standard deviation

ROC showed that compared to MAP–CVP and MAP–Plateau, MAP–CPV–PL had the highest AUC (Fig. 1, panel D). Thus, MAP–CPV–PL was used as the main perfusion index in the current study. The associations between the other two indexes (MAP–CVP, MAP–Plateau) and AKI incidence in linear spline and category analysis were presented in supplementary Tables S1 and S2.

MAP–CPV–PL and AKI incidence

A non-linear relationship between MAP–CPV–PL and AKI was detected in RCS analysis (Fig. 1, panel C),

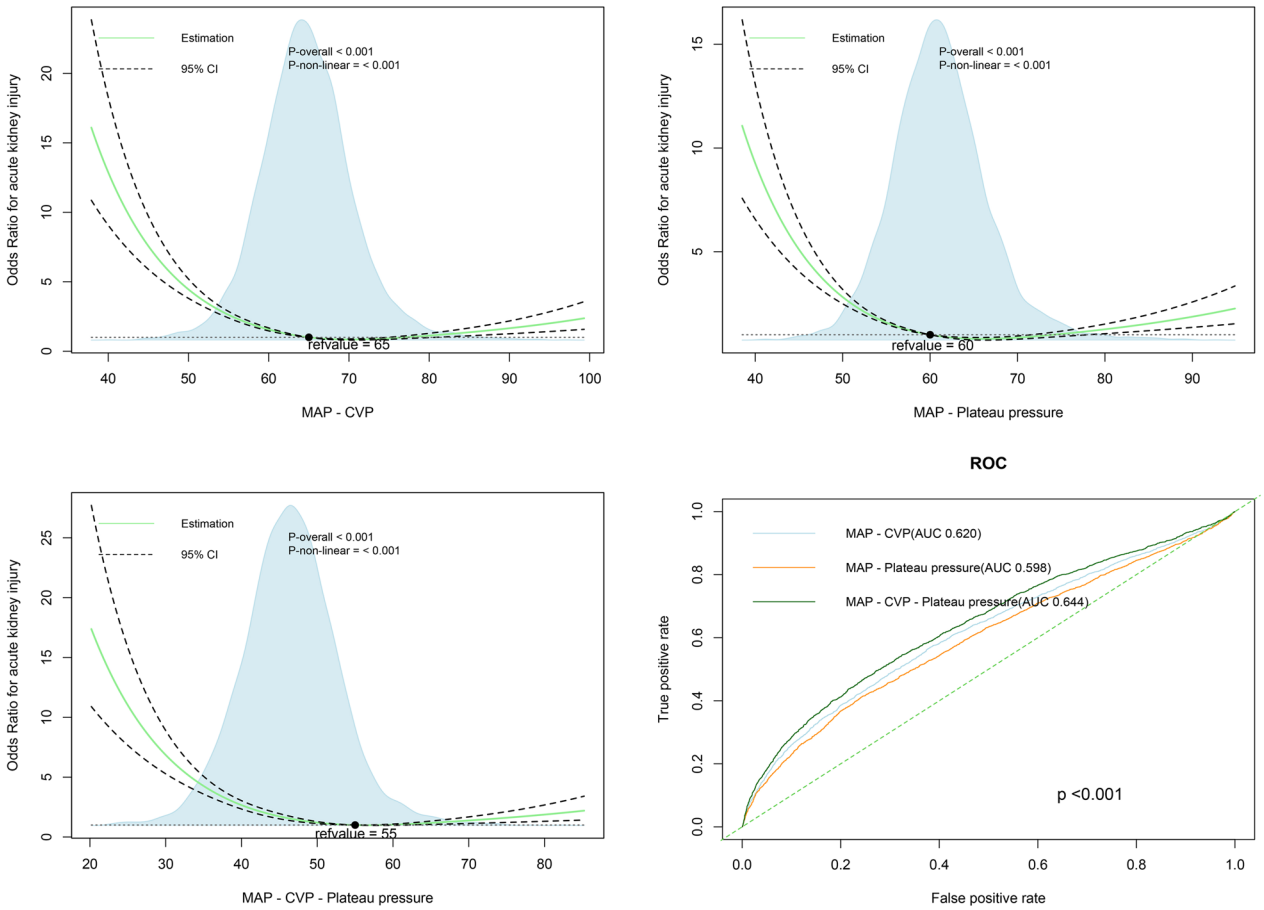

Fig. 1 Non-linear association between MAP–CVP, MAP–PL, MAP–CVP–PL and incidence rate and ROC analysis. *MAP* mean arterial pressure, *CVP* central venous pressure, *PL* platform pressure, *ROC* the receiver operating characteristic

with a cutoff value of 55. In the linear spline function analysis (Table 2), high MAP–CPV–PL was significantly associated with low risk of AKI when the MAP–CPV–PL was < 55 (OR 0.95, 95% CI 0.94–0.96, $p < 0.01$), while this relationship inversed when MAP–CPV–PL was > 55 (OR 1.02, 95% CI 1.01–1.03, $p < 0.01$). In the category analysis (Table 2), MAP–CPV–PL was divided into four categories: level-1: > 65; level-2: 55 ~ 65; level-3: 45 ~ 55; level-4: < 45. Compared to level 2, the other three levels were significantly associated with high AKI incidence, and there was a stepwise increase from level-3 (OR 1.35, 95% CI 1.19–1.53, $p < 0.01$) to level-4 (OR 1.94, 95% CI 1.67–2.25, $p < 0.01$), which was consistent with the non-linear relationship in RCS. Sensitivity analysis in patients without chronic kidney disease also showed similar results (Table S3 and Figure S1). Subgroup analyses was performed based on sepsis status (Figure S2) and a significant interaction was observed (p = 0.009). However, the difference between subgroups was relatively small. In the sepsis subgroup, the OR for AKI was 0.96 (95% CI 0.95–0.97, $p < 0.01$) when MAP–CVP–plateau pressure was < 55 mmHg, and 1.02 (95% CI 1.00–1.03, $p < 0.01$) when MAP–CVP–plateau pressure was > 55 mmHg. Similarly, in the non-sepsis subgroup, the OR for AKI was 0.94 (95% CI 0.92–0.96, $p < 0.01$) when MAP–CVP–plateau pressure was < 55 mmHg, and 1.03 (95% CI 1.01–1.06, $p < 0.01$) when MAP–CVP–plateau pressure was > 55 mmHg. In addition, the association between perfusion indexes and AKI or severe AKI incidence, as defined by both urine output (UO) and serum creatinine criteria, are presented in Tables S4–6 and Figures S3–4. The results remained stable.

MAP–CPV–PL and AKI recovery

Similarly, a non-linear relationship was also detected between MAP–CPV–PL and AKI recovery in RCS analysis (Fig. 2), with a cutoff value of 55. The linear spline function analysis (Table 3) showed that high MAP–CPV–PL was significantly associated with a high AKI recovery rate when the MAP–CPV–PL was < 55 (1.02, 95% CI 1.01–1.04, $p < 0.01$). However, when MAP–CPV–PL was > 55, high MAP–CPV–PL

Table 2 Associations between MAP–CPV–PL pressure and AKI incidence in linear spline function and quartile analysis

Linear spline analysis	Crude OR (95% CI)	*p*	Quartile analysis	Crude OR (95% CI)	*p*
MAP–CVP–PL (< 55)	0.91 (0.90–0.92)	< 0.01	Q1 (MAP–CVP–PL > 65)	1.53 (1.34–1.90)	< 0.01
MAP–CVP–PL (> 55)	1.01 (1.01–1.03)	< 0.01	Q2 (55 < MAP–CVP–PL < 65)	Ref	
			Q3 (45 < MAP–CVP–PL < 55)	1.69 (1.50–1.89)	< 0.01
			Q4 (MAP–CVP–PL < 45)	4.21 (3.71–4.78)	< 0.01
Linear spline analysis	**Adjusted OR (95% CI)**	***p***	**Quartile analysis**	**Adjusted OR (95% CI)**	***p***
MAP–CVP–PL (< 55)	0.95 (0.94–0.96)	< 0.01	Q1 (MAP–CVP–PL > 65)	1.68 (1.33–2.11)	< 0.01
MAP–CVP–PL (> 55)	1.02 (1.01–1.03)	< 0.01	Q2 (55 < MAP–CVP–PL < 65)	Ref	
			Q3 (45 < MAP–CVP–PL < 55)	1.35 (1.19–1.53)	< 0.01
			Q4 (MAP–CVP–PL < 45)	1.94 (1.67–2.25)	< 0.01
Age	1.01 (1.01–1.02)	< 0.01	Age	1.01 (1.01–1.02)	< 0.01
Initial hemoglobin	0.97 (0.95–0.99)	0.01	Initial hemoglobin	0.97 (0.95–0.99)	< 0.01
Diabetes	1.27 (1.14–1.40)	< 0.01	Diabetes	1.27 (1.14–1.40)	< 0.01
Coronary disease	0.78 (0.70–0.86)	< 0.01	Coronary disease	0.77 (0.69–0.85)	< 0.01
Vasopressor use	1.06 (0.94–1.19)	0.30	Vasopressor use	1.07 (0.95–1.20)	0.22
Hypertension	0.71 (0.65–0.79)	< 0.01	Hypertension	0.71 (0.65–0.79)	< 0.01
Initial SOFA	1.22 (1.20–1.25)	< 0.01	Initial SOFA	1.23 (1.20–1.25)	< 0.01
Duration of hypotension	1.02 (1.01–1.03)	< 0.01	Duration of hypotension	1.02 (1.01–1.03)	< 0.01

MAP mean artery pressure, *CVP* central venous pressure, *PL* plateau pressure, *OR* odds ratio, *CI* confidence interval, *SOFA* sequential organ failure assessment

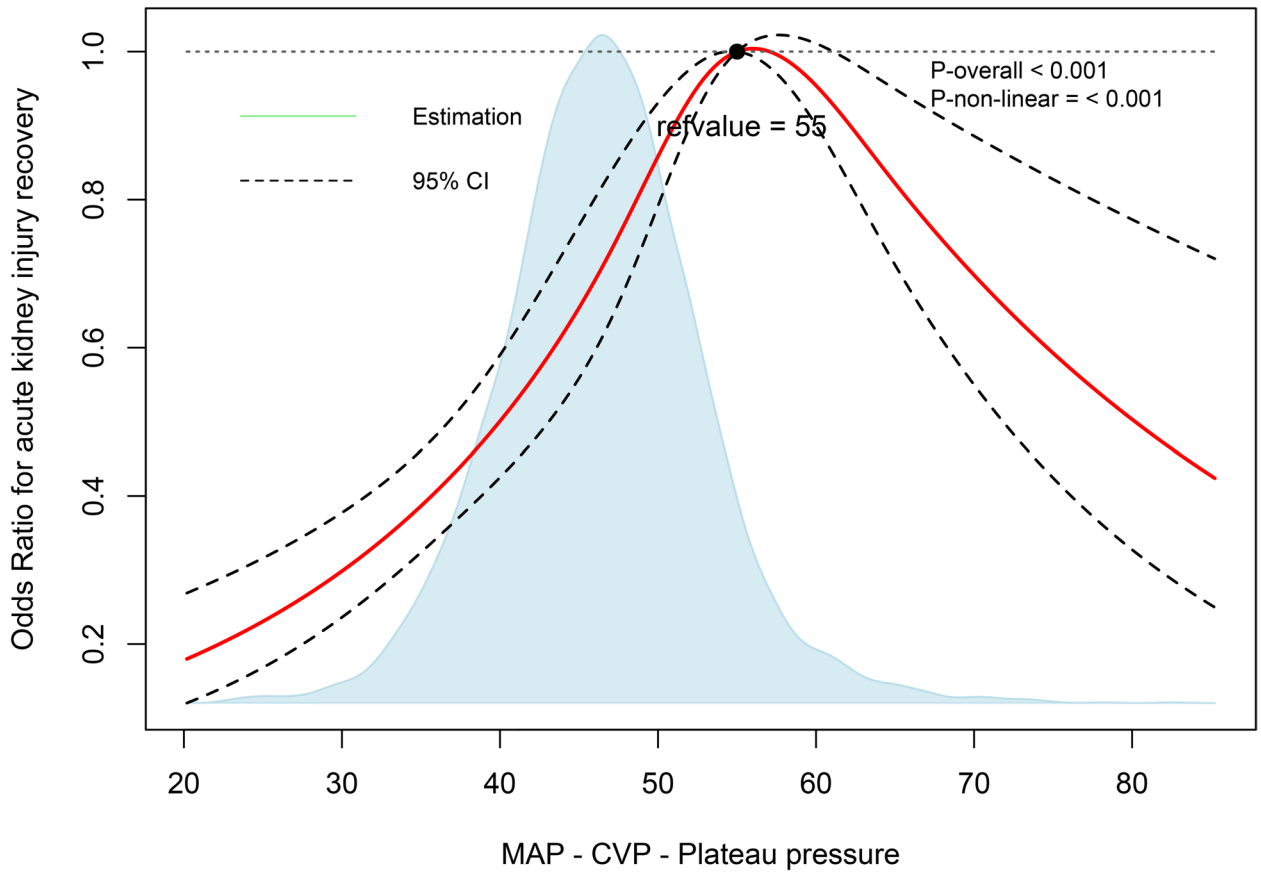

Fig. 2 MAP–CPV–PL and AKI recovery in RCS analysis. *MAP* mean arterial pressure, *CVP* central venous pressure, *PL* platform pressure, *RCS* restricted cubic spline analysis

Table 3 Associations between MAP–CPV–PL pressure and AKI recovery rate in linear spline function and quartile analysis

Linear spline analysis	Crude OR (95% CI)	*p*	Quartile analysis	Crude OR (95% CI)	*p*
MAP–CVP–PL (< 55)	1.05 (1.04–1.06)	< 0.01	Q1 (MAP–CVP–PL > 65)	0.61 (0.44–0.85)	< 0.01
MAP–CVP–PL (> 55)	0.97 (0.95–0.98)	< 0.01	Q2 (50 < MAP–CVP–PL < 65)	Ref	
			Q3 (40 < MAP–CVP–PL < 55)	0.80 (0.66–0.96)	0.01
			Q4 (MAP–CVP–PL < 45)	0.44 (0.37–0.53)	< 0.01
Linear spline analysis	**Adjusted OR (95% CI)**	***p***	**Quartile analysis**	**Adjusted OR (95% CI)**	***p***
MAP–CVP–PL (< 55)	1.02 (1.01–1.04)	< 0.01	Q1 (MAP–CVP–PL > 65)	0.55 (0.40–0.77)	< 0.01
MAP–CVP–PL (> 55)	0.96 (0.94–0.98)	< 0.01	Q2 (50 < MAP–CVP–PL < 65)	Ref	
			Q3 (40 < MAP–CVP–PL < 55)	0.90 (0.74–1.09)	0.29
			Q4 (MAP–CVP–PL < 45)	0.64 (0.52–0.78)	< 0.01
Age	0.98 (0.97–0.99)	< 0.01	Age	0.98 (0.97–0.99)	< 0.01
Initial hemoglobin	1.07 (1.03–1.10)	< 0.01	Initial hemoglobin	1.07 (1.03–1.10)	< 0.01
Diabetes	0.87 (0.76–1.00)	0.05	Diabetes	0.88 (0.76–1.00)	0.07
Coronary disease	1.11 (0.96–1.28)	0.13	Coronary disease	1.12 (0.97–1.29)	0.09
Vasopressor use	0.93 (0.79–1.10)	0.43	Vasopressor use	0.94 (0.80–1.10)	0.48
Hypertension	1.04 (0.91–1.18)	0.55	Hypertension	1.03 (0.90–1.18)	0.58
Initial SOFA	0.92 (0.89–0.94)	< 0.01	Initial SOFA	0.91 (0.89–0.93)	< 0.01
Duration of hypotension	0.99 (0.98–1.00)	0.20	Duration of hypotension	0.99 (0.98–1.00)	0.16

MAP mean artery pressure, *CVP* central venous pressure, *PL* plateau pressure, *OR* odds ratio, *CI* confidence interval, *SOFA* sequential organ failure assessment

was associated with a lower AKI recovery rate (OR 0.96, 95% CI 0.94–0.98, $p < 0.01$). The category analysis (Table 3) also showed that compared to level-2 (55 ~ 65), both low [level-3, OR 0.90, 95% CI 0.74–1.09, p < 0.01; level-4, OR 0.64, 95% CI 0.52–0.78, $p < 0.01$) and high (level-1, OR 0.55, 95% CI 0.40–0.77, $p < 0.01$)] MAP–CPV–PL were significantly associated with lower AKI recovery rate.

Discussion

This study has several key strengths: first, it integrate respiratory parameters into the assessment of AKI occurrence and recovery. We demonstrated that respiratory parameters significantly influence renal perfusion pressure and renal function, offering a more precise reference than traditional indices. In addition, we identified and validated a non-linear relationship between MAP–CPV–PL and AKI occurrence and recovery rate through RCS, linear spline function, and categorical logistic regression, emphasizing the need to maintain MAP–CPV–PL within an optimal range for AKI prevention and recovery. As one of the few studies to incorporate respiratory parameters into renal perfusion pressure calculations, our findings further advance valuable insights into the relationship between perfusion pressure, kidney injury, and recovery.

Respiratory parameter, CVP, MAP and AKI

The innovation of this study is the inclusion of respiratory parameters in assessing renal perfusion pressure. Associations between different respiratory parameters and renal function have been evaluated, and the incorporation of plateau pressure into the surrogate index of renal perfusion pressure is based on compelling evidence. First, a meta-analysis conducted by Johannes et al. [15] revealed a significant association between invasive mechanical ventilation and an increased incidence of AKI, with a threefold increase in the odds of developing AKI in those receiving mechanical ventilation. However, other factors such as tidal volume (Vt) and positive end-expiratory pressure (PEEP) were not associated with AKI risk. However, the ARMA trial in JAMA [16] demonstrated that patients with low VT and limited plateau pressure exhibited a greater number of renal failure-free days. Meanwhile, a recent review [17] summarizing the lung physiological bases of esophageal pressure monitoring showed that plateau pressure is the respiratory parameter with the longest duration and is closer in time to the lowest negative intrathoracic pressure, suggesting that it may be better correlated with CVP. Based on these findings, plateau pressure was used as the primary respiratory parameter in the current study.

Meanwhile, hemodynamic indices such as CVP and MAP have also been extensively studied in the context of AKI. For example, Matthieu et al. [18] and Marlies et al. [9] highlighted the critical role of CVP in the onset

and progression of AKI. Regardless of fluid balance or PEEP levels, CVP was identified as the parameter most closely linked to AKI development and progression. As a key component of mean perfusion pressure (MPP), CVP exerts an independent influence on the risk of AKI progression. In contrast, the role of blood pressure in AKI development remains uncertain. In prospective studies, Michael et al. [19] and Meri et al. [20] reported a significantly higher incidence of AKI in the intensive blood pressure control group (target SBP < 120 mmHg) compared to the standard blood pressure control group (target SBP < 140 mmHg). However, other studies [21–23] report otherwise that a reduction in MAP alone was not an independent risk factor for AKI progression. The reasons for these inconsistent findings are unclear. We suggest that lack of consideration of the non-linear association may be one important factor.

Perfusion pressure and AKI incidence

In the current study, MAP–CPV–PL was identified as the most robust predictor of AKI incidence, validated through ROC analysis and further supported by a non-linear association revealed in restricted cubic spline (RCS) analyses. A threshold of 55 mmHg was established, with both MAP–CPV–PL values below and above this threshold associated with an increased risk of AKI. Notably, low MAP–CPV–PL levels were particularly significant in contributing to this risk. These findings underscore the critical importance of maintaining optimal, rather than maximal, perfusion pressure to mitigate AKI risk.

Although several perfusion pressure indexes have been proposed in previous studies, the non-linear relationship between perfusion pressure and AKI risk had been rarely reported. Xie et al.'s observational cohort study [11], which utilized data from the MIMIC and eICU databases, demonstrated a non-linear association between optimal blood pressure targets and AKI. Using a Lasso regression model, they showed that elevated MAP and DBP (MAP > 177 mmHg and DBP > 132 mmHg) were associated with kidney injury, particularly in patients without chronic hypertension. In addition, insufficient MAP and DBP (MAP < 65 mmHg and DBP < 50 mmHg) led to renal hypoperfusion and increased AKI risk, providing robust evidence of the non-linear relationship between perfusion pressure and AKI incidence. Another study [24], involving 84 patients undergoing major abdominal surgery, used MAP—2 × IAP–CVP–Pmean as the renal perfusion pressure and demonstrated that this index had the best predictive value for AKI. Similarly, a study [6] of 23 patients undergoing cardiac surgery found that MAP–(CVP + Pmean + IAP) was linearly associated with postoperative AKI, with higher perfusion pressures correlating with lower AKI incidence. However, these perfusion indexes differ from ours, and the potential non-linear associations were not investigated due to the small sample sizes.

In this study, the non-linear association between MAP–CVP–PL and AKI was confirmed through RCS analysis, linear spline functions, and category analysis. Based on these findings, we recommend maintaining MAP–CVP–PL within the reference range of 55–65 mmHg. This emphasizes the critical importance of maintaining perfusion pressure within an optimal range to protect kidney function, aligning with prior studies [11] while offering detailed insights into the non-linear dynamics of perfusion pressure and AKI risk.

The mechanisms underlying AKI due to low perfusion pressure have been relatively well-studied, but those related to high perfusion pressure remain unclear. The relationship between high perfusion pressure and increased AKI risk may involve complex interactions among MAP, CVP, and PL. For instance, in clinical practice, fluid infusion or increased circulatory resistance can lead to simultaneous elevations in MAP and CVP. In cases with volume responsiveness, the rise in MAP may exceed that of CVP [25], resulting in higher perfusion pressure. However, factors such as excessive fluid resuscitation or increase in circulatory resistance may also contribute to the occurrence of AKI. Under such circumstances, elevated perfusion pressure could act as a risk factor for AKI. Of course, these hypothesis require further investigation to be clarified in future studies.

Perfusion pressure and AKI recovery

This study is among the first to explore the link between perfusion pressure and AKI recovery. Similar to its role in AKI incidence, both excessively high and low perfusion pressures hinder recovery. Low perfusion pressure exacerbates renal hypoperfusion, while high perfusion pressure, often due to elevated MAP or CVP, particularly in patients with impaired autoregulation. For instance, excessive fluid resuscitation to raise perfusion pressure can also cause renal congestion, further delaying recovery. These findings underscore the importance of maintaining optimal perfusion pressure to support renal recovery while avoiding adverse effects from over-resuscitation [26, 27].

Clinical implications

Our findings have significant clinical implications for the management of critically ill patients at risk for AKI. The non-linear associations between perfusion pressure and both AKI incidence and recovery suggest that targeting an MAP–CPV–PL range of 55–65 mmHg may be optimal for reducing AKI risk and enhancing recovery.

Additional research is necessary to validate these findings in larger, diverse populations and to explore the mechanisms behind the non-linear relationships observed. Future studies should assess dynamic perfusion pressure monitoring and individualized adjustments, as well as how factors, such as fluid status and vasopressor use impact AKI management.

Limitations

This study has several limitations. First, other parameters, such as intra-abdominal pressure (IAP) and Pmean—both potential factors influencing renal perfusion—were not included in the analysis due to the high rate of missing data in the current database. Addressing this limitation in future studies may enhance our understanding of the interplay between IAP, Pmean, and renal perfusion. Second, using the mean values of CVP, MAP, and Plateau Pressure during the first 24 h after ICU admission to calculate kidney perfusion pressure may minimize bias compared to using the first recorded value, it does not entirely eliminate the potential bias introduced by transient measurements (e.g., default ventilator settings). Third, this study used only serum creatinine, not the full KDIGO criteria (including urine output), potentially underestimating AKI incidence and introduced potential bias. Forth, the study population consisted exclusively of critically ill patients, which may limit the generalizability of the findings to other patient groups due to heterogeneity. Nevertheless, we evaluated and compared three perfusion pressure indices, identifying the most robust predictor. Further research should aim to refine perfusion pressure thresholds across diverse patient populations, improving the applicability of these findings in various clinical contexts.

Conclusion

This study highlights the crucial role of perfusion pressure, particularly MAP–CPV–PL, in both the occurrence and recovery of AKI in critically ill patients. The non-linear relationships observed between MAP–CPV–PL and AKI outcomes suggest that maintaining perfusion pressures within an optimal range is essential for minimizing AKI risk and promoting recovery. These findings provide a strong rationale for future research aimed at developing individualized hemodynamic strategies to improve kidney outcomes in critically ill patients.

Supplementary Information

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Supplementary material 1.

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Author contributions
Y.S., X.D. and G.C. drafted the manuscript and performed the statistical analysis; L.Z. and S.C. revised the manuscript; C.Z., Q.L., Q.L. and Q.J. designed and examined the re-search;Y.S. examined the integrity and accuracy of the data. All authors have read and ap-proved the final manuscript.

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Availability of data and materials
Full data set available from the corresponding author at snow.shen@hotmail.com. However, reanalysis of the full data needs to be approved by MIMIC Institute.

Declarations

Competing interests
The authors declare no competing interests.

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References

1. Gameiro J, Neves JB, Rodrigues N, Bekerman C, Melo MJ, Pereira M, Teixeira C, Mendes I, Jorge S, Rosa R, et al. Acute kidney injury, long-term renal function and mortality in patients undergoing major abdominal surgery: a cohort analysis. Clin Kidney J. 2016;9(2):192–200.
2. Li Y, Zheng T, Zhu J, Chen Y, Chen Y, Sun S. Variability of blood pressure and risk of postoperative acute kidney injury in patients undergoing surgery for acute aortic dissection: a 11-year single-center study. J Clin Hypertens. 2023;25(5):463–9.
3. Hu R, Kalam Y, Broad J, Ho T, Parker F, Lee M, Bellomo R. Decreased mean perfusion pressure as an independent predictor of acute kidney injury after cardiac surgery. Heart Vessel. 2020;35(8):1154–63.
4. Sato R, Luthe SK, Nasu M. Blood pressure and acute kidney injury. Crit Care. 2017;21(1):28.
5. Huh J, Kwon H, Park H, Park SC, Yun SS, Chae MS. Impact of norepinephrine and dopamine infusion on renal arterial resistive index during pre-emptive living donor kidney transplantation: propensity score matching analysis. Medicina. 2024;60(7):1066.
6. Dang PT, Lopez BE, Togashi K. A decrease in effective renal perfusion pressure is associated with increased acute kidney injury in patients undergoing cardiac surgery. Cureus. 2023;15(9):e45036.

7. Asfar P, Meziani F, Hamel JF, Grelon F, Megarbane B, Anguel N, Mira JP, Dequin PF, Gergaud S, Weiss N, et al. High versus low blood-pressure target in patients with septic shock. N Engl J Med. 2014;370(17):1583–93.
8. Panitchote A, Mehkri O, Hastings A, Hanane T, Demirjian S, Torbic H, Mireles-Cabodevila E, Krishnan S, Duggal A. Factors associated with acute kidney injury in acute respiratory distress syndrome. Ann Intensive Care. 2019;9(1):74.
9. Ostermann M, Hall A, Crichton S. Low mean perfusion pressure is a risk factor for progression of acute kidney injury in critically ill patients - a retrospective analysis. BMC Nephrol. 2017;18(1):151.
10. Kato R, Pinsky MR. Personalizing blood pressure management in septic shock. Ann Intensive Care. 2015;5(1):41.
11. Zhao L, Fan Y, Wang Z, Wei Z, Zhang Y, Li Y, Xie K. The blood pressure targets in sepsis patients with acute kidney injury: an observational cohort study of multiple ICUs. Front Immunol. 2022;13:1060612.
12. Johnson AEW, Bulgarelli L, Shen L, Gayles A, Shammout A, Horng S, Pollard TJ, Hao S, Moody B, Gow B, et al. MIMIC-IV, a freely accessible electronic health record dataset. Sci Data. 2023;10(1):1.
13. Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013;17(1):204.
14. Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, Angus DC, Rubenfeld GD, Singer M, Sepsis Definitions Task F. Developing a new definition and assessing new clinical criteria for septic shock: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):775–87.
15. van den Akker JP, Egal M, Groeneveld AB. 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(3):R98.
16. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301–8.
17. Ball L, Talmor D, Pelosi P. Transpulmonary pressure monitoring in critically ill patients: pros and cons. Crit Care. 2024;28(1):177.
18. Legrand M, Dupuis C, Simon C, Gayat E, Mateo J, Lukaszewicz AC, Payen D. Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study. Crit Care. 2013;17(6):R278.
19. Rocco MV, Sink KM, Lovato LC, Wolfgram DF, Wiegmann TB, Wall BM, Umanath K, Rahbari-Oskoui F, Porter AC, Pisoni R, et al. Effects of intensive blood pressure treatment on acute kidney injury events in the systolic blood pressure intervention trial (SPRINT). Am J Kidney Dis. 2018;71(3):352–61.
20. Poukkanen M, Wilkman E, Vaara ST, Pettilä V, Kaukonen KM, Korhonen AM, Uusaro A, Hovilehto S, Inkinen O, Laru-Sompa R, et al. Hemodynamic variables and progression of acute kidney injury in critically ill patients with severe sepsis: data from the prospective observational FINNAKI study. Crit Care. 2013;17(6):R295.
21. Gambardella I, Gaudino M, Ronco C, Lau C, Ivascu N, Girardi LN. Congestive kidney failure in cardiac surgery: the relationship between central venous pressure and acute kidney injury. Interact Cardiovasc Thorac Surg. 2016;23(5):800–5.
22. Nohria A, Hasselblad V, Stebbins A, Pauly DF, Fonarow GC, Shah M, Yancy CW, Califf RM, Stevenson LW, Hill JA. Cardiorenal interactions: insights from the ESCAPE trial. J Am Coll Cardiol. 2008;51(13):1268–74.
23. Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC, Young JB, Tang WHW. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. J Am Coll Cardiol. 2009;53(7):589–96.
24. Kopitko C, Medve L, Gondos T. Renoprotective postoperative monitoring: what is the best method for computing renal perfusion pressure? An observational, prospective, multicentre study. Nephron. 2018;139(3):228–36.
25. Okyere P, Okyere I, Ndanu TA, Osafo C, Amankwaa B. Factors associated with acute kidney injury recovery in a tertiary hospital in Ghana: a prospective study. Pan Afr Med J. 2019;33:236.
26. Dewitte A, Labat A, Duvignaud PA, Bouche G, Joannes-Boyau O, Ripoche J, Hilbert G, Gruson D, Rubin S, Ouattara A, et al. High mean arterial pressure target to improve sepsis-associated acute kidney injury in patients with prior hypertension: a feasibility study. Ann Intensive Care. 2021;11(1):139.
27. Raimundo M, Crichton S, Syed Y, Martin JR, Beale R, Treacher D, Ostermann M. Low systemic oxygen delivery and bp and risk of progression of early AKI. Clin J Am Soc Nephrol. 2015;10(8):1340–9.

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