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Association between Clinician-selected Mean Arterial Pressure Targets and Acute Kidney Injury in Patients with Septic Shock: A Prospective Cohort Study

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ABSTRACT: Background: Optimal mean arterial pressure (MAP) targets for preventing acute kidney injury (AKI) in patients with septic shock remain uncertain. This study compared the incidence of AKI between lower and higher MAP targets in patients with septic shock admitted to the intensive care unit (ICU) and explored factors associated with AKI.

Methods: This observational analytic comparative study used a prospective cohort design and was conducted in the ICU of Dr. Wahidin Sudirohusodo Hospital from May to July 2026. MAP targets were determined by the treating ICU team as part of routine clinical care, according to the hospital protocol. The investigators did not assign treatment targets. Patients were classified according to the prescribed MAP target (65–70 or 80–85 mmHg) at the 6-hour evaluation after initial resuscitation, provided that the target was achieved at that evaluation. Forty adult patients with septic shock were included and classified according to clinician-selected MAP targets of 65–70 mmHg (lower-target group, n=20) or 80–85 mmHg (higher-target group, n=20). The clinical and laboratory data, vasoactive-inotropic score (VIS), AKI incidence, and neutrophil gelatinase-associated lipocalin (NGAL) levels were assessed. Exploratory logistic regression analysis was performed to examine factors associated with AKI.

Results: AKI occurred in 4 patients (20.0%) in the low-MAP group and 7 patients (35.0%) in the high-MAP group; the difference was not statistically significant (Fisher's exact $P=0.480$). The risk difference was 15 percentage points (95% CI –12.3 to 42.3) and the risk ratio was 1.75 (95% CI 0.61–5.05), indicating an imprecise estimate. VIS was significantly higher in the high-MAP group throughout the observation period ($p<0.001$). NGAL levels were consistently higher among patients who developed AKI in both MAP groups. In exploratory logistic regression, Δ NGAL was associated with AKI (OR 1.08, 95% CI 1.03–1.14; $p=0.003$); the final model contained Δ NGAL alone.

Conclusions: In this small prospective cohort of patients with septic shock, no statistically significant difference in AKI occurrence was detected between the lower- and higher-MAP target groups. The estimate was imprecise, and the study was not designed to establish equivalence or causality. Higher MAP was accompanied by greater vasoactive-inotropic support. Changes in serum NGAL were associated with AKI in exploratory analyses and require validation in larger cohorts.

1. INTRODUCTION

Sepsis-associated acute kidney injury (S-AKI) is a common and life-threatening complication among critically ill patients. Acute kidney injury (AKI) develops in approximately two-thirds of patients with septic shock and is associated with substantially increased mortality, a higher risk of chronic kidney disease, and an increased need for renal replacement therapy [1]. Because the kidneys are particularly vulnerable to alterations in systemic and microcirculatory perfusion during sepsis, early recognition and prevention of AKI are important components of septic shock management.

Maintaining adequate organ perfusion is a primary objective of hemodynamic resuscitation in septic shock. Mean arterial pressure (MAP) is commonly used as a therapeutic target for vasopressor administration because it reflects the driving pressure for systemic organ perfusion. Current recommendations generally suggest an initial MAP target of at least 65 mmHg in adults with septic shock receiving vasopressors [2]. However, the optimal MAP target may vary according to individual patient characteristics and the underlying state of vascular autoregulation. Previous randomized trials have reported no consistent overall benefit of higher MAP targets compared with lower targets, although selected patients, particularly those with pre-existing hypertension, may have different renal perfusion requirements [3,4].

The relationship between MAP and AKI is clinically relevant because both inadequate perfusion pressure and excessive vasopressor exposure may adversely affect renal function. Lower arterial pressure may compromise renal perfusion, whereas achieving a higher MAP may require greater vasopressor doses, potentially increasing vasoconstriction and impairing microcirculatory blood flow [5]. Thus, determining an appropriate MAP target remains an important clinical issue in patients with septic shock who are at risk of AKI.

Early identification of renal injury is another challenge in septic shock. Serum creatinine, the conventional biomarker used to diagnose AKI, may increase only after substantial renal injury has occurred and can be influenced by factors unrelated to the acute renal insult. Neutrophil gelatinase-associated lipocalin (NGAL) is an emerging biomarker that may increase earlier following renal tubular injury and has demonstrated potential for predicting AKI in critically ill patients [6,7]. Studies have also demonstrated an association between NGAL concentrations and the development or persistence of AKI in critically ill and septic patients [8].

Despite the importance of hemodynamic optimization and early AKI detection, the relationship between different MAP targets and AKI, particularly when evaluated alongside serial NGAL measurements, remains incompletely defined. Therefore, this study aimed to compare the incidence of AKI between septic shock patients classified to a lower MAP target of 65–70 mmHg and those classified to a higher target of 80–85 mmHg. The study also evaluated serial NGAL concentrations and changes in NGAL as markers associated with AKI during ICU treatment.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This study used an observational analytic comparative design with a prospective cohort approach to examine the association between clinician-selected MAP targets and AKI incidence in adult patients with septic shock. The study was conducted in the ICU of Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia, from May to July 2026. MAP targets were determined by the treating ICU team as part of routine clinical care, according to the hospital protocol. The investigators did not assign treatment targets. Patients were classified according to the prescribed MAP target (65–70 or 80–85 mmHg) at the 6-hour evaluation after initial resuscitation, provided that the target was achieved at that evaluation.

2.2 Study Population and Sampling

The target population comprised adult patients with septic shock admitted to the ICU during the study period. The study sample consisted of patients with septic shock who fulfilled the eligibility criteria. Consecutive sampling was used, whereby eligible patients were recruited according to the order of ICU admission or septic shock diagnosis. The sample size was determined using the Lemeshow formula for estimating a single proportion in a finite population (population size $N=59$; expected proportion 31.68% hypertension prevalence; $Z=1.96$ for $\alpha=0.05$; precision 10%), yielding 40.28, rounded to a minimum of 40 participants. The calculation was not designed to detect a between-group difference; the study was exploratory and was not designed to establish equivalence between MAP groups. The final analytic cohort comprised 20 patients in each group.

2.3 Eligibility Criteria

All adult patients with septic shock admitted to the ICU during the study period were consecutively screened for eligibility and enrolled using consecutive sampling according to the order of ICU admission or septic shock diagnosis. Patients were eligible if they were aged ≥ 18 years, diagnosed with septic shock, had complete clinical data for mean arterial pressure (MAP) and clinical outcomes, were expected to remain in the ICU for at least 24 hours, and provided informed consent either personally or through an authorized family member or representative. Following initial resuscitation, patients were evaluated at 6 hours and classified according to the MAP target prescribed by the treating ICU team, provided that the prescribed target had been achieved at that evaluation. Patients with pre-existing moderate-to-severe chronic kidney disease (CKD stage ≥ 3), previous renal transplantation, end-stage renal disease requiring routine dialysis before ICU admission, or incomplete medical records were excluded. Patients were also excluded from the final analytic cohort if they failed to achieve the prescribed MAP target despite fluid resuscitation and vasopressor therapy, died within the first 24 hours, or experienced a change in MAP target during the first 24 hours. Time zero was defined as the completion of initial resuscitation and served as the reference point for MAP and vasopressor-inotropic score (VIS) measurements. The participant flow and reasons for exclusion are presented in Figure 1. These post-baseline exclusions may have introduced selection and survivor bias and may limit the generalizability of the findings to all patients presenting with septic shock. No sensitivity analysis including the excluded patients was performed.

Sepsis was defined according to Sepsis-3 (an increase in SOFA score of ≥ 2 from baseline due to infection). Septic shock was defined as sepsis requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate > 2 mmol/L despite adequate fluid resuscitation. Both criteria were verified from the clinical records. Lactate was used to establish eligibility but was not included as an analytic variable, initial resuscitation followed the ICU standard operating procedure. Baseline SOFA was assessed within the first 24 hours of ICU care. Chronic hypertension, diabetes mellitus, cardiovascular disease, and CKD were identified from documented diagnoses in the medical records; CKD stage ≥ 3 was defined as in the exclusion criteria. Infection source, lactate, fluid balance, and nephrotoxin exposure were not recorded for analysis.

2.4 Hemodynamic Management and MAP Targets

Patients underwent standard fluid resuscitation and vasopressor therapy according to the ICU protocol. MAP targets were determined by the treating ICU team based on routine clinical care and the institutional protocol; the investigators did not assign or randomize MAP targets. At the 6-hour evaluation, patients were classified according to the prescribed MAP target into a lower-MAP group (65–70 mmHg) or a higher-MAP group (80–85 mmHg), provided that the prescribed target had been achieved at that evaluation. Patients who failed to achieve the prescribed target despite fluid resuscitation and vasopressor therapy, or whose MAP target changed during the first 24 hours, were excluded from the final analysis. Prescribed MAP targets and subsequently achieved MAP values were recorded and reported separately. After classification, patients remained in their assigned group regardless of subsequent deviations from the target range, and no corrective rule was applied. The proportion of observations within each target range was not analyzed.

MAP was measured by arterial-line monitoring (invasive) or cuff-based monitoring (non-invasive) and recorded hourly by ICU nurses on a MAP monitoring form, with NIBP monitoring in 40 patients. MAP values at 6, 12, 18, and 24 hours were calculated as the means of hourly recordings within each corresponding 6-hour interval. Mean MAP during ICU treatment was calculated from the hourly recordings over the 24-hour observation period. No adjustment for changes in monitoring modality was documented.

2.5 Assessment of Vasoactive-Inotropic Support

The vasoactive-inotropic score (VIS) was used to quantify the intensity of vasoactive and inotropic support required to maintain the target MAP. VIS was calculated as dopamine + dobutamine + $100 \times$ epinephrine + $100 \times$ norepinephrine + $10,000 \times$ vasopressin + $10 \times$ milrinone [15], with catecholamine and milrinone doses in $\mu\text{g}/\text{kg}/\text{min}$ and vasopressin in $\text{U}/\text{kg}/\text{min}$. Doses were taken from hourly titration records in the ICU observation form, using the dose recorded at each measurement hour. The mean VIS was the average of the four 6-hour scores.

2.6 Assessment of AKI

Baseline serum creatinine was defined as the value obtained within the first 24 hours of ICU care (Table 1). AKI occurrence was assessed during the first 48 hours of ICU care using a KDIGO-based operational definition: a serum creatinine increase of ≥ 0.3 mg/dL within 48 hours and/or urine output < 0.5 mL/kg/hour for at least 6 hours. The criterion of serum creatinine ≥ 1.5 times baseline within 7 days was not included, and AKI stage was not assessed. Because AKI status at the time of MAP classification and the precise timing of AKI onset were not separately documented, patients were categorized as having AKI occurrence or no AKI occurrence, and the outcome was reported as “AKI occurrence” rather than “incident AKI.” Accordingly, no causal interpretation was made regarding the relationship between MAP target and AKI occurrence.

2.7 NGAL Measurement

Neutrophil gelatinase-associated lipocalin (NGAL) was evaluated as an early biomarker of renal injury. Serum NGAL was measured at 6 and 12 hours after completion of initial resuscitation using a commercially available human NGAL ELISA kit (Elabscience, E-EL-H6127). Blood samples were collected at the specified time points, allowed to clot for 1 hour at room temperature, and then centrifuged at $1,000 \times g$ for 20 minutes at $2-8^{\circ}\text{C}$. The resulting serum supernatant was collected for analysis, and samples were analyzed according to the manufacturer's instructions. NGAL concentrations were expressed in pg/mL. ΔNGAL was calculated as the 12-hour NGAL concentration minus the 6-hour NGAL concentration. Because the temporal relationship between NGAL sampling and AKI onset could not be established, both NGAL and ΔNGAL were interpreted as biomarkers associated with AKI rather than as predictors of incident AKI.

2.8 Data Collection

Clinical and laboratory data were obtained from medical records and ICU monitoring forms. Collected variables included demographic characteristics, comorbidities, MAP, vasoactive and inotropic medication requirements, VIS, Sequential Organ Failure Assessment (SOFA) score, serum electrolytes, random blood glucose, serum creatinine, NGAL concentrations, AKI occurrence, length of ICU stay, and mortality. ICU length of stay was measured in days from ICU admission to ICU discharge or death, and mortality referred to in-ICU mortality.

2.9 Statistical Analysis

Continuous variables were assessed for distribution using the Kolmogorov–Smirnov test. Normally distributed variables were expressed as mean $\pm$ standard deviation, whereas non-normally distributed variables were summarized using median and interquartile range. Categorical variables were presented as frequencies and percentages. Continuous variables were compared using the independent-samples t-test when normally distributed and the Mann–Whitney U test otherwise. Categorical variables were compared using Pearson's chi-square test when all expected cell counts were ≥ 5 and Fisher's exact test otherwise; for the primary AKI comparison, Fisher's exact test was reported ($P=0.480$; Pearson chi-square $P=0.288$). Patients with incomplete medical records were excluded, so analyses were complete case. No adjustment for multiple comparisons was applied. The number of observations is shown in each table. Serial MAP and VIS trajectories were summarized descriptively; separate time-point comparisons were exploratory.

Exploratory logistic regression analysis was performed to examine factors associated with AKI and was intended to be hypothesis-generating rather than to develop a prediction model or establish independent causal associations. Variables with univariable $P < 0.25$ (MAP target, BMI, hypertension, type 2 diabetes mellitus, random blood glucose, 6-hour NGAL, and ΔNGAL) were entered into a backward stepwise multivariable logistic regression model. Given only 11 AKI events, the selection procedure was potentially unstable, and the sample size prevented comprehensive adjustment for confounders. The final selected model contained ΔNGAL alone; therefore, its odds ratio (OR) should not be interpreted as an adjusted estimate controlling for other patient characteristics. Linearity of the logit for continuous predictors and the correlation between baseline NGAL and ΔNGAL were not formally assessed.

The results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs); for continuous variables, ORs were expressed per 1-unit increase (kg/m² for BMI, mg/dL for random blood glucose, and ng/mL for 6-hour NGAL and ΔNGAL). A two-sided P value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 30 (IBM Corp., Armonk, NY, USA). The study is reported according to the STROBE guidelines for cohort studies [16].

The primary outcome was the occurrence of AKI (KDIGO-based) during the first 48 hours of ICU care, compared between MAP target groups. Analyses of serial NGAL, other AKI-associated factors, ICU length of stay, mortality, and within-group comparisons were secondary and exploratory, and no multiplicity adjustment was applied; exploratory findings were interpreted as hypothesis-generating.

3. RESULTS AND DISCUSSION

3.1 Study Population and Baseline Characteristics

During the study period, 59 adult patients with septic shock were screened, of whom 50 met the initial inclusion criteria. Three patients were excluded because of pre-existing CKD stage ≥3 (n=1) or end-stage renal disease requiring routine dialysis (n=2). Of the remaining 47 patients, five were excluded after initial resuscitation because they failed to achieve the target MAP (n=4) or died within the first 24 hours (n=1). Forty-two patients achieved the predefined MAP targets, comprising 22 patients in the low-MAP group and 20 in the high-MAP group. At the 24-hour reassessment, two patients in the low-MAP group were excluded because of a change in MAP status. The final analysis therefore included 40 patients, with 20 patients in each group. Participant flow is shown in Figure 1.

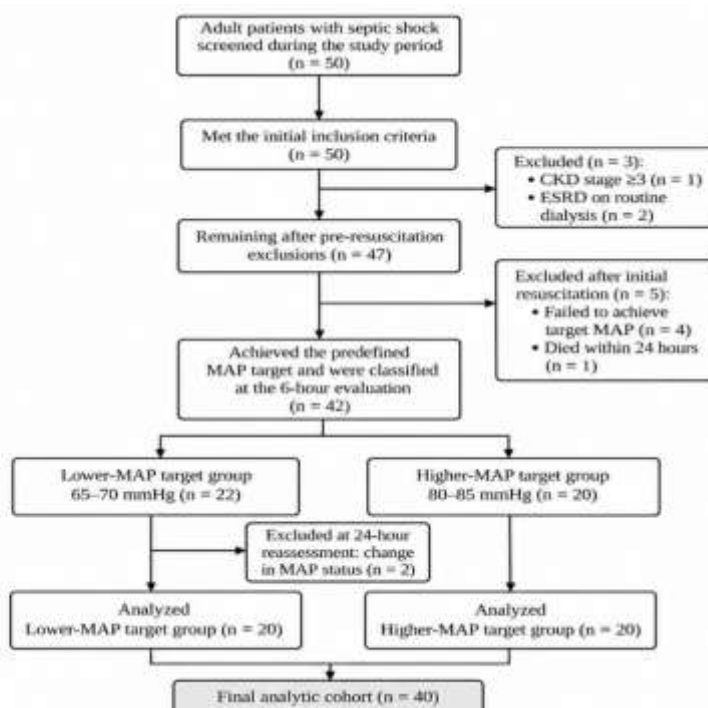


Figure 1. Flow diagram of patient screening, exclusion, and classification into the lower- and higher-MAP target groups.

Table 1 presents baseline characteristics of subjects. The mean age was significantly higher in the high-MAP group than in the low-MAP group (69.9 ± 13.2 vs 61.6 ± 12.4 years; $P=0.048$). The proportion of patients aged ≥60 years did not differ significantly between groups (60.0% vs 55.0%; $P=0.750$). Men comprised 80.0% of the high-MAP group and 55.0% of the low-MAP group ($P=0.091$). The prevalence of hypertension was significantly higher in the high-MAP group than in the low-MAP group (70.0% vs 30.0%; $P=0.014$). Baseline imbalances in age and hypertension (standardized mean differences 0.65 and 0.87, respectively) suggest possible confounding by indication, and the observed AKI difference cannot be attributed to MAP alone. There were

no significant between-group differences in body mass index, type 2 diabetes mellitus, cardiovascular disease, serum electrolytes, random blood glucose, serum creatinine, or SOFA score.

Table 1. Patient clinical characteristics

Characteristics	MAP Target		P value
	Low (n=20)	High (n=20)	
Age (years)	61.6 ± 12.4	69.9 ± 13.2	0.048*
<60	9 (45.0)	8 (40.0)	0.750
≥60	11 (55.0)	12 (60.0)	
Sex			0.091
Male	11 (55.0)	16 (80.0)	
Female	9 (45.0)	4 (20.0)	
BMI (kg/m ²)	24.8 ± 2.1	25.1 ± 3.3	0.710
<25	12 (60.0)	9 (45.0)	0.342
≥25	8 (40.0)	11 (55.0)	
Incidence of AKI during the first 48 hours (KDIGO)	4 (20.0%)	7 (35.0%)	0.480
AKI	4 (20.0%)	7 (35.0%)	
Non-AKI	16 (80.0%)	13 (65.0%)	
Hypertension	6 (30.0)	14 (70.0)	0.014*
DM type 2	7 (35.0)	8 (40.0)	0.744
Cardiovascular Disease	4 (20.0)	4 (20.0)	1.000
Electrolyte (mmol/L)			
Sodium	134.6 ± 4.1	135.6 ± 2.9	0.354
Potassium	4.3 ± 0.2	4.4 ± 0.3	0.139
Chloride	109.0 ± 3.0	110.6 ± 2.9	0.081
Random Blood Glucose (mg/dL)	146.7 ± 26.7	160.3 ± 21.2	0.079
Serum Creatinine (mg/dL)	0.9 ± 0.1	0.9 ± 0.1	0.844
SOFA score	12.7 ± 1.5	13.0 ± 1.4	0.732
MAP (mmHg)			
At 6 hours	69.2 ± 3.6	76.5 ± 4.5	<0.001*
At 12 hours	71.1 ± 3.7	84.9 ± 4.7	<0.001*
At 18 hours	72.7 ± 2.5	84.4 ± 4.8	<0.001*
At 24 hours	71.5 ± 2.9	86.9 ± 4.3	<0.001*
Mean (during ICU treatment)	71.4 ± 1.8	83.7 ± 2.6	<0.001*
VIS score			
At 6 hours	28.5 ± 6.3	36.8 ± 6.3	<0.001*
At 12 hours	28.8 ± 5.1	37.8 ± 5.7	<0.001*
At 18 hours	29.5 ± 5.4	39.3 ± 4.7	<0.001*
At 24 hours	33.0 ± 5.2	41.5 ± 6.1	<0.001*
Mean (during ICU treatment)	29.9 ± 4.2	38.8 ± 4.2	<0.001*

Values are presented as mean±standard deviation or frequency (percentage); MAP and VIS time-point comparisons are exploratory; Pearson chi-square P=0.288 for AKI.

Abbreviations: MAP: mean arterial pressure; BMI: body mass index; DM: diabetes mellitus; SOFA: Sequential Organ Failure Assessment. VIS: Vasoactive-Inotropic Score

*P value was significant at <0.05

3.2 MAP and Vasoactive-Inotropic Score

The achieved MAP differed significantly between groups throughout the observation period. Mean MAP values at 6, 12, 18, and 24 hours were 69.2 ± 3.6 , 71.1 ± 3.7 , 72.7 ± 2.5 , and 71.5 ± 2.9 mmHg, respectively, in the low-MAP group and 76.5 ± 4.5 , 84.9 ± 4.7 , 84.4 ± 4.8 , and 86.9 ± 4.3 mmHg, respectively, in the high-MAP group ($P < 0.001$ for all comparisons). The mean MAP during ICU treatment was 71.4 ± 1.8 mmHg in the low-MAP group and 83.7 ± 2.6 mmHg in the high-MAP group ($P < 0.001$). Mean MAP at 6 hours in the higher-MAP group (76.5 ± 4.5 mmHg) was below the prescribed range of 80–85 mmHg, whereas mean MAP in the lower-MAP group exceeded 70 mmHg at 12, 18, and 24 hours (71.1 , 72.7 , and 71.5 mmHg). Prescribed targets were therefore not strictly maintained after classification.

VIS was consistently higher in the high-MAP group. At 6, 12, 18, and 24 hours, mean VIS values were 28.5 ± 6.3 , 28.8 ± 5.1 , 29.5 ± 5.4 , and 33.0 ± 5.2 in the low-MAP group compared with 36.8 ± 6.3 , 37.8 ± 5.7 , 39.3 ± 4.7 , and 41.5 ± 6.1 in the high-MAP group, respectively ($P < 0.001$ for all comparisons). The mean VIS during the observation period was 29.9 ± 4.2 versus 38.8 ± 4.2 , respectively ($P < 0.001$). The trends of MAP and VIS scores of both groups were presented in Figure 2 and Figure 3.

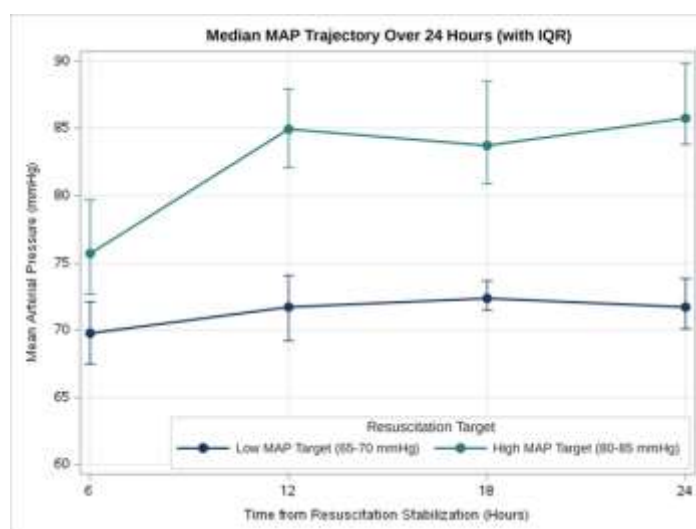


Figure 2. Trend of mean arterial pressure (MAP) at 6-hour intervals from completion of initial resuscitation, by MAP target group (65–70 mmHg vs 80–85 mmHg). Data are presented as median and interquartile range (IQR); Table 1 presents mean $\pm$ SD.

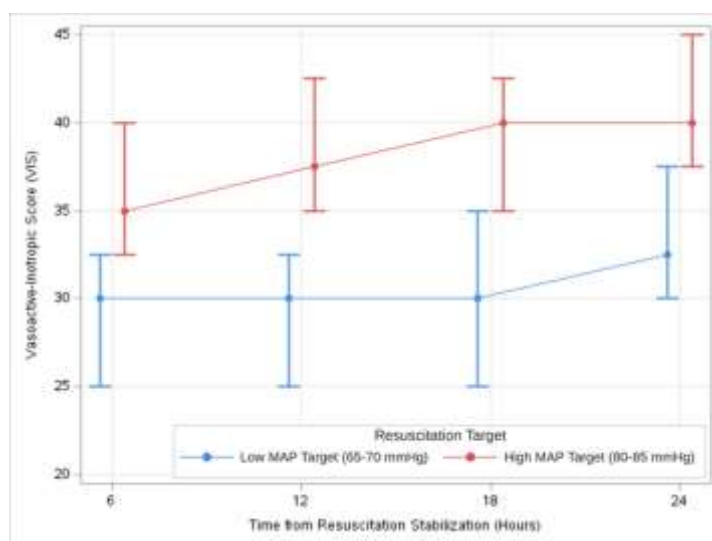


Figure 3. Vasoactive-inotropic score (VIS) at 6-hour intervals from completion of initial resuscitation, by MAP target group. Data are presented as median with error bars representing the interquartile range.

3.3 Incidence of AKI

AKI occurred in 4 of 20 patients (20.0%) in the low-MAP group and 7 of 20 patients (35.0%) in the high-MAP group. The absolute risk difference was 15 percentage points (95% CI -12.3 to 42.3) and the risk ratio was 1.75 (95% CI 0.61–5.05); Fisher's exact $P=0.480$. The estimated association was imprecise, and the confidence interval did not exclude clinically important differences. The study was not designed to establish equivalence. Within the low-MAP group, patients who developed AKI had a higher mean body mass index than those without AKI (26.8 ± 1.6 vs 24.3 ± 2.0 kg/m²; $P=0.029$), a numerically higher prevalence of hypertension (75.0% vs 18.8%; $P=0.061$), and higher random blood glucose levels (175.0 ± 16.9 vs 139.6 ± 23.4 mg/dL; $P=0.011$). Within the high-MAP group, type 2 diabetes mellitus was more frequent among patients with AKI than among those without AKI (85.7% vs 15.4%; $P=0.004$). Within-group analyses were exploratory because only four and seven AKI events occurred in the lower- and higher-MAP groups, respectively. Differences in statistical significance between groups do not demonstrate an interaction (Table 2).

Table 2. Baseline characteristics, outcomes, and serum NGAL according to AKI status within MAP target groups.

Characteristics	Low MAP Target (n=20)			High MAP Target (n=20)		
	AKI (n=4)	Non-AKI (n=16)	P value	AKI (n=7)	Non-AKI (n=13)	P value
Age (years)	58.5 ± 10.1	62.3 ± 13.1	0.597	74.3 ± 8.8	67.5 ± 14.9	0.280
Sex						
Male	1 (25.0)	10 (62.5)	0.284	5 (71.4)	11 (84.6)	0.586
Female	3 (75.0)	6 (37.5)		2 (28.6)	2 (15.4)	
BMI (kg/m ²)	26.8 ± 1.6	24.3 ± 2.0	0.029*	26.2 ± 2.2	24.5 ± 3.7	0.296
Hypertension	3 (75.0)	3 (18.8)	0.061	7 (100.0)	8 (61.5)	0.113
DM type 2	1 (25.0)	6 (37.5)	1.000	6 (85.7)	2 (15.4)	0.004*
Cardiovascular Disease	1 (25.0)	3 (18.8)	1.000	1 (14.3)	3 (23.1)	1.000
Electrolyte (mmol/L)						
Sodium	135.6 ± 4.4	134.3 ± 4.1	0.584	136.1 ± 3.2	135.4 ± 2.9	0.650
Potassium	4.3 ± 0.2	4.3 ± 0.2	0.585	4.4 ± 0.3	4.4 ± 0.3	0.749
Chloride	109.8 ± 3.1	108.8 ± 3.0	0.553	110.4 ± 3.1	110.8 ± 3.0	0.794
Random Blood Glucose (mg/dL)	175.0 ± 16.9	139.6 ± 23.4	0.011*	172.6 ± 17.2	153.6 ± 20.6	0.053
SOFA score	13.0 ± 2.3	12.6 ± 1.4	0.622	12.4 ± 0.4	13.3 ± 0.4	0.192
LOS (days)	10.8 ± 2.2	5.9 ± 1.7	<0.001*	9.6 ± 2.9	6.2 ± 2.4	0.016*
Mortality	1 (25.0)	4 (25.0)	1.000	3 (42.9)	5 (38.5)	1.000
Serum NGAL level (ng/mL)						
6 hours	129.5 ± 30.1	76.3 ± 19.8	0.007*	110.4 ± 29.6	76.2 ± 13.9	0.002*
12 hours	270.0 ± 71.7	117.1 ± 31.6	0.002*	234.4 ± 36.6	151.4 ± 29.7	<0.001*
ΔNGAL	140.5 ± 44.3	40.9 ± 18.1	0.002*	124.0 ± 24.2	75.2 ± 31.7	<0.001*

Values are presented as mean±standard deviation or frequency (percentage)

Abbreviations: MAP: mean arterial pressure; BMI: body mass index; DM: diabetes mellitus; SOFA: Sequential Organ Failure Assessment; LOS: Length of Stay; VIS: Vasoactive-Inotropic Score; NGAL: neutrophil gelatinase-associated lipocalin

*P value was significant at <0.05

3.4 NGAL Concentrations

NGAL concentrations were consistently higher among patients who developed AKI in both MAP groups. In the low-MAP group, NGAL concentrations at 6 and 12 hours were 129.5±30.1 and 270.0±71.7 ng/mL, respectively, in patients with AKI compared with 76.3±19.8 and 117.1±31.6 in patients without AKI (P=0.007 and P=0.002, respectively). The corresponding ΔNGAL values were 140.5±44.3 and 40.9±18.1, respectively (P=0.002).

In the high-MAP group, NGAL concentrations at 6 and 12 hours were 110.4±29.6 and 234.4±36.6 in patients with AKI compared with 76.2±13.9 and 151.4±29.7 in patients without AKI (P=0.002 and P<0.001, respectively). ΔNGAL was also significantly higher in patients with AKI (124.0±24.2 vs 75.2±31.7; P<0.001).

3.5 Length of ICU Stay and Mortality

Patients with AKI had significantly longer ICU stays than patients without AKI in both MAP groups. In the low-MAP group, ICU stay was 10.8±2.2 days in patients with AKI compared with 5.9±1.7 days in patients without AKI (P<0.001). In the high-MAP group, corresponding values were 9.6±2.9 and 6.2±2.4 days, respectively (P=0.016). Length-of-stay comparisons were interpreted cautiously because death may truncate ICU stay.

Mortality did not differ significantly according to AKI status in either the low-MAP group (25.0% vs 25.0%; P=1.000) or the high-MAP group (42.9% vs 38.5%; P=1.000). Mortality analyses were exploratory, and the limited number of deaths precluded reliable inference about independent associations.

3.6 Factors Associated with AKI

In univariable logistic regression, higher body mass index (OR 1.25, 95% CI 1.00–1.56; P=0.046), hypertension (OR 16.36, 95% CI 1.85–144.81; P=0.012), type 2 diabetes mellitus (OR 4.59, 95% CI 1.06–19.94; P=0.042), random blood glucose (OR 1.07, 95% CI 1.02–1.12; P=0.008), 6-hour NGAL (OR 1.10, 95% CI 1.03–1.17; P=0.004), and ΔNGAL (OR 1.08, 95% CI 1.03–1.14; P=0.003) were associated with AKI. The very wide confidence interval for hypertension indicates substantial imprecision. The high-MAP target was not significantly associated with AKI (OR 2.15, 95% CI 0.52–8.96; P=0.293). In the final selected model, which contained ΔNGAL alone, ΔNGAL was associated with AKI (OR 1.08, 95% CI 1.03–1.14; P=0.003) (Table 3). Because this model contained no other covariates, this estimate should not be interpreted as adjusted for other patient characteristics.

Table 3. Factors associated with acute kidney injury in the Intensive Care Unit

Variables	Univariable Analysis		Final model (ΔNGAL only)	
	OR (95% CI)	P value	OR (95% CI)	P value
High MAP target	2.15 (0.52–8.96)	0.293	-	-
BMI (per 1 kg/m ² increase)	1.25 (1.00–1.56)	0.046*	-	-
Hypertension	16.36 (1.85–144.81)	0.012*	-	-
DM type 2	4.59 (1.06–19.94)	0.042*	-	-
Random Blood Glucose (per 1 mg/dL increase)	1.07 (1.02–1.12)	0.008*	-	-
Serum NGAL level at 6 hours (per 1 ng/mL increase)	1.10 (1.03–1.17)	0.004*	-	-
ΔNGAL (per 1 ng/mL increase)	1.08 (1.03–1.14)	0.003*	1.08 (1.03–1.14)	0.003*

OR: odds ratio; CI: confidence interval; MAP: mean arterial pressure; BMI: body mass index; DM: diabetes mellitus; NGAL: neutrophil gelatinase-associated lipocalin; Δ NGAL: change in serum NGAL between 6 and 12 hours. "–": variable not included in the final model.

* P value was significant at <0.05

3.7 Discussion

The principal findings of this study were that the incidence of AKI did not differ significantly between patients classified to a low MAP target of 65–70 mmHg and those classified to a high MAP target of 80–85 mmHg. Although AKI occurred numerically more frequently in the high-MAP group, the difference was not statistically significant. In contrast, the high-MAP strategy was associated with consistently greater vasoactive-inotropic requirements, as reflected by significantly higher VIS values. Furthermore, NGAL concentrations were consistently higher among patients who developed AKI, and Δ NGAL was associated with AKI in exploratory regression analysis (final model containing Δ NGAL alone).

The study population was predominantly composed of older adults, with mean ages of 61.6 and 69.9 years in the low- and high-MAP groups, respectively. The high-MAP group was significantly older. However, the proportion of patients aged ≥ 60 years did not differ significantly between groups. The predominance of older patients is consistent with the increased susceptibility of aging populations to sepsis and septic shock, which may be related to immunosenescence, comorbidity burden, and reduced physiological reserve [9]. In addition, the high-MAP group had a greater prevalence of chronic hypertension (standardized mean differences 0.65 for age and 0.87 for hypertension). Although men were more frequently represented in both groups, the difference in sex distribution was not statistically significant. This finding is consistent with previous observations from the SEPSISPAM study, which did not demonstrate a significant difference in sex distribution between MAP target groups [3]. Sex-related differences in sepsis outcomes have been described, but their clinical significance may vary according to age, comorbidity, disease severity, and treatment characteristics [10].

MAP Target and AKI

The incidence of AKI was 20.0% in the low-MAP group and 35.0% in the high-MAP group, with no statistically significant difference (Table 1). Thus, this study did not demonstrate a significant association between the prescribed MAP target and AKI incidence. The numerical difference should be interpreted cautiously because the sample size was small and the confidence interval around the estimated effect of the high-MAP target was wide. The absence of statistical significance should therefore not be interpreted as evidence of equivalence between the two MAP strategies. Because the higher-MAP group was older and had more chronic hypertension, possible confounding by indication cannot be excluded, and the observed AKI difference cannot be attributed to MAP alone. The relationship between arterial pressure and renal injury in septic shock is complex. Renal perfusion is influenced not only by systemic MAP but also by venous pressure, intra-abdominal pressure, cardiac output, vascular tone, microcirculatory function, and pre-existing renal autoregulatory changes. Consequently, increasing MAP does not necessarily translate into improved renal perfusion in every patient. The numerically higher prevalence of hypertension among patients with AKI in the low-MAP group ($P=0.061$) warrants cautious interpretation. Previous literature has suggested that patients with chronic hypertension may have an altered renal autoregulatory threshold and may therefore require individualized perfusion pressures [11]. Within-group analyses were exploratory because only four and seven AKI events occurred in the lower- and higher-MAP groups, respectively. Differences in statistical significance between groups do not demonstrate an interaction. This study was not designed or adequately powered to establish whether chronic hypertension modifies the association between MAP and AKI.

NGAL and AKI

A consistent finding in this study was the higher NGAL concentration among patients who developed AKI. In both MAP groups, patients with AKI had significantly higher NGAL concentrations at both measured time points. Δ NGAL was also significantly greater in patients with AKI. These findings are consistent with previous studies demonstrating that NGAL may increase earlier than conventional markers of renal dysfunction and may provide additional information for the early identification of AKI in critically ill patients [6,7]. In septic patients specifically, NGAL has been investigated as a potential predictor of AKI and may provide clinically relevant information during the early phase of ICU treatment [8]. Serial serum NGAL concentrations and their changes were evaluated as markers associated with AKI. Their ability to predict incident AKI requires confirmation in a cohort with clearly established biomarker-to-outcome timing. Δ NGAL was associated with AKI in

exploratory regression analysis (OR 1.08, 95% CI 1.03–1.14; $P=0.003$). Because the final selected model contained Δ NGAL alone, this estimate should not be interpreted as adjusted for other patient characteristics. This finding suggests that the dynamic change in NGAL might contain additional information beyond a single NGAL measurement, which requires confirmation. Serial biomarker assessment has previously been proposed as a means of improving AKI prediction compared with reliance on a single measurement [12]. Nevertheless, NGAL is not entirely specific to renal injury and may be influenced by systemic inflammation and other clinical conditions. Therefore, NGAL should be interpreted in conjunction with clinical findings, urine output, serum creatinine, and hemodynamic status rather than being used as an isolated diagnostic marker.

Other Factors Associated with AKI

Higher body mass index, hypertension, type 2 diabetes mellitus, random blood glucose, and NGAL were associated with AKI in univariable analyses. These findings highlight the multifactorial nature of renal injury in septic shock. The association between diabetes and AKI is biologically plausible because diabetes may be accompanied by endothelial dysfunction, altered microcirculation, and increased renal susceptibility to hemodynamic stress [13]. In the present study, type 2 diabetes was particularly frequent among patients who developed AKI in the high-MAP group. However, this subgroup consisted of a small number of patients, and the finding should therefore be interpreted cautiously. Random blood glucose was also associated with AKI. This observation is consistent with recent evidence demonstrating an association between diabetes, glucose control, and early sepsis-associated AKI [14]. However, because glucose concentrations in critically ill patients may be affected by stress responses, nutritional status, diabetes treatment, and severity of illness, the relationship should not be interpreted as causal.

Length of ICU Stay and Mortality

Patients who developed AKI had significantly longer ICU stays than those without AKI in both MAP groups. This finding is clinically important because AKI may contribute to prolonged critical illness through persistent organ dysfunction, increased monitoring requirements, and the need for additional supportive therapies. Length-of-stay comparisons were interpreted cautiously because death may truncate ICU stay. Mortality did not differ significantly according to AKI status within either MAP group. This lack of association may reflect the small number of AKI events and deaths in the present study. Consequently, the study was not sufficiently powered to determine whether AKI or MAP target independently affected mortality.

Clinical Implications

The findings suggest that a higher MAP target of 80–85 mmHg was not associated with a statistically significant difference in AKI occurrence compared with a target of 65–70 mmHg in this study population. At the same time, higher MAP was accompanied by greater vasoactive-inotropic support in this cohort. The findings are compatible with individualized hemodynamic management but cannot establish the superiority or harm of either MAP approach. Serial NGAL assessment might provide additional information regarding patients at increased risk of AKI, but this was not established in the present study. The association between Δ NGAL and AKI observed in this exploratory analysis supports further investigation of dynamic NGAL monitoring in septic shock; these findings remain hypothesis-generating.

Limitations

Several limitations should be considered. First, the observational analytic design does not allow causal inference, and MAP targets were selected by treating clinicians according to the clinical protocol rather than assigned through randomization. Consequently, confounding by indication cannot be excluded; notably, patients in the higher-MAP group were older and had a substantially higher prevalence of chronic hypertension. Although potential AKI-associated variables were explored using logistic regression, the small number of AKI events ($n=11$) precluded comprehensive multivariable adjustment and limited the stability of exploratory regression estimates. Residual confounding therefore remains possible, and differences in AKI occurrence should not be attributed to the MAP target alone. No multiplicity adjustment was applied.

Second, the sample size was relatively small, with only 40 patients included in the final analysis, limiting statistical power and generalizability. Post-baseline exclusions may have introduced selection and survivor bias, while differences in monitoring methods (arterial line versus cuff) and possible overlap between biomarker sampling and AKI onset further limit interpretation. Baseline creatinine was obtained within the first 24 hours of ICU care rather than before ICU admission. Infection source, lactate, fluid balance, and nephrotoxin exposure were not recorded for analysis. Additionally, hemodynamic monitoring and NGAL measurements were primarily focused on the first 24 hours of ICU treatment. Future multicenter studies with larger

sample sizes and randomized allocation of MAP targets are needed to determine whether individualized MAP strategies influence AKI and other clinical outcomes in septic shock.

4. CONCLUSION

In this prospective cohort of patients with septic shock, no statistically significant difference in AKI occurrence was detected between the lower- and higher-MAP target groups. The estimate was imprecise, and the study was not designed to establish equivalence or causality. Higher MAP was accompanied by greater vasoactive-inotropic support. Changes in serum NGAL were associated with AKI in exploratory analyses and require validation in larger cohorts.

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Author Contributions

AAR contributed to the study conception and design, conducted data collection, performed data analysis, and prepared the original manuscript draft. FM and SG contributed to the methodology, investigation, formal analysis, and critical revision of the manuscript. AAR, FM, HS, SG, MR, ASP, and HN contributed to the study supervision, critical revision of the manuscript, and final approval of the submitted version. All authors have read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

This research adhered to the ethical guidelines outlined in the Declaration of Helsinki. Approval for the study was granted by the Health Research Ethics Committee at Hasanuddin University, Makassar, Indonesia (Approval No. 624/UN4.6.4.5.31/PP36/2026; approved on 8 May 2026). Prior to participants being enrolled, written informed consent was obtained from their parents or legal guardians.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

REFERENCES

- [1] Manrique-Caballero CL, Del Rio-Pertuz G, Gomez H. Sepsis-associated acute kidney injury. *Crit Care Clin* 2021;37:279-301.
- [2] Prescott HC, Antonelli M, Alhazzani W, Möller MH, Alshamsi F, Azevedo LCP, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026. *Crit Care Med* 2026;54:725-812.
- [3] Asfar P, Meziani F, Hamel JF, Grelon F, Megarbane B, Anguel N, et al. High versus low blood-pressure target in patients with septic shock. *N Engl J Med* 2014;370:1583-93.
- [4] Panwar R, Hardie M, Bellomo R, Barrot L, Eastwood GM, Young PJ, et al. Near-normal versus lower mean arterial pressure target in patients with septic shock: a randomized controlled trial. *Am J Respir Crit Care Med* 2016;193:43-51.
- [5] Russell JA. Is there a good MAP for septic shock? *N Engl J Med* 2014;370:1649-51.
- [6] Jahaj E, Vassiliou A, Pratikaki M, Gallos P, Mastora Z, Dimopoulou I, et al. Serum neutrophil gelatinase-associated lipocalin (NGAL) could provide better accuracy than creatinine in predicting acute kidney injury development in critically ill patients. *J Clin Med* 2021;10:5379.
- [7] Yi A, Lee C, Yun Y, Kim H, Moon H, Hur M. Effectiveness of plasma and urine neutrophil gelatinase-associated lipocalin for predicting acute kidney injury in high-risk patients. *Ann Lab Med* 2021;41:60-7.
- [8] Aulia MF, Lubis AP, Silaen EL, Harahap J. The relationship of neutrophil gelatinase-associated lipocalin (NGAL) as a predictor of events acute kidney injury (AKI) in septic patients treated in ICU. *Crit Care Shock* 2025;28:53-60.
- [9] Alhamyani AH, Alamri MS, Aljuaid NW, Aloubthani AH, Alzahrani S, Alghamdi AA, et al. Sepsis in aging populations: a review of risk factors, diagnosis, and management. *Cureus* 2024;16:e74973.

- [10] Min SY, Yong HJ, Kim D. Sex or gender differences in treatment outcomes of sepsis and septic shock. *Acute Crit Care* 2024;39:207-13.
- [11] Othman MI, Mustafa EM, Abdelwahab AE, Hssain AA, Nashwan AJ. Optimizing mean arterial pressure targets for septic shock patients with chronic hypertension: a narrative review. *Health Sci Rep* 2025;8:e70696.
- [12] Introcaso G, Nafi M, Bonomi A, L'Acqua C, Salvi L, Ceriani R, et al. Improvement of neutrophil gelatinase-associated lipocalin sensitivity and specificity by two plasma measurements in predicting acute kidney injury after cardiac surgery. *Biochem Med (Zagreb)* 2018;28:030701.
- [13] Kaur A, Sharma GS, Kumbala DR. Acute kidney injury in diabetic patients: a narrative review. *Medicine (Baltimore)* 2023;102:e33888.
- [14] Zhao L, Cui Q, Dong S, Wang H, Yang F, Wang Y, et al. Impact of diabetes mellitus and glucose level control on early sepsis-associated acute kidney injury: a multicenter retrospective observational study. *Front Med (Lausanne)* 2026;13:1878791.
- [15] Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med* 2010;11:234-8.
- [16] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453-7.