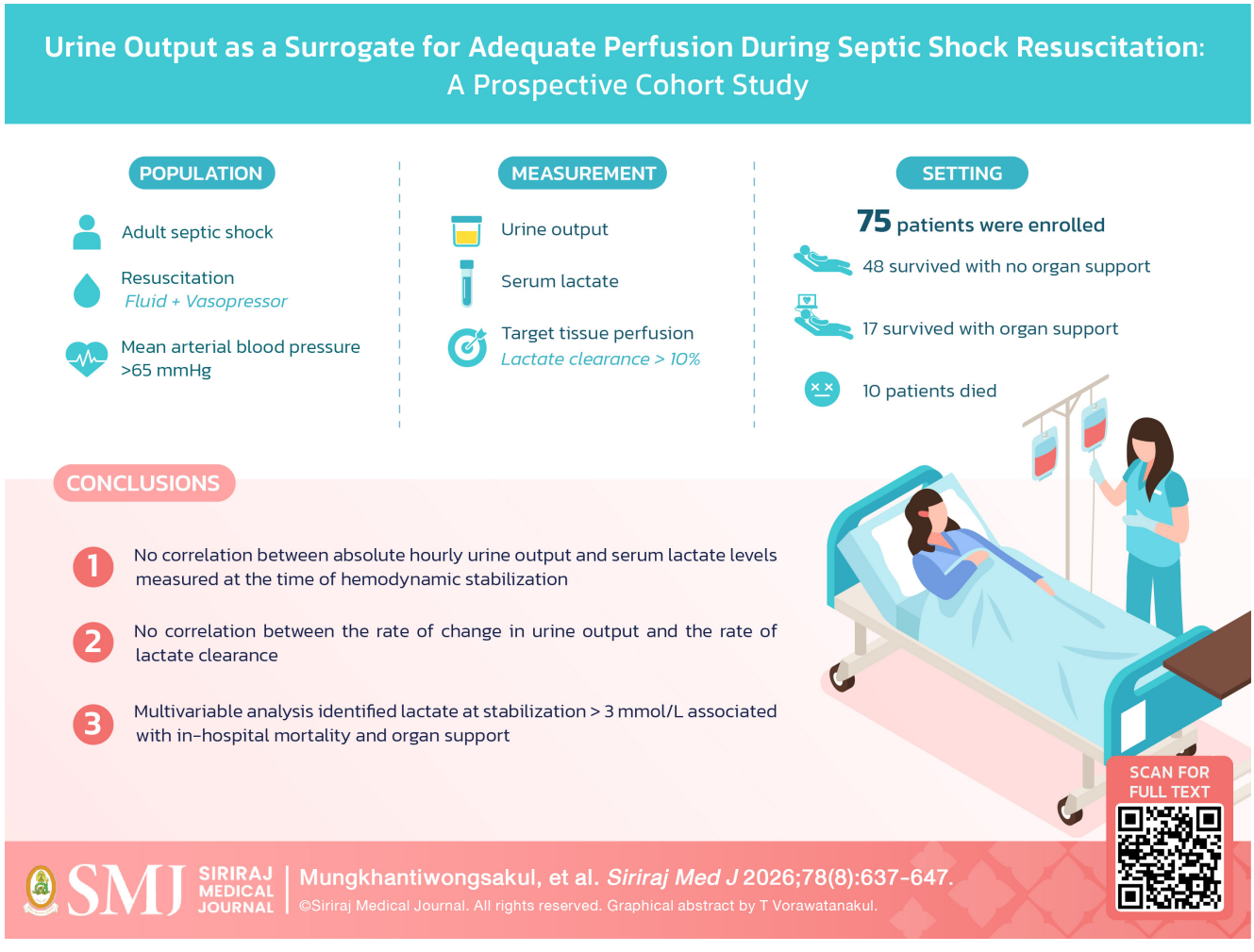
Urine Output as a Surrogate for Adequate Perfusion During Septic Shock Resuscitation: A Prospective Cohort Study

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ABSTRACT

Objective: Septic shock resuscitation targets hemodynamic stabilization (mean arterial pressure 65 mmHg) and tissue perfusion, defined by lactate < 2 mmol/L or lactate clearance > 10%. Because urine output is widely used as an organ perfusion goal, we examined its behavior during resuscitation and its association with lactate kinetics and outcomes.

Materials and Methods: We conducted a prospective cohort study of patients with intact urine flow during resuscitation. Serum lactate was measured at resuscitation start and at hemodynamic stabilization, and hourly urine flow was recorded. The primary outcome was survival without organ support at 28 days after septic shock diagnosis. We assessed correlations between urine flow and lactate clearance at stabilization.

Results: From January to July 2024, 95 patients were screened; 20 were excluded. The remaining 75 achieved hemodynamic stabilization within 12 hours, and all but 2 met tissue oxygenation goals regardless of urine flow rate. The proportion with urine output < 0.5 mL/kg/hour did not differ between survivors and the death/organ support group. In multivariable analysis, urine output at stabilization <0.4 mL/kg/hour was not associated with unfavorable outcomes, whereas lactate at stabilization > 3 mmol/L was associated with in-hospital mortality and organ support.

Conclusions: During septic shock resuscitation, intact urine flow at hemodynamic restoration may serve as a surrogate of adequate tissue perfusion when infection is controlled. However, lactate remains a key milestone for confirming perfusion restoration.

Keywords: Septic shock; urine output; serum lactate; tissue perfusion; resuscitation (Siriraj Med J 2026;78(8): 637-647)

INTRODUCTION

A 2017 World Health Organization report estimated 48.9 million incident sepsis cases and 11.0 million sepsis-related deaths worldwide in that year.[1,2] The World Health Organization, therefore, identified sepsis as a critical global health issue requiring urgent action.[1,2] In Thailand, our medical-ward report for 2014–2020 showed 18,030 sepsis cases among 98,359 admissions (18.3%) and an in-hospital mortality of 19.6%.[3] Among children, retrospective data from the Thai National Health Security Office for 2015 to 2022 reported a prevalence of 190–280 per 100,000 people, with mortality of 20.2%–30.7%.[4] In response, international guidelines have been promulgated to improve outcomes by restoring perfusion pressure, providing organ support, and controlling infection.[5-7] In our prior report, patients who met targets for blood pressure, urine output, and tissue oxygenation within the first 6 hours had higher survival, and meeting more targets correlated with better outcomes.[8] These data emphasize the need for timely interventions toward hemodynamic goals.

The 2021 Surviving Sepsis Campaign guidelines specify hemodynamic resuscitation targets: a mean arterial pressure ≥ 65 mmHg and tissue perfusion evidenced by lactate ≤ 2 mmol/L or lactate clearance ≥ 10%.[5] An earlier version of the Surviving Sepsis Campaign guidelines incorporated urine output as a resuscitation target, and our prior study operationalized that approach.[6,8] A urine output threshold of ≥ 0.5 mL/kg/hour is widely referenced in guidelines, notably KDIGO, and in observational studies across diverse populations as a favorable prognostic marker.[9-12] However, reported urine-output responses and thresholds vary across cohorts, which complicates its use as a stand-alone surrogate for tissue perfusion, particularly in patients without overt hypovolemia.[13-16] If urine output could substitute for serum lactate in selected patients, it would be practical in resource-limited settings. Accordingly, our primary objective was to characterize urine flow at hemodynamic stabilization and evaluate its correlation with outcomes after septic shock resuscitation.

MATERIALS AND METHODS

Study design

We conducted a prospective cohort study enrolling adults with septic shock admitted to medical and surgical intensive care units. The study was approved by the Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (Certificate of approval number: Si 625/2023). Written informed consent was obtained from each patient or legal representative before enrollment.

Study population

The inclusion criteria were age ≥ 18 years, septic shock per the Sepsis-3 definition, and a requirement for

vasopressor or inotrope therapy. The exclusion criteria were prolonged shock (> 12 hours), anuria at presentation, end-stage renal disease, and other causes of acute kidney injury, such as nephrotoxin exposure or obstructive nephropathy.

Protocol

All patients were managed according to standard treatment protocols by their attending physicians. Serum lactate was measured at resuscitation onset and again at hemodynamic stabilization, defined as a mean arterial pressure ≥ 65 mmHg with a stable vasopressor rate for > 1 hour. Restoration of tissue perfusion was defined as lactate clearance > 10% in accordance with guideline recommendations.[5] Hourly urine output was recorded from resuscitation onset through 12 hours. We collected outcomes and details of organ support through day 28 after enrollment.

Outcomes

The primary outcome was survival without organ support at 28 days after septic shock diagnosis. Organ support included mechanical ventilation, renal replacement therapy, and extracorporeal membrane oxygenation. The secondary outcomes were hourly urine output and its trajectory at hemodynamic stabilization, as well as lactate clearance.

Sample size calculation

The sample size was derived from our prior work linking achievement of resuscitation goals, including urine output, to outcomes in septic shock.[8] In that cohort, median urine output was 595 mL/day (interquartile range [IQR] 186–1264) in the death group and 1,400 mL/day (IQR 825–2,317) in survivors.[8] Because these distributions were non-normal, we used the Mann–Whitney *U* test to estimate the required sample size. Assuming a two-sided α of 5% (Z = 1.96) and 80% power, and using nQuery statistical software, the calculated sample size was 75 patients.

Statistical analysis

We summarized baseline characteristics using descriptive statistics. Categorical variables were reported as counts and percentages and compared with the chi-square test or Fisher's exact test. Normally distributed continuous variables were reported as mean with standard deviation; nonnormal variables were reported as median and IQR. We compared hourly and average urine output during resuscitation between patients who survived without organ support at 28 days (favorable outcome) and those who died or required organ support (unfavorable outcome). Comparisons used the independent *t*-test or the Mann–Whitney *U* test, as appropriate.

For continuous variables that differed significantly between groups, we performed receiver operating characteristic analysis to determine cutoff values. We used Youden's index to identify the optimal cutoff and reported its sensitivity and specificity. We then reclassified variables by these cutoffs and conducted univariate analyses, expressing risk as unadjusted odds ratios with 95% confidence intervals (CIs). Variables with $P \leq 0.1$, together with clinically relevant covariates, entered a binary logistic regression model. Multivariable results are presented as adjusted odds ratios with 95% CIs and *P* values. Factors were considered independently predictive of 28-day mortality when $P \leq 0.05$. All analyses were performed with IBM SPSS Statistics version 26 (IBM Corp, Armonk, NY, USA).

RESULTS

Patient screening and enrollment

From January to July 2024, 95 patients in the medical and surgical intensive care units were screened, as shown in Fig 1. Twenty were excluded. The two predominant reasons were end-stage renal disease ($n = 6$) and anuria at enrollment ($n = 6$). Additional exclusions were shock duration > 12 hours ($n = 5$), nephrotoxin exposure ($n = 2$), and post-acute kidney injury ($n = 1$). All of the remaining 75 patients achieved hemodynamic stabilization within 12 hours (mean arterial pressure ≥ 65 mmHg) with a stable vasopressor rate for > 1 hour. All had continuous urine output and were included in the analysis.

Baseline characteristics

Baseline characteristics are shown in Table 1. The mean age was 70.25 ± 17.3 years, and 50 patients (66.7%) were male. Common comorbidities were hypertension (43, 57.3%), diabetes mellitus (28, 37.3%), and chronic kidney disease (23, 30.7%).

Clinical outcomes at 28 days

Forty-eight patients survived at 28 days without organ support (favorable outcome group), and 27 had an unfavorable outcome. Ten patients (13.3%) died despite initial reversal of shock: 8 from ventilator-associated pneumonia, 1 from bowel ischemia, and 1 from gangrenous cholecystitis. The remaining 17 patients (22.7%) required organ support: mechanical ventilation in 11 and both mechanical ventilation and renal replacement therapy in 6.

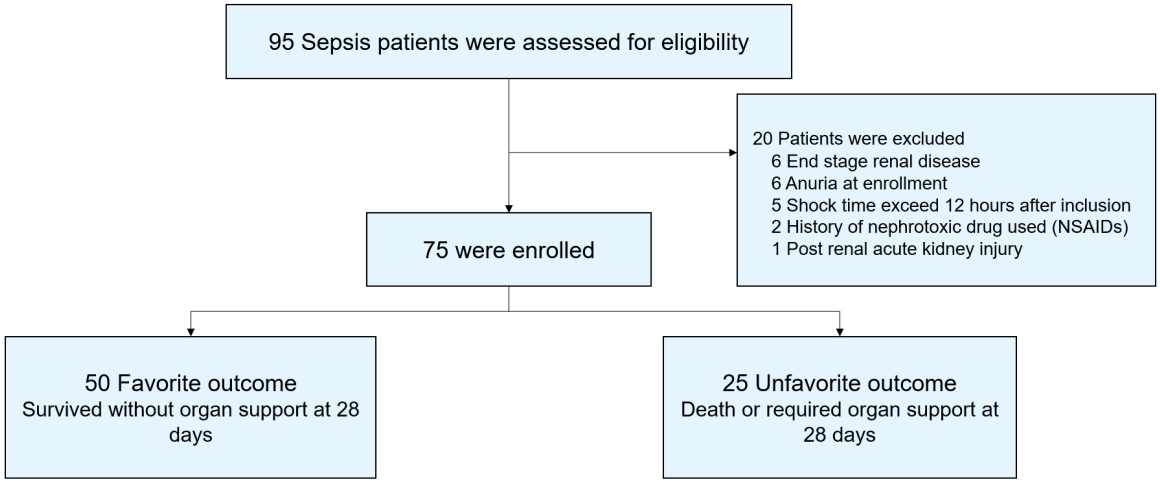


Fig 1. Flow diagram of screening, exclusions, and analytic cohort (January–July 2024).

TABLE 1. Baseline characteristics at enrollment (*N* = 75).

Clinical parameters	Total (*N* = 75)	Favorable outcome (*N* = 48)	Unfavorable outcome (*N* = 27)	*P* value
Age, mean (SD), y	70.25 ± 17.3	68.9 ± 18.8	72.70 ± 14.3	0.369
Male, *n* (%)	50 (66.7%)	32 (66.7%)	18 (66.7%)	1.00
APACHE II, mean (SD)	20.1 ± 7.5	18.4 ± 5.9	23.2 ± 9.1	0.017
SOFA, mean (SD)	8.8 ± 2.8	8.1 ± 1.9	10.1 ± 3.7	0.012
Ward, *n* (%)				
Internal medicine	46 (61.3%)	31 (64.6%)	15 (55.6%)	0.441
Surgery	29 (38.7%)	17 (35.4%)	12 (44.4%)	0.441
Underlying disease, *n* (%)				
Diabetes mellitus	28 (37.3%)	17 (35.4%)	11 (40.7%)	0.647
Hypertension	43 (57.3%)	26 (54.2%)	17 (63.0%)	0.460
Chronic kidney disease	23 (30.7%)	15 (31.2%)	8 (29.6%)	0.971
Cerebrovascular disease	10 (13.3%)	6 (12.5%)	4 (14.8%)	0.777
Cardiovascular disease	9 (12.0%)	6 (12.5%)	3 (11.1%)	0.859
Cirrhosis	4 (5.3%)	2 (4.2%)	2 (7.4%)	0.549
Malignancy	11 (14.7%)	5 (10.4%)	6 (22.2%)	0.188
Diuretic use, *n* (%)	9 (12.0%)	6 (12.5%)	3 (11.1%)	0.859
Source of infection, *n* (%)				
Pneumonia	29 (38.7%)	14 (29.2%)	15 (55.6%)	0.024
Urinary tract infection	7 (9.3%)	5 (10.4%)	2 (7.4%)	1.000
Abdominal infection	25 (33.3%)	18 (37.5%)	7 (25.9%)	0.307
Septicemia	13 (17.3%)	10 (20.8%)	3 (11.1%)	0.355
Soft tissue	3 (4.0%)	1 (2.1%)	2 (7.4%)	0.293

TABLE 1. Baseline characteristics at enrollment (*N* = 75). (Continued)

Clinical parameters	Total (*N* = 75)	Favorable outcome (*N* = 48)	Unfavorable outcome (*N* = 27)	*P* value
Vital signs baseline, mean (SD)				
Body temperature (°C)	38.3 ± 1.6	38.4 ± 1.5	38.2 ± 1.8	0.556
Heart rate (beats per minute)	121.7 ± 23.6	118.0 ± 25.2	128.4 ± 19.1	0.049
Respiratory rate (times per minute)	27.0 ± 4.8	26.0 ± 4.4	28.6 ± 5.1	0.027
Mean arterial blood pressure (mmHg)	57.8 ± 6.3	57.4 ± 6.2	58.4 ± 6.5	0.491
Oxygen saturation (%)	96.3 ± 2.2	96.8 ± 1.6	95.5 ± 2.8	0.039
Laboratory investigations baseline				
Hematocrit, mean (SD), %	29.2 ± 6.9	30.2 ± 6.3	27.4 ± 7.7	0.113
White blood cell count, mean (SD), cells/mm³	16 438.5 ± 15 728.5	16 702.5 ± 14 574.4	17 881.9 ± 15 969.3	0.848
Platelet count, mean (SD), cells/mm³	193 346.7 ± 186 573.9	174 790.2 ± 214 750.1	150 444.4 ± 112 787.9	0.136
Creatinine, mean (SD), mg/dL	1.55 ± 0.84	1.49 ± 0.82	1.65 ± 0.87	0.433
Arterial blood gas pH, mean (SD)	7.38 ± 0.08	7.38 ± 0.09	7.39 ± 0.06	0.749
PaO_2, mean (SD), mmHg	143.9 ± 48.6	151.5 ± 50.1	130.3 ± 43.5	0.069
Lactate, mean (SD), mmol/L	5.4 ± 3.0	5.0 ± 2.9	6.1 ± 2.9	0.115
Treatment				
Fluid, mean (SD), ml/kg				
Balanced crystalloid	30.0 ± 17.6	30.7 ± 20.0	28.3 ± 9.2	0.661
Non-balanced crystalloid	40.1 ± 25.8	37.4 ± 23.6	44.9 ± 22.0	0.264
Colloid albumin	6.2 ± 4.4	6.6 ± 3.7	5.7 ± 5.3	0.553
Non-albumin colloid solution	13.6 ± 10.3	13.1 ± 10.3	14.4 ± 10.7	0.733
Vasopressor/inotropic drug				
Norepinephrine, *n* (%)	75 (100%)	48 (100%)	27 (100%)	1.000
Adrenaline, *n* (%)	13 (17.3%)	8 (16.7%)	5 (18.5%)	1.000
Norepinephrine, mean (SD), mcg/kg/min	0.18 ± 0.14	0.17 ± 0.16	0.19 ± 0.11	0.636
Adrenaline, mean (SD), mcg/kg/min	0.49 ± 0.57	0.33 ± 0.23	0.74 ± 0.87	0.226
All, mean (SD), mcg/kg/min	0.26 ± 0.36	0.23 ± 0.24	0.32 ± 0.52	0.267

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; IQR, interquartile range; MAP, mean arterial pressure; PaO_2, partial pressure of oxygen in arterial blood; SD, standard deviation; SOFA, Sequential Organ Failure Assessment

Group comparisons

Initial heart rate was lower in the favorable group (118.0 ± 25.2 vs 128.4 ± 19.1 per minute; P = 0.049). Respiratory rate was also lower (26.0 ± 4.4 vs 28.6 ± 5.1 per minute; P = 0.027). Oxygen saturation was higher (96.8% ± 1.6% vs 95.5% ± 2.8%; P = 0.039). Severity scores were lower in the favorable group (APACHE II 18.4 ± 5.9 vs 23.2 ± 9.1, with P = 0.017; SOFA 8.1 ± 1.9 vs 10.1 ± 3.7, with P = 0.012). Pneumonia was less frequent in the favorable than in the unfavorable group (14, 29.2% vs 15, 55.6%; P = 0.024).

Urine flow as an indicator of adequate tissue perfusion

Urine output at hemodynamic stabilization for 75 patients was plotted against lactate level (Fig 2). All but 2 patients achieved the tissue perfusion goal of lactate clearance ≥ 10%. These 2 patients had diagnoses of bowel ischemia and acute gangrenous cholecystitis and they subsequently died. Urine output at stabilization ranged 0.18–3.08 mL/kg/hour, with a mean of 0.86 ± 0.63 mL/kg/hour. Plots of lactate clearance versus mean arterial pressure showed similar findings (Fig 3). When lactate clearance was ≥ 10%, 31 patients (41.3%) still had urine output < 0.5 mL/kg/hour. The proportion with urine output < 0.5 mL/kg/hour did not differ between the favorable and unfavorable outcome groups (P = 0.165; Table 2 and Fig 2). Urine flow trajectories also did not differ between groups (Table 2). Lactate at stabilization was higher in the unfavorable group (3.0 ± 1.9 vs 3.9 ± 2.6). The proportion with llactate > 3 mmol/L was likewise higher (31.3% vs 51.9%), although neither difference reached statistical significance (Table 2).

There was no significant correlation between absolute hourly urine output at the time of hemodynamic stabilization and serum lactate levels measured at the same time point. Spearman's rho demonstrated a very

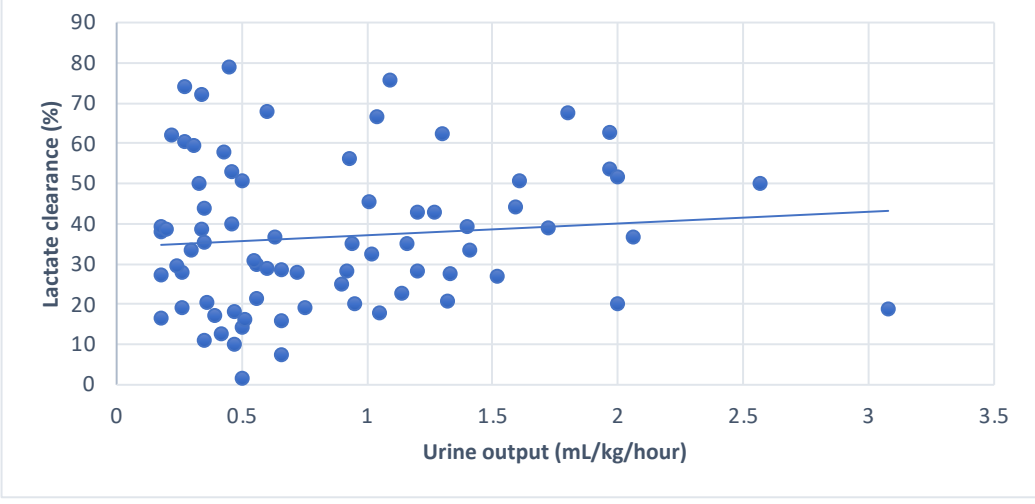


Fig 2. Scatterplot of urine output vs lactate clearance at hemodynamic stabilization.

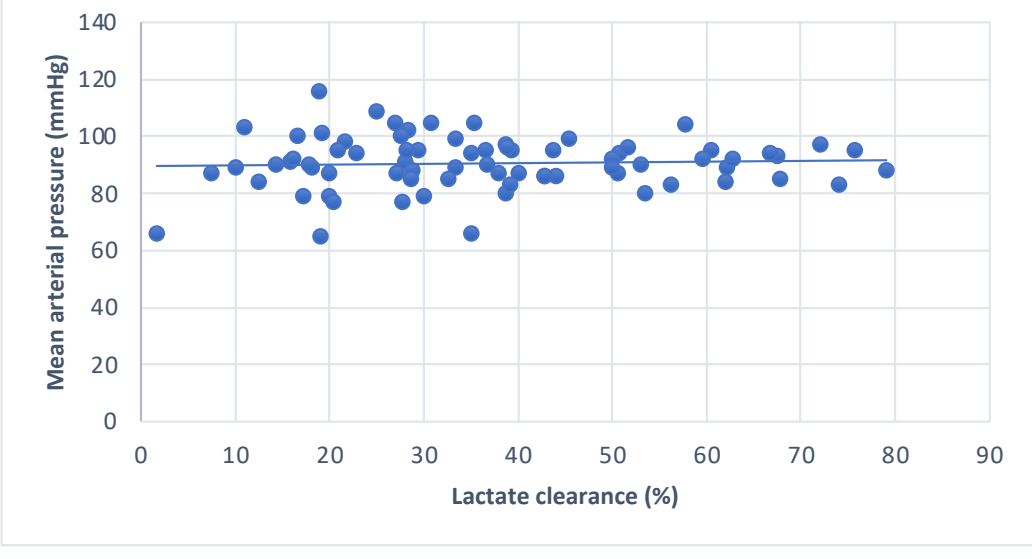


Fig 3. Scatterplot of lactate clearance vs mean arterial pressure at hemodynamic stabilization.

TABLE 2. Outcomes, organ support, and perfusion parameters.

Hemodynamic parameters	Total (*N* = 75)	Favorable outcome (*N* = 48)	Unfavorable outcome (*N* = 27)	*P* value
Time to hemodynamic stabilization, mean (SD), hours	6.5 ± 1.2	6.4 ± 1.1	6.7 ± 1.3	0.314
Hemodialysis, *n* (%)	6 (8.0%)	0 (0%)	6 (22.2%)	0.001
Ventilator support, *n* (%)	17 (22.7%)	0 (0%)	17 (63.0%)	0.001
Urine output				
Urine at time of stabilization, mL/kg/hour	0.86 ± 0.63	0.92 ± 0.65	0.74 ± 0.56	0.233
Urine 1st hour, mL/kg/hour	0.44 ± 0.25	0.47 ± 0.24	0.40 ± 0.26	0.259
Urine 2nd hour, mL/kg/hour	0.46 ± 0.29	0.49 ± 0.30	0.40 ± 0.28	0.175
Urine 3rd hour, mL/kg/hour	0.47 ± 0.34	0.49 ± 0.38	0.43 ± 0.27	0.458
Urine 4th hour, mL/kg/hour	0.49 ± 0.33	0.52 ± 0.35	0.43 ± 0.29	0.275
Urine 5th hour, mL/kg/hour	0.63 ± 0.46	0.69 ± 0.47	0.50 ± 0.41	0.069
Urine 6th hour, mL/kg/hour	0.72 ± 0.47	0.76 ± 0.48	0.64 ± 0.46	0.331
Urine at time of stabilization < 0.5 ml/kg/hour, *n* (%)	31 (41.3%)	17 (35.4%)	14 (51.9%)	0.165
Lactate				
Lactate at time of stabilization, mean (SD), mmol/L	3.3 ± 2.2	3.0 ± 1.9	3.9 ± 2.6	0.090
Lactate clearance, mean (SD), %	36.8 ± 18.3	37.9 ± 16.7	34.8 ± 21.1	0.491
Lactate > 3 mmol/L, *n* (%)	29 (38.7%)	15 (31.3%)	14 (51.9%)	0.079

Favorable outcome = survival without organ support at 28 days; unfavorable outcome = death or survival with organ support at 28 days. Organ support includes mechanical ventilation and renal replacement therapy; no patients received extracorporeal membrane oxygenation in this cohort.

Abbreviation: SD, standard deviation

weak negative association (correlation coefficient = -0.05, *P*=0.355). Also, there was no significant correlation between the rate of change in urine output and the rate of lactate clearance. Spearman's rho demonstrated a very weak positive association (correlation coefficient =0.06, *P*=0.320). We performed a sensitivity analysis excluding the two patients with uncontrolled septic foci (bowel ischemia and gangrenous cholecystitis), the overall findings remained unchanged.

Predictors of unfavorable outcome

In univariate analyses, initial oxygen saturation < 94%, APACHE II > 20, SOFA > 8, pneumonia, and lactate at stabilization > 3 mg/dL were associated with mortality or organ support at 28 days (Table 3). In multivariable logistic regression, only lactate at stabilization > 3 mg/dL remained significant (odds ratio 4.48, 95% CI 1.23–16.31; *P* = 0.023; Table 4).

DISCUSSION

The primary objective was to characterize urine output during septic shock resuscitation; we therefore limited inclusion to patients with intact urine output at the time of hemodynamic stabilization (mean arterial pressure ≥ 65 mmHg). Key findings are as follows. At stabilization, all but 2 patients achieved tissue oxygenation targets—lactate clearance ≥ 10%—regardless of urine flow rate; both exceptions had uncontrolled infection and died. Urine output at stabilization ranged 0.18–3.08 mL/kg/hour, and 31 patients (41.3%) had a urine output

TABLE 3. Univariate analysis of predictors of unfavorable outcome at 28 days.

	Total (*N* = 75)	Favorable outcome (*N* = 48)	Unfavorable outcome (*N* = 27)	*P* value	Relative risk
APACHE-II scores > 20, *n* (%)	36 (48%)	19 (39.6%)	17 (63.0%)	0.052	1.14 (0.98–2.02)
SOFA score > 8, *n* (%)	31 (49.3%)	16 (33.3%)	15 (55.6%)	0.061	1.41 (0.96–2.07)
Oxygen saturation < 94%, *n* (%)	14 (18.7%)	5 (10.4%)	9 (33.3%)	0.028	1.97 (0.96–4.06)
Respiratory rate > 28 times/min, *n* (%)	17 (22.7%)	8 (16.7%)	9 (33.3%)	0.098	1.47 (0.86–2.50)
Heart rate > 110 beats/min, *n* (%)	47 (62.7%)	27 (56.3%)	20 (74.1%)	0.099	1.30 (0.94–1.80)
Pneumonia	29 (38.7%)	14 (29.2%)	15 (55.6%)	0.024	1.53 (1.01–2.32)
Urine at time of stabilization < 0.4 mL/kg/hour, *n* (%)	21 (28.0%)	10 (20.8%)	11 (40.7%)	0.065	1.48 (0.91–2.39)
Lactate at time of stabilization > 3 mg/dL, *n* (%)	29 (38.7%)	15 (31.3%)	14 (51.9%)	0.079	1.39 (0.93–2.06)

Cutoffs reflect receiver operating characteristic–derived thresholds where applicable. *P* values are two-sided.
Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment

TABLE 4. Multivariable logistic regression of predictors of unfavorable outcome at 28 days.

	Relative risk	95% CI	*P* value
APACHE-II scores > 20, *n* (%)	1.77	0.52–6.03	0.358
SOFA score > 8, *n* (%)	2.05	0.57–7.32	0.269
Oxygen saturation < 94%, *n* (%)	4.18	0.95–18.47	0.059
Respiratory rate > 28 times/min, *n* (%)	1.63	0.38–6.94	0.509
Heart rate > 110 beats/min, *n* (%)	0.94	0.23–3.78	0.925
Pneumonia	3.39	0.89–12.89	0.074
Urine at time of stabilization < 0.4 mL/kg/hour, *n* (%)	1.86	0.50–6.96	0.357
Lactate at time of stabilization > 3 mg/dL, *n* (%)	4.48	1.23–16.31	0.023

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment

< 0.5 mL/kg/hour. Nevertheless, the proportions did not differ between survivors without organ support and those who died or required organ support (Table 2 and Fig 2). In multivariable analysis, urine output at stabilization < 0.4 mL/kg/hour was not associated with unfavorable outcomes (Table 4). Despite reversal of shock in all patients, a subset died or needed organ support, and lactate at stabilization > 3 mmol/L was independently associated with death or organ support (Table 4).

Our findings address the primary research question and add new information. During septic shock resuscitation, nearly all patients with intact urine flow at hemodynamic stabilization also achieved adequate tissue perfusion, irrespective of urine output rate. Hence, in this context, whether the presence of urine flow serves as a reliable practical surrogate of perfusion adequacy remains a hypothesis requiring prospective validation in broader, unrestricted cohorts. Such use aligns with recommendations for adult sepsis care in resource-limited settings and offers operational simplicity because it requires no additional testing or cost.[17] However, infection control is a prerequisite; the 2 patients with uncontrolled infection failed to clear lactate and later died, underscoring that urine flow alone cannot confirm perfusion when source control is incomplete. Consequently, urine flow at hemodynamic stabilization should be interpreted as a surrogate of adequate perfusion. Lactate remains an essential marker for confirming restoration of tissue perfusion and is emphasized in contemporary guidelines.[5-7] Serum lactate was used as a pragmatic and widely accepted surrogate marker of tissue hypoperfusion rather than a definitive gold standard of microcirculatory function. Urine output and lactate likely represent complementary rather than interchangeable physiological parameters, as renal urine production may also be influenced by multiple factors beyond systemic perfusion, including neurohormonal regulation, intrinsic renal susceptibility, baseline kidney function, fluid balance, and vasopressor exposure.

Urine output at hemodynamic stabilization spanned 0.18–3.08 mL/kg/hour (Fig 2). Using the guideline threshold of 0.5 mL/kg/hour, 31 of 75 patients (41.3%) fell below this value, yet proportions did not differ between survivors without organ support and those with unfavorable outcomes (Table 2). Multivariable analysis likewise showed no association for urine output < 0.4 mL/kg/hour at stabilization (Table 4). These observations suggest the canonical 0.5 mL/kg/hour cutoff—endorsed by prior guideline iterations—may be overly conservative for defining adequate organ perfusion.[6,7,17] Our findings align with external datasets: an analysis of the Medical Information Mart for Intensive Care (MIMIC)-IV database identified an inflection near 0.39 mL/kg/hour[13], and a separate retrospective cohort suggested a threshold near 0.2 mL/kg/hour averaged over 4–6 hours.[15] Taken together, these data support recalibrating urine-output targets; in patients with source control, the presence of sustained urine flow at hemodynamic stabilization may be sufficient, whereas lactate remains essential for confirmation.

We found no clear correlation between cumulative resuscitation fluid and urine output at hemodynamic stabilization. This heterogeneity likely reflects differences in baseline volume status, intrinsic renal disease, diuretic exposure, neurohormonal stress responses, and patient-level variation. Although oliguria during resuscitation has been linked to progression of renal failure and mortality[15,16], our cohort showed no such association once perfusion had been restored. These observations support reports that fluid boluses given for oliguria seldom increase urine output after perfusion is reestablished[18] and may promote over-resuscitation with fluid accumulation syndrome.[19,20]

Despite hemodynamic stabilization and restoration of urine flow, a subset of patients died or required organ support. Most deaths were infection related, and multivariable analysis identified lactate at stabilization > 3 mmol/L as an independent risk factor.[19-21] This aligns with prior work, including ours, and suggests that elevated lactate at presumed stabilization reflects ongoing dysoxia, microcirculatory shunting, or mitochondrial dysfunction that portends poorer outcomes.

Limitations

This study has limitations. Although the study achieved the predefined sample size, the relatively small cohort may have limited the statistical power of the multivariable analysis and reduced the ability to detect additional independent predictors of unfavorable outcomes. Therefore, the findings should be interpreted cautiously and require validation in larger multicenter cohorts. We defined hemodynamic stabilization as a mean arterial pressure ≥ 65 mmHg with a stable vasopressor rate for > 1 hour. However, this pragmatic threshold may misclassify patients who require higher mean arterial pressure targets to restore perfusion, particularly older adults or those with chronic hypertension.

CONCLUSIONS

In conclusion, these data support practical, application of urine output thresholds in clinical practice while reaffirming that lactate remains essential for confirmation. Low urine output in the presence of meeting lactate goals

does not necessarily indicate inadequate resuscitation. Persistent hyperlactatemia at presumed hemodynamic stability should be prioritized as a warning signal of residual pathophysiological insult.

Data Availability Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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DECLARATIONS

Grants and Funding Information

Not applicable.

Conflict of Interest

The authors declare that they have no competing interests.

Registration Number of Clinical Trial

Not applicable.

Author Contributions

Conceptualization and methodology, T.M., C.P., and S.T. ; Investigation, T.M.; Formal analysis, T.M., C.P. and S.T. ; Visualization and writing – original draft, T.M., C.P., and S.T.; Writing – review and editing, T.M., C.P., and S.T. ; Funding acquisition, T.M., C.P., and S.T.; Supervision, C.P. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

During the preparation of this work, the author(s) did not use generative AI in any writing process.

Institutional Review Board Statement

The study was approved by the Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (Certificate of approval number: Si 625/2023).

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