ORIGINAL ARTICLE

Peripheral perfusion-guided versus routine fluid therapy in sepsis: A randomized controlled pilot trial

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Background: Sepsis remains a leading cause of morbidity and mortality among critically ill patients. Fluid resuscitation is essential, but conventional protocols often lack individualized assessment of tissue perfusion, risking underresuscitation or fluid overload. The peripheral perfusion index (PPI), derived from pulse oximetry, offers a practical, noninvasive way to dynamically guide fluid therapy and may improve outcomes. The objective of the study was to evaluate whether PPI-guided targeted fluid therapy improves clinical and microvascular outcomes in septic intensive care unit patients compared with conventional fluid therapy. **Materials and Methods:** In a prospective, randomized trial, 60 septic adults were assigned to standard fluid therapy or PPI-guided resuscitation. The primary outcome was microvascular perfusion improvement within 72 h. The secondary outcomes included 7-day mortality, acute kidney injury (AKI), fluid balance, lactate clearance, and renal biomarkers (including cystatin C). **Results:** PPI-guided therapy significantly improved microvascular perfusion ($P = 0.001$) and reduced cystatin C levels by day 7 ($P = 0.0001$), suggesting renal protection. Although there were fewer deaths at 7 days and less AKI in the intervention group, these differences did not reach statistical significance. Trends favored lactate clearance and more favorable fluid balance with PPI guidance. **Conclusion:** PPI-guided fluid therapy is a feasible, low-cost approach to individualized resuscitation in septic patients, associated with short-term improvements in microvascular perfusion and renal biomarkers. The observed physiological benefits warrant confirmation in larger multicenter trials to determine any impact on long-term clinical outcomes.

Key words: Fluid therapy, oximetry, sepsis

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INTRODUCTION

Sepsis remains a leading cause of morbidity and mortality in critically ill patients worldwide, posing a major challenge in intensive care units (ICUs).[1,2] Management of sepsis includes antibiotics, fluid resuscitation, and corticosteroids.[3] With effective fluid therapy crucial for restoring tissue perfusion and preventing organ dysfunction.[4] Traditional fluid protocols often lack individualized perfusion assessment.[5,6] However, excessive or insufficient fluid administration can lead to adverse outcomes, including fluid overload or persistent hypoperfusion.[7] Studies in resource-limited settings show that early fluid boluses may increase mortality, highlighting uncertainty in optimal early resuscitation.[8,9] Excessive fluids poststabilization can lead to edema and organ dysfunction.[8,9] In resource-limited settings where hemodynamic monitoring capabilities are restricted, fluid therapy should be guided by patient response to a fluid challenge, pulse pressure variation (PPV), tidal volume challenge, passive leg raise test (used alongside pulse pressure or PPV), and ultrasonography if available.[8,9] Dynamic tools such as passive leg raise and peripheral perfusion index (PPI) better predict hemodynamic response than static measures such as central venous

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pressure.[9,10] To address this, targeted fluid therapy based on dynamic perfusion parameters has gained attention, offering the potential to guide resuscitation more precisely.[10,11] Macrovascular indicators, heart rate (HR), respiratory rate, blood pressure (BP), and lactate, reflect cardiovascular status but may not capture microvascular perfusion.[12]

The PPI, a noninvasive, pulse oximetry-derived measure, offers real-time evaluation of tissue perfusion.[10,13] Several studies have indicated that PPI correlates with microcirculatory and hemodynamic changes, making it a valuable indicator in guiding fluid responsiveness in septic patient.[10,14] Despite its potential, comparative data between routine and PPI-guided fluid therapy remain limited.[15]

This study evaluates and compares routine versus PPI-guided targeted fluid therapy in ICU patients with sepsis at Al-Zahra Teaching Hospital, Isfahan, Iran, assessing the effectiveness of PPI-guided resuscitation on clinical outcomes.

METHODS

This prospective, single-center, randomized controlled trial was conducted in the ICU of Alzahra Hospital, between July and December 2024. The study was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR. MUI. PHANUT. REC.1403.061). The trial was registered in the Iranian Registry of Clinical Trials (IRCT20240804062637N1) and approved by the local institutional review board. Written informed consent was obtained from all participants; when a patient lacked decision-making capacity, consent was obtained from a legally authorized representative.

Enrollment occurred within 24 h of meeting Sepsis-3 criteria. Eligible patients were aged 18 years or older and admitted to the ICU with sepsis, defined as confirmed or suspected infection plus acute organ dysfunction, indicated by a ≥2-point increase in the Sequential Organ Failure Assessment (SOFA) score from baseline.[16] Baseline SOFA and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were recorded at ICU admission. Sixty patients were enrolled and randomized equally into intervention and control groups (30 patients each).

Inclusion criteria

Adults aged 18 years or older diagnosed with sepsis defined as infection accompanied by new organ dysfunction, indicated by a SOFA score of 2 or higher admitted to the ICU.

Exclusion criteria

Pregnant women, conditions preventing reliable peripheral perfusion monitoring (such as severe hypothermia, Raynaud's phenomenon, advanced peripheral arterial disease, or scleroderma), Stage 5 chronic kidney disease requiring dialysis, and patient or legal surrogate refusal.

Patients were randomized 1:1 to control (routine fluid therapy) or intervention (PI-guided therapy) via block randomization (block size = 4) using computer-generated sequences; allocation was sealed in opaque envelopes and managed by the principal investigator. ICU clinicians were blinded to PI, which was measured by a trained investigator.

During the assessment, patients were positioned supine in a room with a controlled temperature of approximately 22°C. The pulse oximeter probe was placed on an upper limb, typically on the index or middle finger, avoiding limbs with arterial lines to ensure accurate PPI measurements.

All patients received standard sepsis care as per the Surviving Sepsis Campaign guidelines,[17] including an initial 30 mL/kg isotonic crystalloid bolus and vasopressors as needed to maintain mean arterial pressure (MAP) ≥65 mmHg and urine output >0.5 mL/kg/h.[18]

Control group

In the control group, fluid management after the initial 30 mL/kg crystalloid bolus followed standard sepsis care protocols and relied solely on conventional clinical markers rather than PI-guided assessment. Treating physicians determined the need for additional fluid boluses based on traditional indicators of tissue perfusion and hemodynamic status, including BP, HR, urine output, lactate levels, capillary refill time, skin temperature, and overall fluid balance. When these parameters suggested ongoing hypoperfusion, patients received further aliquots of crystalloid fluids (typically 250–500 mL), and if hemodynamic targets remained unmet, vasopressor therapy was initiated or titrated to maintain a MAP ≥65 mmHg. All therapeutic decisions were made according to standard bedside evaluations and physician judgment without the use of PI monitoring.

Intervention group

PI was measured with a fingertip pulse oximeter (Cardioline, China) every 30 s for 5 min postinitial bolus; the mean defined baseline PI. Measurements were repeated on days 1–3. PI <1.4 indicated abnormal perfusion. Protocol steps are as follows:

If PI <1.4, a 250–500 mL crystalloid bolus was infused over 30–60 min, considering age, comorbidities, fluid intolerance signs, and ultrasound if available.

One-hour postbolus, HR, MAP, and PI were reassessed.

Additional boluses were given until PI≥1.4 when maintaining MAP ≥65 mmHg and urine output >0.5 mL/kg/h.

Vasopressors were initiated only if hypoperfusion persisted.

Baseline demographic and clinical data included age, sex, ICU admission diagnosis, infection source, and comorbidities. Illness severity was recorded using APACHE II and SOFA scores at enrollment. Patients were evaluated within 24 h of ICU admission or sepsis onset.

Measurements

Hemodynamic parameters (MAP and HR) and metabolic variables (arterial lactate) were assessed 6–24 h after initial resuscitation. Daily cumulative fluid balance was calculated as total intake (enteral + IV) minus output (urine, drains, and gastric aspirate). Renal function was monitored via serum creatinine, urine output, and cystatin C at baseline and on day 7. Patients were followed for up to 28 days or until discharge. Lactate samples were collected 6–24 h postresuscitation and converted from mg/dL to mmol/L (mg/dL: 9) for reporting.

The primary outcomes were incidence of peripheral hypoperfusion, hospital mortality (7 days), and incidence of acute kidney injury (AKI) within 7 days. AKI was defined by any of the following criteria: increase in serum creatinine ≥0.3 mg/dL within 48 h, or ≥1.5 times baseline within 7 days, or urine output <0.5 mL/kg/h for 6 h (KDIGO criteria). Serum cystatin C was measured as an additional marker of glomerular filtration, and the secondary outcomes was correlation between cumulative fluid balance and PI in the intervention group; prognostic significance of serial PI changes during the first 72 h of sepsis in the intervention group; and multivariate analysis of peripheral perfusion parameters as independent predictors of clinical outcomes.

The sample size was determined based on a prior study examining peripheral hypoperfusion in septic patients with AKI and its association with mortality and fluid balance.[19] Assuming an expected survival rate of P1 = 65.5% in the intervention group and P2 = 35.5% in the control group, with a two-sided α of 0.05 and power (1–β) of 0.80, the required sample size per group was calculated using the formula:

$$N = (z\alpha/2 + z\beta)2 * [P1(1-P1) + P2(1-P2)] / (P1-P2)2$$

Substituting $Z_{\alpha/2} = 1.96$, $Z_{\beta} = 0.84$, P1 = 0.655, and P2 = 0.355 yielded approximately 27 patients per group. Accounting for a 10% dropout rate, we planned to enroll 30 patients per arm ($n = 60$).

Statistical analysis

Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed data were presented as mean ± standard deviation and were compared between groups using the independent-samples *t*-test; within-group comparisons over time were made using repeated-measures ANOVA. Nonparametric data were presented as median (interquartile range) and were compared between groups using the Mann–Whitney *U*-test and within groups using the Wilcoxon signed-rank test. Categorical variables were expressed as counts (percentages) and were compared using the Chi-square test or Fisher's exact test, as appropriate. All statistical analyses were performed using SPSS software (SPSS Inc; Chicago, IL, USA). A two-sided $P \leq 0.05$ was considered statistically significant.

RESULTS

This prospective randomized study was conducted between July and December 2024, during which 180 patients were screened for eligibility. Following the application of inclusion and exclusion criteria (details shown in Figure 1), a total of 60 patients were enrolled in the ICU of Al-Zahra Hospital and randomly assigned in equal numbers to either the routine fluid therapy group ($n = 30$) or the targeted fluid therapy group guided by PPI ($n = 30$).

Baseline demographic and clinical characteristics, including age, gender distribution, vital signs (temperature, HR, respiratory rate, MAP, and oxygen saturation), and initial laboratory values, were well balanced between the two groups with no statistically significant differences [Table 1]. Both the groups received empirical broad-spectrum antibiotics upon admission following ICU and Surviving Sepsis Campaign guidelines, with no significant difference in antibiotic regimens or sources of infection observed ($P = 0.78$).

The primary clinical outcomes included the incidence of peripheral hypoperfusion, in-hospital mortality, and the development of AKI during the ICU stay. The secondary outcomes comprised cumulative fluid balance, urine output, and serum lactate levels evaluated at day 1 and day 7 postadmission. As summarized in Table 2, the intervention group demonstrated significantly improved tissue PI values at three different time points compared to the control group ($P = 0.001$). However, within-group analysis did not show significant temporal changes ($P = 0.23$). Mortality rates were lower in the intervention group, but did not reach statistical significance ($P = 0.30$).

AKI incidence was assessed using serum creatinine, cystatin C, and KDIGO criteria. No significant differences were found between groups based on creatinine levels at day

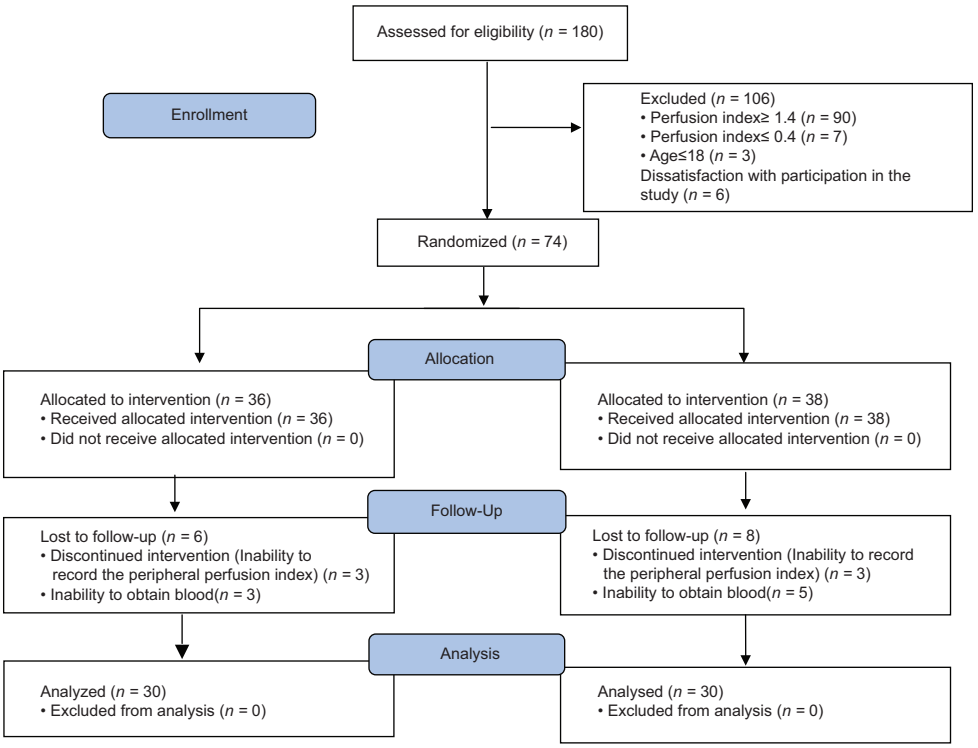

Figure 1: The CONSORT flow diagram of the study

1 ($P = 0.60$) or day 7 ($P = 0.10$), nor in cystatin C-based AKI diagnosis at either time point (day 1 $P = 0.23$; day 7 $P = 1.00$). Notably, the mean cystatin C levels differed significantly between groups over time ($P = 0.0001$), with a significant within-group decrease observed in the intervention arm ($P = 0.02$) [Table 3]. In addition, creatinine and blood urea nitrogen levels showed no significant intergroup differences on days 1 and 7, although numerically lower values were noted in the PPI-guided group.

Serum lactate concentrations did not differ significantly between groups ($P = 0.26$), yet a significant reduction over time was detected within both the groups, reaching statistical significance in the intervention group ($P = 0.025$). Fluid intake, cumulative fluid balance, and urine output, normalized per weight and time, were comparable between groups on both the 1st and 7th days (all $P > 0.2$), with no significant within-group variations.

DISCUSSION

PPI-guided therapy improved microvascular perfusion, but showed no significant impact on mortality, AKI, or lactate clearance. This likely reflects limited statistical power, low event rates, and the short 7-day follow-up. While prior studies link better peripheral perfusion to improved sepsis prognosis, our findings should be viewed as short-term physiological effects rather than evidence of long-term benefit.

Our findings align with those of Hernández *et al.*, who reported that targeted fluid therapy improved microvascular indices with significant intergroup differences, while mortality decreased without statistical significance.[20] Similarly, Marik *et al.* showed that excessive fluid administration increased mortality, organ failure, and ICU stay, underscoring the need for individualized strategies and continuous monitoring of vascular indices.[21] Consistent with these results, our study demonstrated that using the PPI reduced mortality in the intervention group.

The European Society of Critical Care Medicine recommends guiding ICU fluid therapy with hemodynamic or clinical indicators, such as Capillary refilling time (CRT), rather than relying solely on BP or fixed volumes.[22] Given resource constraints in Iran, we used the PPI, a simple, cost-effective tool compatible with CRT, which may enhance treatment, reduce complications, and lower mortality.

Narayanan *et al.* demonstrated that the PPI is a practical tool for predicting fluid therapy responses in ICU patients, supporting its role in evaluating therapeutic adequacy.[10] Our findings similarly highlight PPI's value in guiding fluid management, showing improvements in microvascular parameters. While Narayanan *et al.* reported effects primarily on macrovascular indicators, our study found that PPI-guided therapy influenced markers such as MAP

Table 1: Baseline characteristics of the study population

	Intervention group	Control group	P[a]
n	30	30	
Age (years)	0.66±0.22	0.66±0.22	0.98
Gender			
Female	14	13	0.50
Male	16	17	
CRP	0.8±0.05	0.63±0.05	0.19
ESR	0.49±0.04	0.52±0.04	0.76
Lactate-1 (mg/dl)	0.21±0.01	0.25±0.01	0.26
SOFA score	0.08±0.03	0.07±0.02	0.22
APACHE II Score	0.18±0.05	0.19±0.07	0.68
SPO_2	1.2±0.04	1.19±0.04	0.37
HR	1.16±0.03	1.15±0.03	0.89
FiO_2	0.52±0.03	0.51±0.04	0.93
MAP (mmHg)	1.12±0.02	1.05±0.02	0.19
Use of vasopressor	0	0	1
Past medical history			
CNS disease	6	2	0.44
Cardiovascular disease	4	1	
Diabetes	1	2	
Dyslipidemia	1	1	
Kidney disease	1	2	
Cancer	1	2	
Pulmonary disease	1	0	
Other	2	2	
Pneumonia (community- or hospital-acquired), *n* (%)	12 (40.0)	13 (43.3)	0.9
Urinary tract infection, *n* (%)	9 (30.0)	8 (26.7)	
Intra-abdominal infection, *n* (%)	4 (13.3)	5 (16.7)	
Skin/soft tissue infection, *n* (%)	2 (6.7)	2 (6.7)	
Bloodstream infection (primary), *n* (%)	2 (6.7)	1 (3.3)	
Other/undetermined, *n* (%)	1 (3.3)	1 (3.3)	

[a]Data were analyzed by ANOVA test. MAP=Mean arterial pressure; HR=Heart rate; SpO_2=Peripheral oxygen saturation; SOFA=Sequential Organ Failure Assessment; APACHE II=Acute Physiology and Chronic Health Evaluation II; CRP=C-reactive protein; ESR=Erythrocyte sedimentation rate; FiO_2=Fraction of inspired oxygen; CNS=Central nervous system

Table 2: Peripheral hypoperfusion, mortality, acute kidney injury in both randomization arms during the study period

	Intervention group	Control group	P[a]
PI_1*	0.88±0.28	0.98±0.34	0.001
PI_2**	1.48±0.66	1.05±0.46	
PI_3***	2.07±0.6	1.34±0.63	
Mortality			
Death	1	3	0.50
Alive	29	27	
Number of AKI based on creatinine#	2	4	0.60
Number of AKI based on creatinine##	0	1	1
Number of AKI based on Cystatin c#	0	3	0.23
Number of AKI based on Cystatin c##	0	0	1

*PI at first day; **PI at second day; ***PI at third day; [a]Independent-samples *t*-test; #First day; ##7th day. Data are presented as mean±SD. AKI=Acute kidney injury; SD=Standard deviation; PI=Perfusion index

and HR, though intergroup differences were not statistically significant.

Multiple studies have linked positive fluid balance to higher sepsis mortality.[23,24] In our study, although more patients in the intervention group had positive fluid balance, this was not statistically significant, and mortality was higher in the control group.[23-27] A contributing factor to this discrepancy is the difference in the length of the mortality assessment period, with Kharadi *et al*.[27] evaluating up to 90 days compared to the 7-day assessment in the current study. Additionally, variations in sample size may have influenced the conflicting results, as Sakr *et al*.[26] included 1,808 participants whereas the present study involved only 60.

The Sepsis-3 guidelines highlight tissue perfusion as a key measure of treatment response and follow-up. Consistent with these recommendations, our study used the PPI to evaluate fluid therapy adequacy, emphasizing simple, cost-effective alternatives to complex, expensive techniques.[23]

Abraham *et al*. reported that higher serum cystatin C levels at ICU admission predict AKI occurrence and renal recovery in sepsis, offering greater sensitivity than creatinine. As sepsis-related AKI markedly increases mortality, early and accurate detection is critical.[28] In our study, cystatin C levels differed significantly between groups on days 1 and 7 (P = 0.0001): intervention group 1.73 ± 0.35 and 1.53 ± 0.32 vs. control group 2.14 ± 0.47 and 2.01 ± 0.46. However, AKI incidence by cystatin C showed no significant difference (P = 0.23 on day 1, P = 1 on day 7). These findings diverge from Abraham *et al*., likely due to our smaller sample size.

Jones *et al*. reported no mortality difference in severe sepsis or septic shock patients resuscitated using lactate clearance versus $ScvO_2$-guided protocols.[29] Similarly, our study found no significant differences in serum lactate over 3 days (P = 0.26) or mortality between intervention and control groups (P = 0.30), though mortality was numerically lower in the intervention group. A key strength of our study is its randomized design combined with simple, cost-effective monitoring for fluid therapy management.

A key strength of this randomized clinical trial is the use of accessible, cost-effective monitoring for fluid therapy management.

Limitations include a small sample size, short follow-up, limited postdischarge clinical data, and incomplete PI measurements due to extremity coldness.

Table 3: Creatinine and cystatin C level, lactate level, fluid intake, fluid balance, and urinary output in both randomization arms during the study period

	Intervention group	Control group	P^a
Creatinine$_1$*	1.17±0.49	1.59±0.17	0.19
Creatinine$_2$**	1.13±0.40	1.27±0.83	0.39
BUN$_1$*	29.27±1.78	34.80±3.07	0.40
BUN$_2$**	26.39±1.29	27.54±1.72	0.78
Cystatin c$_1$*	1.73±0.35	2.14±0.47	0.0001
Cystatin c$_2$**	1.53±0.32	2.01±0.46	
Number of AKI based on creatinine*	2	4	0.60
Number of AKI based on creatinine**	0	1	1
Number of AKI based on Cystatin c$_1$*	0	3	0.23
Number of AKI based on Cystatin c$_2$**	0	0	1
Lactate level (mg/dl)			
First day	16.89±0.78	20.14±1.07	0.26
Second day	15.31±0.64	18.95±0.95	
Third day	15.99±0.95	16.88±0.91	
Fluid intake$_1$*	3621.67±67.49	3545.63±66.92	0.66
Fluid intake$_2$**	3489.00±78.42	3477.00±64.36	0.95
Urinary output$_1$*	2951.33±83.73	2617.50±141.70	0.27
Urinary output$_2$**	2910.67±70.68	2695.67±120.84	0.404
Urinary output/kg/h*	1.67±0.076	1.57±0.086	0.603
Urinary output/kg/h**	1.68±0.067	1.63±0.077	0.80
Fluid balance*			
Positive	26	26	1
Negative	4	4	
Fluid balance**			
Positive	26	23	0.5
Negative	4	7	

*First day of study; **Last day of study. Data are presented as mean±SD. [a]Between-group comparisons used Independent-samples *t*-test. AKI=Acute kidney injury; SD=Standard deviation; BUN=Blood urea nitrogen

CONCLUSION

Based on the findings, it is recommended that targeted fluid therapy guided by the PPI is incorporated into sepsis treatment protocols, alongside more traditional assessment methods such as capillary refill time. In addition, further research involving larger patient cohorts and extended follow-up periods is necessary to validate these findings and optimize sepsis management strategies.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, *et al*. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA 2016;315:801-10.
2. Brown RM, Semler MW. Fluid management in sepsis. J Intensive Care Med 2019;34:364-73.
3. Polat G, Ugan RA, Cadirci E, Halici Z. Sepsis and septic shock: Current treatment strategies and new approaches. Eurasian J Med 2017;49:53-8.
4. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, *et al*. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008;36:296-327.
5. Marik PE, Lemson J. Fluid responsiveness: An evolution of our understanding. Br J Anaesth 2014;112:617-20.
6. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, *et al*. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 2017;43:304-77.
7. Genga K, Russell JA. Early liberal fluids for sepsis patients are harmful. Crit Care Med 2016;44:2258-62.
8. Dondorp AM, Dünser MW, Schultz MJ, editors. Sepsis Management in Resource-Limited Settings. Cham (CH): Springer;

2019.
9. Thwaites L, Nasa P, Abbenbroek B, Dat VQ, Finfer S, Kwizera A, *et al*. Management of adult sepsis in resource-limited settings: Global expert consensus statements using a Delphi method. Intensive Care Med 2025;51:21-38.
10. Narayanan BJ, Rao SV, Kandasamy S. Peripheral perfusion index for prediction of fluid responsiveness in spontaneously breathing critically ill patients: A prospective observational study. Indian J Crit Care Med 2025;29:151-4.
11. Guarino M, Perna B, Cesaro AE, Maritati M, Spampinato MD, Contini C, *et al*. 2023 update on sepsis and septic shock in adult patients: Management in the emergency department. J Clin Med 2023;12:3188.
12. Mahmoodpoor A, Sheikhzadeh D, Golzari SE. Microcirculation versus macrocirculation for the management of septic shock: Is hyperoxia any good? ABCmed 2017;5:1-2.
13. Lima AP, Beelen P, Bakker J. Use of a peripheral perfusion index derived from the pulse oximetry signal as a noninvasive indicator of perfusion. Crit Care Med 2002;30:1210-3.
14. Singh RB, Shekhar S, Sinha S, Singh S, Singh R, Kumar Nayan S. An observational study to correlate peripheral perfusion index as a predictor of hypotension and mortality in sepsis patients. Cureus 2025;17:e80431.
15. Monnet X, Marik PE, Teboul JL. Prediction of fluid responsiveness: An update. Ann Intensive Care 2016;6:111.
16. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, *et al.* Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. Crit Care Med 2021;49:e1063-143.
17. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, *et al*. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181-247.
18. Dellinger RP, Rhodes A, Evans L, Alhazzani W, Beale R, Jaeschke R, *et al*. Surviving sepsis campaign. Crit Care Med 2023;51:431-44.
19. de Miranda AC, de Menezes IA, Junior HC, Luy AM, do Nascimento MM. Monitoring peripheral perfusion in sepsis associated acute kidney injury: Analysis of mortality. PLoS One 2020;15:e0239770.
20. Hernández G, Ospina-Tascón GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J, *et al*. Effect of a resuscitation strategy targeting peripheral perfusion status versus serum lactate levels on 28-day mortality among patients with septic shock: The ANDROMEDA-SHOCK randomized clinical trial. JAMA 2019;321:654-64.
21. Marik PE, Levitov A, Young A, Andrews L. The use of bioreactance and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. Chest 2013;143:364-70.
22. Agudelo Torres DE, Navarro-Martinez J, Galiana-Ivars M, Alarcon Martinez C. Comments on Cecconi *et al*.: Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med 2015;41:570.
23. Howitt SH, Herring M, Malagon I, McCollum CN, Grant SW. Incidence and outcomes of sepsis after cardiac surgery as defined by the sepsis-3 guidelines. Br J Anaesth 2018;120:509-16.
24. Rosenberg AL, Dechert RE, Park PK, Bartlett RH, NIH NHLBI ARDS Network. Review of a large clinical series: Association of cumulative fluid balance on outcome in acute lung injury: A retrospective review of the ARDSnet tidal volume study cohort. J Intensive Care Med 2009;24:35-46.
25. Messmer AS, Zingg C, Müller M, Gerber JL, Schefold JC, Pfortmueller CA. Fluid overload and mortality in adult critical care patients-a systematic review and meta-analysis of observational studies. Crit Care Med 2020;48:1862-70.
26. Sakr Y, Rubatto Birri PN, Kotfis K, Nanchal R, Shah B, Kluge S, *et al*. Higher fluid balance increases the risk of death from sepsis: Results from a large international audit. Crit Care Med 2017;45:386-94.
27. Kharadi N, Mehreen T, Habib M, Rasheed G, Ilyas A, Akhtar A, *et al*. Evaluating the impact of positive fluid balance on mortality and length of stay in septic shock patients. Cureus 2022;14:e24809.
28. Abraham BP, Frazier EA, Morrow WR, Blaszak RT, Devarajan P, Mitsnefes M, *et al*. Cystatin C and neutrophil gelatinase-associated lipocalin as markers of renal function in pediatric heart transplant recipients. Pediatr Transplant 2011;15:564-9.
29. Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA, *et al*. Lactate clearance versus central venous oxygen saturation as goals of early sepsis therapy: A randomized clinical trial. JAMA 2010;303:739-46.