Clinical research protocol

Project name: The value of critical care ultrasound and noninvasive cardiac output monitoring in guiding fluid resuscitation for septic shock in the emergency department

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Department: Emergency Department

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object name	The value of critical care ultrasound and non-invasive cardiac output monitoring in fluid resuscitation for emergency department patients with septic shock.
goal of study	This study explores the value of critical care ultrasound and non-invasive cardiac output monitoring in fluid resuscitation for emergency department patients with septic shock, providing evidence for optimizing hemodynamic management of septic shock, improving patient prognosis, and guiding clinical selection of appropriate monitoring modalities.
research design	Subjects were recruited from patients with septic shock admitted to the Emergency Department of Guangzhou Panyu District Central Hospital between July 2023 to luly 2025. Demographic data of patients, including gender, age, and underlying diseases, were collected, along with mean arterial pressure, baseline lactate levels, and vital signs at enrollment. Records were made of the total fluid volume administered within the first 6 hours after patients were randomized into groups, the achievement of resuscitation targets, blood lactate levels, blood pressure, and the incidence of complications such as pulmonary edema and renal injury. Additionally, the use of vasoactive agents (e.g., dopamine, epinephrine/norepinephrine), mechanical ventilation support, and antibiotics was documented. Patients were followed up to record the duration of emergency department stay, total hospital stay, 28-day mortality, and adverse events occurring during the study period (e.g., severe arrhythmias, anaphylactic shock).
Total number of cases studied	60 cases (30 cases in each group)

case selection	Inclusion criteria: (1) diagnosis of septic shock in accordance with the Surviving Sepsis Campaign International; (2) receipt of initial fluid resuscitation in the emergency department with a hospital stay of at least 6 hours; (3) age ≥ 18 years; (4) provision of informed consent.
	excluded criteria: (1) contraindications to rapid fluid administration (e.g., end-stage renal disease, end-stage heart failure, acute pulmonary edema); (2) inability to comply with treatment, such as patients with severe trauma, burns, cancer undergoing chemotherapy, pregnant or lactating women, and those with mental illness; (3) withdrawal from treatment or transfer to another facility within 24 hours of admission.
Treatment plan	Both groups were managed according to the 2021 Surviving Sepsis Campaign (SSC) International Guidelines for septic shock resuscitation, including: (1) early antimicrobial therapy, (2) vasopressor support (with norepinephrine as first-line), and (3) organ function support. The key difference between groups lay in the fluid resuscitation monitoring approach (critical care ultrasound vs. noninvasive cardiac output monitoring)
efficacy evaluation	The main efficacy indicators: emergency department length of stay, total hospital stay. Secondary efficacy indicators: regarding total fluid volume within the first 6 hours of resuscitation, early resuscitation efficacy (time to achieve mean arterial pressure ≥65 mmHg, lactate reduction ≥20% from baseline, or lactate clearance ≥ 10%), complication rates (including pulmonary edema, renal injury, and acute respiratory distress syndrome).

	Safety evaluation index: 28-day mortality.
statistical method	This study adopted a prospective randomized controlled design, and the sample size was estimated using PASS 15.0 software. Based on the difference in 6-hour fluid resuscitation volume between the two groups in the pilot study (mean difference 1261 mL, standard deviation 3155 mL), α=0.05 (bilateral) was set β=0.2, Calculated to require 27 cases per group, considering a 20% dropout rate, 60 cases were ultimately included. Use SPSS 26.0 to generate block random sequences (block size 4), and allocate concepts through sealed envelopes. The normality of the measurement data was confirmed by Shapiro Wilk test, and those that conform to the normal distribution were expressed as mean ± standard deviation. Independent sample t-test was used for inter group comparison; non normally distributed individuals are represented by the median (interquartile range) and Mann Whitney U test is used. The categorical data is presented in terms of the number of cases (%), and the comparison between groups is conducted using the chi square test or Fishers exact test (when the theoretical frequency is less than 5). The main outcome (28 day mortality rate) was plotted using Kaplan Meier survival curve, and inter group differences were analyzed using log rank test, and HR (95% CI) was calculated. Secondary outcomes (such as fluid dosage, MAP, etc.) report mean difference (MD) or relative risk (RR) and their 95% confidence intervals. All tests are bilateral, and $P<0.05$ is considered statistically significant. Perform Bonferroni correction on secondary outcomes ($\alpha=0.05/6 \approx 0.008$). Multivariate Cox regression was used to adjust for confounding factors such as age and baseline lactate, and sensitivity analysis included protocol set (PP) and intention to treat (ITT) analyses. The statistical software used is R 4.3.1 (R Foundation) and SPSS 26.0 (IBM).

Research period	July 2023 to luly 2025

(1)Research background

Septic shock represents the severe phase of infection-induced systemic inflammatory response syndrome (SIRS), characterized by a complex pathophysiological mechanism. It is primarily manifested as vasodilation, capillary leakage, and myocardial depression triggered by SIRS, with persistent hypotension, tissue hypoperfusion, and multiple organ dysfunction resulting from insufficient effective circulating blood volume as the main clinical features. With a mortality rate exceeding 40%, it ranks among the common critical illnesses in the emergency department. International guidelines for the management of septic shock highlight that early goal-directed fluid resuscitation is the cornerstone of septic shock treatment. It aims to alleviate the systemic damage caused by shock by rapidly restoring effective circulating blood volume and increasing tissue oxygen delivery, thereby improving prognosis and enhancing quality of life. Consequently, fluid resuscitation holds an irreplaceable role in the management of septic shock, and the first 6 hours after shock recognition, in particular, is designated as the "golden resuscitation period" . However, both excessive and insufficient fluid resuscitation may exacerbate the condition and elevate the risk of complications such as pulmonary edema, acute respiratory distress syndrome (ARDS), and acute kidney injury (AKI). Thus, how to rapidly and accurately assess a patients volume status and cardiac function in the emergency department, formulate individualized fluid resuscitation strategies, achieve precise volume management, and avoid over-resuscitation or under-resuscitation has become an urgent clinical challenge.

Traditional fluid resuscitation strategies rely predominantly on static parameters such as central venous pressure (CVP), mean arterial pressure (MAP), and urine output for guidance. However, these indices have inherent limitations in assessing volume responsiveness and predicting fluid resuscitation efficacy, failing to accurately and dynamically reflect a patients volume status or cardiac preload responsiveness. In recent years, with advances in hemodynamic monitoring technologies, dynamic evaluation of volume responsiveness has emerged as a key strategy for optimizing fluid resuscitation and improving patient outcomes.

Critical care ultrasound, for instance, enables rapid bedside assessment of cardiopulmonary function by real-time visualization of indices including inferior vena cava variability, ventricular wall motion, volume responsiveness, and lung water content, thereby providing visual evidence to guide early fluid resuscitation. Non-invasive cardiac output monitoring, conversely, dynamically tracks circulatory function through quantification of parameters such as cardiac output and stroke volume variability, offering objective data to evaluate resuscitation efficacy. Accordingly, critical care ultrasound and non-invasive cardiac output monitoring have increasingly become valuable clinical adjuncts in guiding fluid resuscitation for patients with septic shock in the emergency department.

(2) research objective

1. Main Objective: This study explores the value of critical care ultrasound and non-invasive cardiac output monitoring in fluid resuscitation for emergency department patients with septic shock, providing evidence for optimizing hemodynamic management of septic shock, improving patient prognosis, and guiding clinical selection of appropriate monitoring modalities.

2.Secondary purpose: This study aims to explore the value of critical care ultrasound and non-invasive cardiac output monitoring in fluid resuscitation for emergency department patients with septic shock, to inform optimized hemodynamic management, improve prognosis, and guide clinical selection ofmonitoring modalities.

(3) Research Design Types, Principles, and Test Procedures

1. Research Design

Subjects were recruited from patients with septic shock admitted to the Emergency Department of Guangzhou Panyu District Central Hospital between July 2023 to luly 2025. Demographic data ofpatients, including gender, age, and underlying diseases, were collected, along with mean arterial pressure, baseline lactate levels, and vital signs at enrollment. Records were made of the total fluid volume administered within the first 6 hours after patients were randomized into groups, the achievement of resuscitation targets,

blood lactate levels, blood pressure, and the incidence of complications such as pulmonary edema and renal injury. Additionally, the use of vasoactive agents (e.g., dopamine, epinephrine/norepinephrine), mechanical ventilation support, and antibiotics was documented. Patients were followed up to record the duration of emergency department stay, total hospital stay, 28-day mortality, and adverse events occurring during the study period (e.g., severe arrhythmias, anaphylactic shock).

After patients met the inclusion criteria and signed the informed consent form, random numbers were generated using SPSS 26.0 statistical software to randomly assign 73 participants to the critical care ultrasound group and the non-invasive cardiac output group. The generated random allocation table was prepared in duplicate, which were sealed and stored by the statistician and research coordinator respectively to prevent premature disclosure of group allocation information.

In the critical care ultrasound group, patients underwent immediate bedside assessment using a Philips EPIQ 5 color Doppler ultrasound system equipped with both phased-array (1.5-4.0 MHz) and convex-array (2.0-5.0 MHz) transducers. The initial ultrasound evaluation was completed within 10 minutes of enrollment and included comprehensive hemodynamic monitoring: inferior vena cava diameter (IVC) and collapsibility index (IVC-CI) for volume status assessment, left ventricular ejection fraction (LVEF) and end-diastolic volume (LVEDV) for cardiac function evaluation, ventricular wall motion analysis, along with pulmonary B-line quantification to assess pulmonary edema. This protocol ensured real-time, comprehensive evaluation of both cardiac function and fluid status to guide resuscitation. Ultrasound reassessment was performed every 1-2 hours to dynamically adjust both the volume and rate of fluid administration until predefined resuscitation targets were achieved.

In the noninvasive cardiac output monitoring group, continuous hemodynamic assessment was performed using the NICOM system based on thoracic bioreactance technology. Following the manufacturers standard operating procedures, four electrode pads were placed at bilateral subclavicular areas and the left subcostal region. Monitoring commenced immediately after

enrollment, with baseline parameters recorded after signal stabilization (≤5 minutes), including cardiac output (CO), stroke volume (SV), stroke volume variation (SVV), and systemic vascular resistance (SVR). The system automatically updated these parameters every 30 seconds and displayed them in real-time on the monitor screen. Fluid resuscitation was dynamically adjusted according to these continuous measurements until achieving the predefined therapeutic targets.

(4) case selection

1. Inclusion criteria:

(1) diagnosis of septic shock in accordance with the Surviving Sepsis Campaign International; (2) receipt of initial fluid resuscitation in the emergency department with a hospital stay of at least 6 hours; (3) age ≥ 18 years; (4) provision of informed consent.

2. excluded criteria:

(1) contraindications to rapid fluid administration (e.g., end-stage renal disease, end-stage heart failure, acute pulmonary edema); (2) inability to comply with treatment, such as patients with severe trauma, burns, cancer undergoing chemotherapy, pregnant or lactating women, and those with mental illness; (3) withdrawal from treatment or transfer to another facility within 24 hours of admission.

3. Elimination criteria

Subjects who have been enrolled in the study but meet one of the following criteria should be excluded:

(1) After inclusion, those who did not meet the inclusion criteria or met the exclusion criteria were found.

(2) Those who have not used test drugs / interventions.

4. Standard for suspension of research

(1) If the following conditions occur during the experiment: cardiac arrest, intestinal perforation, intracranial and other serious complications; (2) the need for rescue is not suitable for experimental related operators; (3) The competent physician believes that the clinical condition is not suitable for continuing the experiment; (4) If the clinical symptoms

and other auxiliary examinations are inconsistent with the relevant non-invasive examination results; (5) Someone did not agree to continue the experiment during the experiment.

5 . Drop-out / exit criteria

Expulsion / withdrawal criteria: (1) the competent physician believes that the clinical condition is not suitable for the continuation ofthe experiment; (2) Ifthe clinical symptoms and other auxiliary examinations are inconsistent with the relevant non-invasive examination results; (3) Someone did not agree to continue the experiment during the experiment.

(5)research method

Subjects were recruited from patients with septic shock admitted to the Emergency Department of Guangzhou Panyu District Central Hospital between December 2022 and January 2026. Demographic data ofpatients, including gender, age, and underlying diseases, were collected, along with mean arterial pressure, baseline lactate levels, and vital signs at enrollment. Records were made of the total fluid volume administered within the first 6 hours after patients were randomized into groups, the achievement of resuscitation targets, blood lactate levels, blood pressure, and the incidence of complications such as pulmonary edema and renal injury. Additionally, the use of vasoactive agents (e.g., dopamine, epinephrine/norepinephrine), mechanical ventilation support, and antibiotics was documented. Patients were followed up to record the duration of Emergency Department stay, total hospital stay, 28-day mortality, and adverse events occurring during the study period (e.g., severe arrhythmias, anaphylactic shock).

(6) Observation items and detection time points

1. Demographic data of patients, including gender, age, and underlying diseases, were collected, along with mean arterial pressure, baseline lactate levels, and vital signs at enrollment.

2. Records were made ofthe total fluid volume administered within the first 6 hours after patients were randomized into groups, the achievement of resuscitation targets, blood

lactate levels, blood pressure, and the incidence of complications such as pulmonary edema and renal injury.

3. Document the use of vasoactive agents (e.g., dopamine, epinephrine/norepinephrine), mechanical ventilation support, and antibiotics.

4. Record the duration of Emergency Department stay, total hospital stay, 28-day mortality, and adverse events occurring during the study period (e.g., severe arrhythmias, anaphylactic shock).

(7) standards for efficacy appraisal

The primary outcome was 28-day mortality

Secondary outcomes included the efficacy of initial resuscitation, duration of hospital stay, incidence of complications, and other relevant parameters.

(8) Observation of adverse events

Observation of adverse events: Clinicians should evaluate the fluid resuscitation of children at any time during the experiment. If the clinical symptoms and other auxiliary examinations (such as heart rate, liver size, mental state, X-ray, blood gas analysis, etc.) If they are inconsistent with the relevant non-invasive examinations, the experiment should be terminated immediately and the superior physician should be found in time to assist.

(9)Data security monitoring

Clinical research will develop a corresponding data security monitoring plan based on the size ofthe risk. All adverse events were recorded in detail, properly handled and tracked until they were properly resolved or stable. Serious adverse events and unexpected events were reported to the ethics committee, competent authorities, sponsors and drug supervision and management departments in a timely manner according to the regulations. The main researchers regularly conduct a cumulative review of all adverse events, and if necessary, convene a meeting of researchers to assess the risks and benefits ofthe study; research that is greater than the minimum risk will arrange independent data monitors to monitor the research data, and high-risk research will establish an independent data security supervisory

committee to monitor the accumulated security data and effectiveness data to make recommendations on whether the research will continue.

(10)Statistical processing

This study adopted a prospective randomized controlled design, and the sample size was estimated using PASS 15.0 software. Based on the difference in 6-hour fluid resuscitation volume between the two groups in the pilot study (mean difference 1261 mL, standard deviation 3155 mL), α=0.05 (bilateral) was set β=0.2, Calculated to require 27 cases per group, considering a 20% dropout rate, 60 cases were ultimately included. Use SPSS 26.0 to generate block random sequences (block size 4), and allocate concepts through sealed envelopes. The normality of the measurement data was confirmed by Shapiro Wilk test, and those that conform to the normal distribution were expressed as mean ± standard deviation. Independent sample t-test was used for inter group comparison; non normally distributed individuals are represented by the median (interquartile range) and Mann Whitney U test is used. The categorical data is presented in terms ofthe number ofcases (%), and the comparison between groups is conducted using the chi square test or Fishers exact test (when the theoretical frequency is less than 5). The main outcome (28 day mortality rate) was plotted using Kaplan Meier survival curve, and inter group differences were analyzed using log rank test, and HR (95% CI) was calculated. Secondary outcomes (such as fluid dosage, MAP, etc.) report mean difference (MD) or relative risk (RR) and their 95% confidence intervals. All tests are bilateral, and $P<0.05$ is considered statistically significant. Perform Bonferroni correction on secondary outcomes ($\alpha=0.05/6 \approx 0.008$). Multivariate Cox regression was used to adjust for confounding factors such as age and baseline lactate, and sensitivity analysis included protocol set (PP) and intention to treat (ITT) analyses. The statistical software used is R 4.3.1 (R Foundation) and SPSS 26.0 (IBM).

(11) Ethics in clinical research

Clinical research will follow the World Medical Congress Helsinki Declaration and other relevant provisions. Before the study began, the clinical study was carried out after the

ethics committee approved the test plan. Before each subject is selected for this study, the researcher has the responsibility to fully and comprehensively introduce the purpose, procedure and possible risks ofthis study to the subjects or their agents, and to sign a written informed consent form. The subjects should be informed that they have the right to withdraw from the study at any time. Informed consent should be retained as a clinical research document for review. The personal privacy and data confidentiality ofthe subjects will be protected during the study.

(12)Research progress

From June 2023 to june 2023 : Preparation stage for the experiment: ① Prepare relevant instruments and equipment, as well as equipment maintenance, testing, and parameter calibration; ② Recruitment and training of staff, clear division of labor and job responsibilities, and familiarity with the experimental process; ③ Complete the pre experiment.

From july 2023 to july 2025 : Recruit research subjects and conduct clinical trials. ① Recruit research subjects and implement interventions in groups according to the randomization plan; ② Record the relevant data of the experiment and follow up on the prognosis for 28 days.

From July 2025 to December 2025 : Organize research data and conduct statistical analysis; Writing and submitting research papers.Summarize research results and write a project summary report.

(13) Reference

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