Clinical Trial Protocol
Iranian Registry of Clinical Trials

25 Aug 2026

Effect of Early HA380 Hemoperfusion on Hemodynamic Recovery and Organ Dysfunction in Adult Patients with Septic Shock

Protocol summary

Study aim

To determine whether early HA380 hemoperfusion reduces vasopressor requirement and improves organ dysfunction compared with standard care alone in adult septic shock patients.

Design

Randomized, parallel-group, open-label, controlled clinical trial on 76 patients (38 in each group). Randomization was by alternating block design with blocks of 4 and 6, 1:1 ratio. Allocation by sealed envelopes, no blinding.

Settings and conduct

After consent, patients are randomized. Intervention: standard sepsis care + HA380 hemoperfusion (standalone machine, within 12 hours, daily 4-hour sessions for 3 days, blood flow 150–200 mL/min, systemic heparin). CRRT if needed after 3 sessions. Control: standard sepsis care without hemoperfusion. CRRT as indicated. Primary outcome: Change in SOFA score from baseline at Days 1, 3, and 7. Secondary outcomes: Change in norepinephrine dose, capillary refill time, VIS, PaO_2/FiO_2 ratio, lactate clearance, 28-day mortality, vasopressor-free days, ventilator-free days. Blinding: Open-label. Statistician blinded (groups A/B). Setting: Adult ICU, Milad Hospital, Urmia Azad University, Iran.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Age ≥ 18 years, septic shock (Sepsis-3), norepinephrine 0.1–0.2 mcg/kg/min, lactate ≥ 2 mmol/L, SOFA ≤ 7, enrollment within 12 hours of shock onset, informed consent. Exclusion criteria: Active major bleeding, platelets < 30,000/µL, severe liver failure (Child-Pugh C), end-stage malignancy, pregnancy, expected death within 24 hours, refusal.

Intervention groups

Intervention group: Standard sepsis care + HA380 hemoperfusion Control group: Standard sepsis care without hemoperfusion. CRRT if needed.

Main outcome variables

Sequential Organ Failure Assessment (SOFA) Score

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20260527069547N1**
Registration date: **2026-08-19, 1405/05/28**
Registration timing: **prospective**

Last update: **2026-08-19, 1405/05/28**
Update count: **0**

Registration date

2026-08-19, 1405/05/28

Registrant information

Name

Amir Saeed

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-08-23, 1405/06/01

Expected recruitment end date

2027-08-23, 1406/06/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title
Effect of Early HA380 Hemoperfusion on Hemodynamic Recovery and Organ Dysfunction in Adult Patients with Septic Shock

Public title
HA380 Hemoperfusion Effects in Septic Shock

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Age ≥ 18 years Septic shock according to Sepsis-3 definition Norepinephrine ≤ 0.2 mcg/kg/min or SOFA ≤ 7 Serum lactate ≥ 2 mmol/L Enrollment within 12 hours of shock diagnosis

Exclusion criteria:
Active major bleeding Platelet count < 30,000/µL Severe chronic liver failure (Child-Pugh C) End-stage malignancy (life expectancy < 3 months) Pregnancy Expected death within 24 hours Refusal of consent Chronic heart disease Chronic kidney failure Patients on long-term immunosuppressive therapy Patients with CAP(Community-acquired pneumonia)

Age
From **18 years** old

Gender
Both

Phase
N/A

Groups that have been masked
No information

Sample size
Target sample size: **38**

Randomization (investigator's opinion)
Randomized

Randomization description
Randomization Method: Permuted block randomization with randomly varying block sizes of 4 or 6 will be used to ensure balanced allocation between the two groups. Allocation Ratio: 1:1 (intervention : control). Allocation Concealment: The randomization sequence will be generated by an independent statistician (not involved in screening, enrollment, or treatment) using statistical software. Allocation codes will be placed in sequentially numbered, opaque, sealed envelopes (SNOSE). Envelopes will be opened by the principal investigator only after informed consent is obtained. Sequence Generation: A random number sequence will be generated using statistical software (e.g., Stata, R, or SAS) with a random seed. Documentation: The randomization list will be kept by the independent statistician and will not be accessible to the clinical research team until data collection and database lock are completed.

Blinding (investigator's opinion)
Not blinded

Blinding description

Placebo
Not used

Assignment
Parallel

Other design features
1. A deliberate enrichment strategy is employed, selecting patients with early, moderate septic shock (norepinephrine ≤ 0.2 mcg/kg/min and SOFA ≤ 7) per sponsor recommendation. This excludes patients with advanced, potentially irreversible organ failure who may not benefit from standalone hemoperfusion .2.Separation of Hemoperfusion from CRRT: Unlike other studies, HA380 is delivered via a standalone hemoperfusion machine, not integrated into a CRRT circuit. This avoids confounding from concurrent CRRT, enhances treatment standardization, and allows clean assessment of HA380 efficacy. CRRT may be initiated in both groups after the 3-day intervention period if clinically indicated. 3. Fixed-Duration Intervention: A fixed 3-day, 4-hour-per-session course is used rather than response-guided duration, enabling assessment of a cumulative effect while avoiding bias from clinician decisions to continue or stop therapy early. 4.Time-Window Design: Hemoperfusion must start within 6–8 hours of shock onset, rigorously defined, to maximize the chance of modulating the inflammatory response before irreversible organ failure occurs. 5.Multi-Timepoint Primary Endpoint with Day 3 Focus: SOFA change is measured at Days 1, 3, and 7 and analyzed using a mixed model for repeated measures. Day 3 (72 hours) is the principal time point of interest, immediately after the 3-day hemoperfusion course and before hospital-acquired infections become a major confounder. 6.Competing Risk Handling: To address the competing risk of death, deceased patients are assigned the maximum SOFA score (24) for subsequent time points. Survival and composite outcome sensitivity analyses are pre-specified. 7.Statistician Blinding: Despite the open-label design, the study statistician performing primary and final analyses remains blinded to group allocation (groups coded as A/B) until the statistical analysis plan is finalized and analyses are complete.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Research Ethics Committees, Research Ethics Committee of Islamic Azad University-Urmia Branch

Street address
Salmas Road (start of the road)

City
Urmia

Province
West Azarbaijan

Postal code
5716963896

Approval date
2026-06-13, 1405/03/23

Ethics committee reference number
IR.IAU.URMIA.REC.1405.035

Health conditions studied

1

Description of health condition studied
Septic Shock
ICD-10 code
R65.21
ICD-10 code description
Severe sepsis with septic shock

Primary outcomes

1

Description
Change in Sequential Organ Failure Assessment (SOFA) Score from Baseline at Days 1, 3, and 7
Timepoint
Baseline (before intervention) and at Days 1, 3, and 7
Method of measurement
Sequential Organ Failure Assessment (SOFA) Score — the standard version recommended by the Sepsis-3 Task Force of the European Society of Intensive Care Medicine (ESICM). The tool grades dysfunction in 6 organ systems (respiratory, coagulation, hepatic, cardiovascular, neurological, renal) on a scale of 0 (normal) to 4 (severe failure). Total score ranges from 0 to 24. Originally developed by Vincent et al. (1996) and validated in numerous critical care studies.

Secondary outcomes

1

Description
Change in Norepinephrine Dose (mcg/kg/min) from Baseline at 24, 48, and 72 Hours
Timepoint
Baseline (before intervention) and at 24, 48, and 72 Hours
Method of measurement
Norepinephrine infusion rate recorded from the syringe infusion pump via the electronic medical record or ICU monitoring chart, expressed as micrograms per kilogram of body weight per minute

2

Description
Vasopressor-Free Days at Day 1, Day 3, and Day 7
Timepoint
Day 1, Day 3, and Day 7
Method of measurement
Number of complete calendar days (24-hour periods) during which the patient is alive and free from any vasopressor infusion (norepinephrine, epinephrine, vasopressin, dopamine, phenylephrine), measured from enrollment to the end of the specified day. If the patient dies, the value is zero. Data are extracted from daily ICU monitoring charts.

3

Description
Capillary Refill Time (CRT) Baseline(before intervention) and at 24, 48, and 72 Hours
Timepoint
Baseline (before intervention) and at 24, 48, and 72 Hours
Method of measurement
Standardized capillary refill time measurement by applying firm pressure to the volar surface of the distal phalanx of the index finger for 5 seconds using a glass slide or examiner's finger, then releasing and measuring the time to return of normal color with a stopwatch in seconds. Room temperature is recorded at the time of measurement. A value of ≥ 3 seconds is considered abnormal.

4

Description
Vasoactive-Inotropic Score (VIS) Baseline(before intervention) and at 24, 48, and 72 Hours
Timepoint
Baseline (before intervention) and at 24, 48, and 72 Hours
Method of measurement
Vasoactive-Inotropic Score (VIS) calculated using the standard formula:VIS = dopamine dose + dobutamine dose + (100 × epinephrine dose) + (100 × norepinephrine dose) + (10,000 × vasopressin dose) + (10 × milrinone dose)All doses are expressed in mcg/kg/min (vasopressin in units/kg/min). Data are extracted from infusion pumps and ICU monitoring charts at the specified time points.

5

Description
Lactate Clearance at 24 Hours
Timepoint
Baseline (before intervention) and at hour 0(before intervention) and 24
Method of measurement
Serum lactate concentration measured from arterial or venous blood gas samples analyzed by the standard ICU blood gas analyzer. Lactate clearance at 24 hours is calculated as:Lactate clearance (%) = [(Baseline lactate − Lactate at 24 h) / Baseline lactate] × 100

6

Description
PaO_2/FiO_2 Ratio at Baseline, 24, 48, and 72 Hours
Timepoint
Baseline (before intervention), 24, 48, and 72 Hours
Method of measurement
PaO_2/FiO_2 ratio calculated from arterial oxygen tension (PaO_2) measured by arterial blood gas analyzer and fraction of inspired oxygen (FiO_2) set on the ventilator or

oxygen delivery device. Both values are recorded simultaneously from the ICU respiratory monitoring chart. Ratio is expressed in mmHg.

7

Description
28-Day All-Cause Mortality
Timepoint
The first 28-Day of ICU admission
Method of measurement
Patient vital status at 28 days after enrollment, ascertained from hospital records, telephone follow-up with family members, or national vital registry. Death from any cause is recorded.

8

Description
ICU (intensive care unit) Length of Stay
Timepoint
Total day of ICU admission
Method of measurement
Number of complete calendar days spent in the ICU, from the date of ICU admission to the date of ICU discharge or death. If the patient dies in the ICU, length of stay equals the number of days from admission to death. Data extracted from the Hospital Information System (HIS).

9

Description
Ventilator-Free Days at Day 28
Timepoint
ICU (intensive care unit) Length of Stay
Method of measurement
Number of complete calendar days (24-hour periods) within the first 28 days after enrollment during which the patient is alive and free from invasive mechanical ventilation (endotracheal tube or tracheostomy). If the patient is extubated during a day and remains extubated until the end of that day (23:59), that day counts as a ventilator-free day. If the patient dies, the value is zero. Data extracted from ICU respiratory monitoring charts.

Intervention groups

1

Description
Intervention group: Patients randomized to the intervention group will receive standard sepsis care plus hemoperfusion with the HA380 cartridge (Jafron Biomedical, China). The intervention specifications are as follows:Timing of Initiation:Hemoperfusion will be initiated within 12 hours of septic shock diagnosis. Shock onset is defined as the time vasopressor infusion (norepinephrine) is started at ≥ 0.1 μg/kg/min in the presence of serum lactate ≥ 2 mmol/L and persistent hypotension despite adequate fluid resuscitation.Mode of Delivery:Hemoperfusion will be performed using a standalone hemoperfusion machine, not integrated into a CRRT circuit. This approach is chosen to enhance treatment consistency and avoid potential confounding from CRRT-related factors. If the patient has no indication for CRRT at enrollment, they will receive standalone hemoperfusion only.Technical Specifications:Cartridge: HA380Blood flow rate: 150–200 mL/minDuration per session: 4 hoursFrequency: Once daily for 3 consecutive days (total of 3 sessions)Vascular Access:A double-lumen central venous catheter (minimum 12 Fr) inserted into the femoral or internal jugular vein.Anticoagulation:Systemic unfractionated heparin according to the ICU standard protocol (target activated partial thromboplastin time: 1.5–2.0 times normal).CRRT After Hemoperfusion:After completion of the 3 HA380 hemoperfusion sessions, if the patient's condition deteriorates and clinical indications for CRRT develop (refractory oliguria, severe metabolic acidosis, refractory hyperkalemia, or fluid overload unresponsive to diuretics), the patient in the intervention group may receive CRRT at the discretion of the treating ICU physician. This decision will be documented in the medical record.
Category
Treatment - Devices

2

Description
Control group: The control group will receive standard septic shock management according to the Surviving Sepsis Campaign international guidelines. CRRT may be initiated at any time if clinically indicated, at the discretion of the treating physician.
Category
N/A

Recruitment centers

1

Recruitment center
Name of recruitment center
Urmia Islamic Azad University, Milad Hospital
Full name of responsible person
Amir Saeed
Street address
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Email
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Islamic Azad University
Full name of responsible person
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
No

Title of funding source
Jafron Biomedical Co., LTD.

Proportion provided by this source
100

Public or private sector
Private

Domestic or foreign origin
Foreign

Category of foreign source of funding
Sponsor: country of origin

Country of origin
CN

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Islamic Azad University
Full name of responsible person
Amir Saeed
Position
Assistant professor
Latest degree
Subspecialist
Other areas of specialty/work
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Latest degree
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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

No - There is not a plan to make this available

Clinical Study Report

Not applicable

Analytic Code

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

Documents and Data Files to be Shared: Study Protocol: The final complete protocol (including background, objectives, design, methods, inclusion/exclusion criteria, interventions, outcomes, and statistical analysis plan) will be submitted for publication in an international peer-reviewed journal (such as BMJ Open or Trials) after ethics approval and trial registration. A PDF copy will also be available upon request via email from the corresponding author. Statistical Code: All statistical programming commands used for primary and secondary outcome analyses (including Stata or R code) will be published as supplementary files alongside the main manuscript. These files contain only statistical commands and no individual patient data. Data Dictionary: A comprehensive variable guide including variable names, definitions (Persian and English), data types (numeric/text/date), permissible values (minimum, maximum, coding), and data sources (ICU chart, laboratory, clinical examination) will be published alongside the statistical code. Individual Participant Data (IPD): The decision regarding sharing of de-identified IPD will be made after consultation with the ethics committee and research team, and based on the requirements of the target journal. If sharing is approved, only fully anonymized data related to the primary and key secondary outcomes (SOFA scores, vasopressor doses, CRT, VIS, lactate, PaO_2/FiO_2, mortality, and length of stay) will be made available to qualified researchers upon formal request to the corresponding author and signature of a Data Sharing Agreement. Detailed demographic data that could enable indirect identification (such as exact age combined with admission date) will not be shared.

When the data will become available and for how long

Study Protocol: The final protocol will be submitted for publication in an international peer-reviewed journal within 6 months of ethics committee approval and IRCT registration. A PDF copy will be available upon request via email from the corresponding author from that time onward. Statistical Code and Data Dictionary: These will be published as supplementary files on the journal's website simultaneously with the main results paper. Estimated timeline: 6 to 12 months after completion of data collection and final analysis. Individual Participant Data (IPD): If the decision to share is made, access to de-identified IPD will begin 12 months after publication of the main results (estimated: Summer 2029) and will remain available for 5 years. Requests during this period will be reviewed by the corresponding author, and data will be provided to qualified applicants upon approval.

To whom data/document is available

1.Study Protocol, Statistical Code, and Data Dictionary: These documents will be openly accessible without restriction via the publishing journal's website or upon request to the corresponding author, available to researchers, clinicians, and students worldwide. 2.Individual Participant Data (IPD): If the decision to share is made, access to de-identified IPD will be restricted to qualified researchers affiliated with accredited academic, scientific, and research institutions (universities, teaching hospitals, research centers). Applicants must: Submit a valid research proposal with clear scientific objectives. Have verifiable research experience in critical care, sepsis, or emergency medicine. Sign a Data Sharing Agreement stipulating that data will be used solely for the stated research purpose and will not be transferred or sold to third parties. Obtain approval from the Ethics Committee of Urmia University of Medical Sciences for use of the data. Industry Personnel: Requests from individuals or entities in industry (including pharmaceutical companies, medical device manufacturers, and health insurers) will be reviewed on a case-by-case basis by the research team and ethics committee, and are contingent upon submission of a scientific proposal with research (not commercial) objectives.

Under which criteria data/document could be used

A) Study Protocol, Statistical Code, and Data Dictionary (Open Access): Use for educational, research, and scientific purposes is freely permitted. Citation of the original publication is mandatory in any use. Commercial use or sale of these documents is prohibited. B) De-identified Individual Participant Data (IPD): 1. Permitted Types of Analysis: Statistical analyses related to sepsis outcomes and organ dysfunction Individual Patient Data Meta-analysis with ethics committee approval Validation studies of prognostic tools in sepsis Pre-specified secondary analyses with clear scientific objectives (not purely exploratory) All analyses must be pre-defined in the submitted proposal. 2. Prohibited Uses: Analysis for commercial purposes, marketing, or product development Re-identification of patients (including attempted re-identification) Transfer or sale of data to third parties Public dissemination of raw data Use in studies without ethics committee approval 3. Request Review and Approval Mechanism: Formal written request to the corresponding author via email Submission of a complete research proposal including: title, objectives, methods, planned analyses, research team, and their credentials Initial approval by the primary research team (assessment of scientific merit and overlap with ongoing analyses) Approval by the Ethics Committee of Urmia University of Medical Sciences Signature of a Data Sharing Agreement including the following clauses: Use solely for the approved research purpose No attempt to identify patients Deletion of data upon completion of the research Reporting of potential violations to the ethics committee Citation of the original study in resulting publications 4. Data Format and Delivery: Data will be provided as password-protected Excel or CSV files. Files

will be sent only to the applicant's institutional email address (personal emails not accepted). Data will be stripped of all direct identifiers (name, national ID, medical record number, exact admission date) and indirect identifiers that could enable identification alone or in combination. 5. Response Timeline: Initial approval or rejection: within 4 weeks of receiving a complete request Data delivery after final approval: within 8 weeks

From where data/document is obtainable

Guidance for Requesting Access to Documents and Data: Applicants may request study documents or data through the following channels, in order of priority: 1. Study Protocol, Statistical Code, and Data Dictionary (Open Access): These documents will be freely available as supplementary files on the publishing journal's website upon publication of the main article. If the journal website is inaccessible, applicants may contact the corresponding author via email. 2. Individual Participant Data (IPD) and Unpublished Documents: All formal requests must be sent to the Corresponding Author: Contact Information Name and Title: Dr. Amir Saeed – Principal Investigator and Corresponding Author Institutional Affiliation: Urmia University of Medical Sciences – Milad Hospital Postal Address: Adult Intensive Care Unit (ICU), Milad Hospital, Urmia, West Azerbaijan Province, Iran Postal Code: 5719151193 Email: Dr.saeedamir@umsu.ac.ir Alternative Email: (Insert alternative institutional email if available) Phone: +98-44-XXXXXXX (Direct line to ICU or Milad Hospital office) Fax: +98-44-XXXXXXX

What processes are involved for a request to access data/document

a) Send a formal email from the applicant's institutional email address with the subject line: "Data Access Request – HA380 Septic Shock Trial" b) Attach the following documents: Complete research proposal (PDF) Summary CV of the lead applicant Names and institutional affiliations of all research team members Ethics committee approval from the applicant's institution (if available) c) Await initial response within 4 weeks. If approved, subsequent steps including signing the Data Sharing Agreement and obtaining approval from the Urmia University of Medical Sciences Ethics Committee will be coordinated via email. 4. Priority of Contact Methods: Priority Method Details 1 Institutional Email Preferably from an academic domain (edu. or ac.ir) 2 Personal Email Only if institutional email is unavailable 3 Formal Letter To the postal address above (in exceptional cases) 4 Telephone For follow-up only, not for initial requests Important Notes: Requests sent from personal emails (Gmail, Yahoo, etc.) will only be reviewed if the applicant has no institutional email. Incomplete requests (lacking a research proposal) will not be reviewed. All correspondence and documents are accepted in English or Persian.

Comments

Additional Information and Comments: Enriched Design: This study deliberately selects patients with early-stage septic shock (norepinephrine ≤ 0.2 and SOFA ≤ 7) to assess the efficacy of standalone HA380 hemoperfusion within the "therapeutic window" before the onset of irreversible organ failure. Patients with advanced organ failure who are likely to require CRRT are excluded. Separation from CRRT: Unlike many similar studies, HA380 is delivered via a standalone machine, not integrated into a CRRT circuit. This approach is designed to avoid confounding by concurrent CRRT and to more precisely evaluate the efficacy of HA380 as an independent therapy. CRRT, if clinically indicated, is initiated only after completion of the 3 hemoperfusion sessions. Funding: This study is funded by [Sponsor name: Jafron Biomedical / Urmia Azad University of Medical Sciences / Other]. HA380 cartridges are provided by Jafron Biomedical (China). The sponsor has no role in data collection, statistical analysis, interpretation of results, or the decision to publish. Conflict of Interest: The investigators declare no financial, personal, or professional conflicts of interest related to this study. Acknowledgments: The research team gratefully acknowledges the cooperation of the ICU staff at Milad Hospital, the Ethics Committee of Urmia University of Medical Sciences, and Jafron Biomedical for providing HA380 cartridges and technical support. Protocol Amendments: Any amendments to the study protocol (including changes to inclusion criteria, intervention, or outcomes) will be updated on IRCT following ethics committee approval.