INPLASY PROTOCOL

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Support: **None.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

Clinical indicators of systemic tissue hypoperfusion ('shock'): A protocol for a systematic review and qualitative analysis of the literature

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Review question / Objective: **The objective of this review is to identify the current scientific evidence on the value of clinical signs to indicate systemic tissue hypoperfusion or shock.**
Condition being studied: **In the literature and clinical studies, shock has traditionally been defined by a drop in arterial blood pressure under a critical threshold, e.g., a systolic blood pressure of 90 mmHg, a mean arterial blood pressure <65 mmHg or a relative drop in systolic blood pressure of ≥40 mmHg. From a pathophysiologic point of view, shock relates to an imbalance between tissue oxygen delivery as well as cellular oxygen consumption and utilization. In most cases, shock results from systemic tissue hypoperfusion with consequent decreased tissue oxygen delivery (commonly referred to as circulatory shock). Impaired cellular oxygen consumption and utilization appear to play contributory roles in specific disease states (e.g., sepsis) or conditions (e.g., intoxications).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 December 2022 and was last updated on 12 December 2022 (registration number INPLASY2022120047).

INTRODUCTION

Review question / Objective: **The objective of this review is to identify the current scientific evidence on the value of clinical signs to indicate systemic tissue hypoperfusion or shock.**

Rationale: **It is unclear which scientific evidence exists to support the use of clinical signs as indicators of systemic tissue hypoperfusion and shock.**

Condition being studied: **In the literature and clinical studies, shock has traditionally been defined by a drop in arterial blood pressure under a critical threshold, e.g., a**

systolic blood pressure of 90 mmHg, a mean arterial blood pressure <65 mmHg or a relative drop in systolic blood pressure of ≥40 mmHg. From a pathophysiologic point of view, shock relates to an imbalance between tissue oxygen delivery as well as cellular oxygen consumption and utilization. In most cases, shock results from systemic tissue hypoperfusion with consequent decreased tissue oxygen delivery (commonly referred to as circulatory shock). Impaired cellular oxygen consumption and utilization appear to play contributory roles in specific disease states (e.g., sepsis) or conditions (e.g., intoxications).

METHODS

Search strategy: This review will be conducted as a scoping systematic review of the current literature (9). The protocol will be registered on the International Prospective Register of Systematic Reviews on December 11th, 2022. The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) (10) guided reporting of this protocol.

We will include retrospective and prospective observational or cohort studies which have been published as full-texts. Randomized controlled trials using a clinical sign as an endpoint to guide haemodynamic management will not be considered unless specific tissue perfusion- or outcome-related correlations are presented (e.g., in the control arm). Commentaries, review articles, editorials, congress abstracts, and case reports or case series enrolling <10 patients will be excluded.

We will include adult patients (19 years or older) who were included in the pre-hospital setting, the emergency department or the intensive care unit. Patients <19 years and those included in studies performed in the operating theatre will not be included in this systematic review.

We will include studies that focus on non-apparative methods to collect clinical symptoms and signs. Studies exclusively conducting data collection via apparative means will be excluded.

We will include eligible studies which report an association or correlation between one or more clinical sign and one or more marker of systemic tissue (hypo-)perfusion (as defined in Table 2). In addition, selected studies will be reviewed if clinical signs were correlated with organ dysfunction and/or mortality.

Participant or population: Human adults > 19 years of age.

Intervention: Assessment of clinical signs and markers of systemic tissue (hypo-)perfusion.

Comparator: Markers of systemic tissue (hypo-)perfusion.

Study designs to be included: Retrospective and prospective observational and cohort studies which are pubished as full-texts; randomized controlled trials using a clinical sign as an endpoint to guide haemodynamic management will only be considered if specific tissue perfusion- or outcome-related correlations are present.

Eligibility criteria: Not reported.

Information sources: MEDLINE database (via PubMed).

Main outcome(s): • tissue hypoperfusion • microcirculatory dysfunction • lactate • shock • central venous oxygen saturation • metabolic acidosis.

Additional outcome(s): Mortality.

Data management: Microsoft Excel will be used to collect and manage records and data.

Quality assessment / Risk of bias analysis: All studies included into the analysis will be evaluated for methodological quality and screened for selection and other confounding biases (e.g., missing data, inclusion criteria, standardized physical examination techniques). In the final publication, all biases identified will be reported in the form of a table.

Strategy of data synthesis: A descriptive/ qualitative analysis of extricated study data will be performed. All general and specific data will be included into two or more tables depending on the number of studies identified.

Subgroup analysis: Not reported.

Sensitivity analysis: Not reported.

Language restriction: Not reported.

Country(ies) involved: Austria.

Other relevant information: As this systematic review will include only studies published in peer-reviewed journals, ethical approval is not required.

Keywords: clinical signs; shock.

Dissemination plans: The results of this research will be reported according to the latest guidelines for the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) and submitted to a peer-reviewed journal for publication.

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