

Assessment of fluid responsiveness via central venous ultrasound measurements: a network meta-analysis

INPLASY202430104

doi: 10.37766/inplasy2024.3.0104

Received: 26 March 2024

Published: 26 March 2024

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ADMINISTRATIVE INFORMATION**Support** - Nil.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202430104**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 March 2024 and was last updated on 26 March 2024.**INTRODUCTION**

Review question / Objective The objective of our study is to assess the prognostic value of ultrasound measurement of various central veins for determining fluid responsiveness.

- (i) population: adult patients.
- (ii) intervention (index test or test method): ultrasound measures of central veins (inferior vena cava [IVC], superior vena cava, subclavian vena, jugular vena)
- (iii) comparator ('gold standard' method): fluid challenge (FC) method for fluid responsiveness assessment.
- (iv) outcomes: area under the receiver operating characteristic (AUROC) for cut-off value.
- (v) study design: prospective cohort studies.

Rationale The issue of hypotension is currently one of the most significant concerns in the medical

field, especially in anesthesiology and critical care. According to the 2022 clinical guidelines, the first stage in assessing the cause of hypotension is the evaluation of fluid responsiveness. While a considerable variety of tests to assess fluid responsiveness exist at present, there remains a lack of unanimous agreement on which test provides the highest diagnostic accuracy. Consequently, there are no endorsed guidelines advocating for the exclusive use of a specific method to evaluate fluid responsiveness. One of the most common methods for assessing fluid responsiveness is the ultrasound measurement of the diameter of certain veins, particularly the inferior vena cava, jugular, femoral, or subclavian veins. The diameters of these veins, especially that of the inferior vena cava, act as indicators for evaluating the effectiveness of venous return. Also, the sizes of these veins are influenced by the level of intrathoracic pressure

and type of respiration, which means their diameters will vary during inhalation and exhalation. As a result, different venous indices have been developed, which include measurements of vein diameters during both inhale and exhale phases, and also consider the pattern of respiration. The tests mentioned above are non-invasive, straightforward to perform, and enable quick conclusion delivery. Based on data from meta-analyses, measuring the indices of the inferior vena cava and internal jugular vein demonstrates considerable diagnostic accuracy and appears to be a promising direction for the initial assessment of hypotension etiology. However, currently, there are no network meta-analyses available that compare the various methods of assessing fluid responsiveness, particularly evaluations of different veins and their indices.

This research represents the world's first network meta-analysis aimed to explore the distinctions in prognostic quality among various fluid responsiveness assessment tests, evaluating different venous diameters and their indices.

Condition being studied The issue of hypotension is currently one of the most significant concerns in the medical field, especially in anesthesiology and critical care. According to the 2022 clinical guidelines, the first stage in assessing the cause of hypotension is the evaluation of fluid responsiveness. While a considerable variety of tests to assess fluid responsiveness exist at present, there remains a lack of unanimous agreement on which test provides the highest diagnostic accuracy. Consequently, there are no endorsed guidelines advocating for the exclusive use of a specific method to evaluate fluid responsiveness.

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inferior vena cava and internal jugular vein demonstrates considerable diagnostic accuracy and appears to be a promising direction for the initial assessment of hypotension etiology. However, currently, there are no network meta-analyses available that compare the various methods of assessing fluid responsiveness, particularly evaluations of different veins and their indices.

This research represents the world's first network meta-analysis aimed to explore the distinctions in prognostic quality among various fluid responsiveness assessment tests, evaluating different venous diameters and their indices.

Condition being studied Fluid responsiveness refers to the capacity of a patient, to increase their cardiac output in response to fluid administration.

METHODS

Search strategy A systematic literature search of prospective studies published from inception to March 2024 was conducted in PubMed, Medline and the Cochrane Central Register of Controlled Trials (CENTRAL) by two independent investigators. Both backward and forward snowballing methods were also used for an exhaustive search (Litmaps service). Language restrictions were not applied.

Participant or population Adult patients (without restrictions on age, sex, race, or ethnicity).

Intervention Index test or test method: venous diameters (IVC, IJV, SCV, and femoral veins) and their indices. The ultrasound measures of central veins (inferior vena cava [IVC], superior vena cava, subclavian vena, jugular vena) assessment to determine fluid responsiveness.

Comparator 'Gold standard' method: fluid challenge (FC) for fluid responsiveness assessment. The FC is a hemodynamic diagnostic test consisting of the administration of a fixed volume of fluids with the purpose of identifying fluid responsive patients.

Study designs to be included We included prospective cohort studies.

Eligibility criteria We focused on prospective cohort studies that explored diagnostic accuracy of the ultrasound measures of central veins (inferior vena cava [IVC], superior vena cava, subclavian vena, jugular vena) for fluid responsiveness defined by FC method. Studies were excluded if they met one of the following criteria: 1) were review articles,

case reports or letters to the editors; 2) used not relevant gold standard; 3) reported no relevant data for network meta-analysis; or 4) used atypical test parameters.

Information sources PubMed, Medline, Cochrane CENTRAL and databases from Litmaps service (Crossref, Semantic Scholar, OpenAlex).

Main outcome(s) The primary outcome for this meta-analysis was the AUROC for venous diameters (IVC, IJV, SCV, and femoral veins) and their indices.

Additional outcome(s) Number of responders and non-responders.

Quality assessment / Risk of bias analysis The internal validity and risk of bias of the included studies was assessed by two independent investigators using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. Publication bias and small-study effects was assessed using Bayesian NMA meta-regression. The certainty of evidence was assessed with the GRADE systematic approach integrated in CINeMA.

Strategy of data synthesis Data extraction was performed by three independent authors. The data extracted included: 1) general information and patient characteristics: first author, setting, sample size, mean age, sex, body mass index (BMI), APACHE II score, baseline central venous pressure (CVP), type of fluid used; 2) information on the index test and 'gold standard': method, parameter, and criterion (cut-off); and 3) outcome data: reported area under receiver-operating characteristic (AUROC), and number of responders and non-responders.

We conducted a frequentist, random-effects Network Meta-Analysis (NMA) using CINeMA (Confidence in Network Meta-Analysis) approach, CINeMA software, and ROB-MEN web application. Articles were included in the NMA if they compare two or more ultrasound test parameters. The Mean Difference (MD) with corresponding 95% CI was calculated for AUROCs. Results of NMA were presented using network plots, league tables, contribution tables and NMA forest plots. To assess between-study heterogeneity, we used Bayesian NMA with τ^2 calculation.

A meta-regression analysis leveraging the restricted maximum-likelihood (REML) random-effects model was conducted to ascertain if the AUROC metrics might be affected by covariates. Statistical significance was set at 0.05 for hypothesis testing.

Subgroup analysis We conducted subgroup analysis using studies with low to moderate risk of bias.

Sensitivity analysis We conducted a subgroup analysis for Caval index test parameter (spontaneous breathing versus mechanical ventilation [MV]).

Language restriction No language limitations.

Country(ies) involved Russian Federation.

Keywords Fluid responsiveness; Caval index; Inferior vena cava; Internal jugular vein.

Contributions of each author

Author 1 - Valery Likhvantsev - conceived and designed the analysis, revised the manuscript, wrote the paper.

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