INPLASY

INPLASY202460038

doi: 10.37766/inplasy2024.6.0038

Received: 11 June 2024

Published: 11 June 2024

**Corresponding author:**
Mikhail Yadgarov

mikhail.yadgarov@gmail.com

**Author Affiliation:**
Department of Clinical Trials and AI technologies, Federal Research and Clinical Centre of Intensive Care Medicine and Rehabilitology, Moscow, Russia.

# Diagnostic Accuracy of Hemodynamic Parameters During the Passive Leg Raising Test for Assessing Fluid Responsiveness in Adult Patients: A Systematic Review and Meta-analysis

Likhvantsev, VV; Berikashvili, LB; Kuznetsov, IV; Yadgarov, MYa; Ryzhkov, PV; Polyakov, PP; Yakovlev, AA.

## ADMINISTRATIVE INFORMATION

**Support -** Nil.

**Review Stage at time of this submission -** Risk of bias assessment.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202460038

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 June 2024 and was last updated on 11 June 2024.

## INTRODUCTION

**Review question / Objective** The objective of our study is to assess the prognostic value of the PLR test for determining fluid responsiveness.
(i) population: adult patients.
(ii) intervention (index test or test method): PLR test
(iii) comparator ('gold standard' method): fluid challenge (FC) method for fluid responsiveness assessment.
(iv) outcomes: responders, non-responders, sensitivity, specificity, area under the receiver operating characteristic (AUROC),
(v) study design: prospective cohort studies.

**Rationale** Hypotension remains a considerable concern in anesthesiology and critical care. Recent clinical guidelines, updated in 2022, for the assessment and management of patients undergoing non-cardiac surgeries highlight the critical role of evaluating fluid responsiveness as an initial step in hypotension treatment. This methodology is increasingly acknowledged as a superior approach for determining the optimal therapeutic strategy.
While various methods exist to assess a patient's response to fluid therapy, many are associated with limitations. For example, precise assessment of cardiac output variability often requires invasive hemodynamic monitoring techniques. Additionally, tests that involve fluid challenges may lead to unnecessary fluid administration in non-responsive patients, given the irreversible nature of these tests.
Against this backdrop, the passive leg raising (PLR) test emerges as a valuable alternative. This non-invasive and reversible technique effectively mimics a temporary autotransfusion by increasing venous return to the heart from the lower limbs

through gravitational forces, offering a practical and safer means to evaluate a patient's fluid responsiveness.
The objective of our study is to assess the prognostic value of the PLR test for determining fluid responsiveness.

**Condition being studied** Fluid responsiveness is defined as the ability of the left ventricle to increase its stroke volume (SV) in response to fluid administration.

## METHODS

**Search strategy** A systematic literature search of studies published from inception until March 18, 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: PLR test. The PLR test is a bedside assessment to determine fluid responsiveness. The test involves raising a patient's legs (to at least 45 degrees) to induce a gravitational transfer of venous blood from the patient's legs into the central circulation.

**Comparator** 'Gold standard' method: FC method 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 PLR test method 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) reported no relevant data; 3) used veno-venous extracorporeal membrane oxygenation (VV-ECMO).

**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 will be reported area under receiver-operating characteristic (AUROC) for PLR test.

**Additional outcome(s)** Number of responders and non-responders, sensitivity, and specificity.

**Quality assessment / Risk of bias analysis** The internal validity and risk of bias of the included studies will be assessed by two independent investigators using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. Publication bias and small-study effects will be assessed using Egger's test and funnel plot analysis. The certainty of evidence will be assessed with the GRADE systematic approach.

**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, APACHE II score, baseline cardiac output (CO), cardiac index (CI), stroke volume (SV), type of fluid used, baseline degree of passive leg raising (PLR) test (head of bed angle), and the time frame for PLR assessment; 2) information on the index test and the reference standard: method, parameter, and criterion (cut-off); and 3) outcome data: number of responders and non-responders, reported area under the receiver operating characteristic curve (AUROC) – with the maximum AUROC selected if multiple were reported, sensitivity, and specificity. We will convert the data to the mean ± standard deviation (SD) format if needed.
We will conduct a frequentist, random-effects NMA using the CINeMA (confidence in network meta-analysis) approach and CINeMA software. Additionally, we will conduct Bayesian random-effects NMA utilizing the ROB-MEN and MetaInsight web applications. Articles will be included in the NMA if they compare two or more test parameters. The mean difference (MD) with the corresponding 95% CI will be calculated for the AUROCs. The results of the NMA will be presented using network plots, league tables, contribution tables and NMA forest plots. The surface under the cumulative ranking curve (SUCRA) values will be obtained to calculate the probability of each test parameter being the most effective in fluid responsiveness prediction. To assess between-study heterogeneity, we will utilize Bayesian NMA with $\tau 2$ calculation. A $\tau 2$ value exceeding the clinically important effect size (MD $\geq$ 0.1) will indicate significant heterogeneity. We will also assess incoherence using the CiNEMA approach.

**Subgroup analysis** We will categorize parameters into the following groups: 1) Cardiac Ejection: ΔCI (%), ΔSVI (%), ΔSV (%), ΔCO (%), ΔABF (%); 2) Arterial Flow: ΔVpeak through the artery (%), ΔVF through the artery (%), Δcarotid blood flow (%); 3) Pressure: ΔPP (%), ΔMAP (%), ΔSAP (%).

**Sensitivity analysis** We will conduct a sensitivity analysis using studies with low to moderate risk of bias.

**Language restriction** No language limitations.

**Country(ies) involved** Russian Federation.

**Keywords** Passive leg raising test, fluid responsiveness, fluid challenge, cardiac output, stroke volume, hemodynamic monitoring.

**Contributions of each author**

Author 1 - Valery Likhvantsev - Contribution: conceived and designed the analysis, revised the manuscript, wrote the paper.
Email: lik0704@gmail.com
Author 2 - Levan Berikashvili - Contribution: contributed data and analysis tools, performed the analysis, certainty of evidence rating, wrote the paper.
Email: levan.berikashvili@mail.ru
Author 3 - Ivan Kuznetsov - Contribution: collected the data, assessed risk of bias, wrote the paper.
Email: ikuznecov@fnkcrr.ru
Author 4 - Mikhail Yadgarov - Contribution: performed the analysis, certainty of evidence rating, wrote the paper.
Email: mikhail.yadgarov@mail.ru
Author 5 - Pavel Ryzhkov - Contribution: collected the data, assessed risk of bias, wrote the paper.
Email: a.pavelhlw@gmail.com
Author 6 - Alexey Yakovlev - Contribution: revised the manuscript, wrote the paper.
Email: ayakovlev@fnkcrr.ru
Author 7 - Petr Polyakov - Contribution: wrote the paper.
Email: petrpoljakov01@gmail.com