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Passive leg raising test – optimal methodology. A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 October 2024 and was last updated on 17 October 2024.

INTRODUCTION

Review question / Objective The objective of our study was to establish criteria for conducting the PLR test based on the diagnostic accuracy of various approaches.
(i) population: adult patients in the ICU.
(ii) intervention (index test or test method): PLR test
(iii) comparator ('gold standard' method): fluid challenge (FC) method for fluid responsiveness assessment.
(iv) outcomes: area under the receiver-operating characteristic (AUROC).
(v) study design: prospective cohort studies.

Rationale Infusion therapy (IT) is one of the most common treatments in intensive care. It is used to manage conditions like hypotension, fluid-electrolyte imbalances, and shock. However, uncontrolled use of IT can lead to fluid overload, causing pulmonary edema and hypotension.
Modern clinical guidelines recommend assessing "fluid responsiveness" before starting IT. This refers to the cardiovascular system's ability to increase cardiac output in response to fluid infusion. Although closely related to hypovolemia, fluid responsiveness is not directly its equivalent, as patients can be responsive even in a normovolemic state, and some hypovolemic patients may not respond with increased cardiac output.
A drawback of fluid challenge is their irreversibility, as it can be difficult to remove excess fluid from the body once complications arise, such as pulmonary edema in patients with latent heart failure. To avoid this, several methods have been developed to assess fluid responsiveness without actual fluid administration. One of the simplest is the passive leg raising (PLR) test, which temporarily increases venous return to the heart and mimics fluid loading.
The PLR test is safe, easy to perform, quick to assess, and does not require actual infusion therapy. However, despite its widespread use, there is no universally accepted method for conducting the PLR test based on evidence-based

medicine. The aim of this work was to establish the principles of conducting the PLR test based on the diagnostic accuracy of its different variations.

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 until March, 2024 was conducted in PubMed (Medline) by two independent investigators. Additionally, the authors used AI-based semantic analysis and both forward and backward snowballing methods using the Litmaps web application in three directions: 1) most frequently cited sources and references, 2) common authorship patterns, and 3) similarity of abstract and title content. No language restrictions were applied.

Participant or population Adult patients in the ICU.

Intervention Index test or test method was PLR (passive leg raising) test.

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 for fluid responsiveness defined by FC method. Studies were excluded if they met one of the following criteria: 1) didn't use FC as a 'gold standard' method; 2) there were no data of assessed outcomes; 3) PLR test effect was not based on the hemodynamics parameters; 4) extracorporeal membrane oxygenation; 5) healthy volunteers.

Information sources PubMed (Medline).

Main outcome(s) The primary outcome for this meta-analysis was the calculated area under receiver-operating characteristic (AUROC) for PLR test.

Additional outcome(s) None.

Quality assessment / Risk of bias analysis The internal validity and risk of bias of the included studies were assessed by two independent investigators using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. Publication bias and small-study effects were 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 two independent authors. The data extracted included: 1) general information and patient characteristics; 2) PLR test conditions and results; 3) methods of assessing heart hemodynamics parameters.
The data were converted to the mean and 95% confidence interval format if needed.
STATA 18.0 (StataCorp LLC, Texas, US) was employed for both calculations and visualizations. The interstudy heterogeneity was assessed via the I-squared (I^2) statistics and the Cochrane Q test. We applied a random-effects model (restricted maximum likelihood [REML]) for the meta-analysis. Statistical significance was set at $p < 0.05$. We also performed univariate meta-regression to assess connection between diagnostic accuracy of PLR test and such covariates as age and sex.

Subgroup analysis The subgroup analyses were conducted to evaluate the AUROC in subgroups formed by: 1) heart hemodynamics assessing method; 2) initial position; and 3) time period between the start of PLR test and parameters measuring.

Sensitivity analysis For the sensitivity analysis the leave-one-out method was applied.

Language restriction No language limitations.

Country(ies) involved Russian Federation.

Keywords Fluid responsiveness, passive leg raise test, meta-analysis.

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