

Diagnostic accuracy of passive leg raising test: systematic review and network meta-analysis

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Abstract

Introduction: The passive leg raising (PLR) test is a non-invasive diagnostic tool for assessing fluid responsiveness, a pivotal aspect in hypotension management. Despite its growing application, a unified comparative assessment of prognostic accuracy for various PLR test parameters is currently lacking.

Objective: Our study aimed to evaluate the efficacy of different PLR test indicators in predicting fluid responsiveness.

Methods: We conducted a network meta-analysis, analyzing prospective studies that explored diagnostic accuracy of PLR test for fluid responsiveness. Electronic databases were searched until March 2024; this search was supplemented by snowballing methods. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to determine the certainty of evidence.

Results: Sixteen prospective cohort studies involving 784 patients were included. The network meta-analysis revealed that cardiac output parameters measured during the PLR test have the highest prognostic significance for assessing fluid responsiveness compared to other parameters (SUCRA score = 88.3). Utilizing arterial blood flow indicators results in a moderate prognostic value for the PLR test (SUCRA score = 72.0). The use of such conventional parameters as arterial blood pressure and inferior vena cava diameter reduces prognostic accuracy to unsatisfactory levels (SUCRA score < 50). The superiority of PLR test prognostic capability when using cardiac output parameters over arterial blood pressure indicators is supported by high-quality evidence.

Conclusion: Our network meta-analysis demonstrated that using PLR test with cardiac output parameters ensures maximum sensitivity and specificity. Consequently, the use of more straightforward and easily obtainable parameters (arterial blood pressure, inferior vena cava diameter) is not recommended for assessing fluid responsiveness.

Keywords: cardiac output; fluid therapy; hemodynamic monitoring; posture; stroke volume; venous return



Диагностическая точность теста с пассивным подъемом ног: систематический обзор и сетевой метаанализ

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Аннотация

Актуальность. Тест с пассивным подъемом ног (passive leg raising, PLR-тест) представляет собой неинвазивный диагностический метод оценки восприимчивости к инфузионной нагрузке, что является ключевым аспектом диагностики гипотензии в анестезиологии и интенсивной терапии. Несмотря на широко распространенное применение его, в настоящее время отсутствует единая сравнительная оценка прогностической точности различных показателей, измеряемых во время проведения PLR-теста.

Цель. Целью нашего исследования было оценить эффективность различных показателей, регистрируемых при проведении PLR-теста, для прогнозирования восприимчивости к инфузионной нагрузке.

Методы. Был проведен сетевой метаанализ, включивший проспективные исследования, изучавшие диагностическую точность PLR-теста для оценки восприимчивости к инфузионной нагрузке. Электронные базы данных были проанализированы до марта 2024 г., поиск дополнялся методом «снежного кома». Для определения уровня доказательств применялся подход Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

Результаты. Были включены 16 проспективных когортных исследований с участием 784 пациентов. Сетевой метаанализ показал, что параметры сердечного выброса, измеренные во время проведения PLR-теста, обладают наибольшей прогностической значимостью при оценке восприимчивости к инфузионной нагрузке в сравнении с другими параметрами (площадь под кривой суммарного ранжирования (SUCRA) score = 88,3). Использование показателей артериального кровотока обеспечивает умеренную прогностическую значимость PLR-теста (SUCRA = 72,0). Использование более традиционных параметров, таких как артериальное давление и диаметр нижней полой вены, снижает прогностическую точность до неудовлетворительного уровня (SUCRA score < 50).

Заключение. Использование параметров сердечного выброса при проведении PLR-теста обеспечивает максимальные значения диагностической точности. Следовательно, применение таких показателей, как артериальное давление и диаметр нижней полой вены, не рекомендуется для оценки восприимчивости к инфузионной нагрузке. Регистрационный номер: INPLASY (International Platform of Registered Systematic Review and Meta-analysis Protocols) 202460038.

Ключевые слова: венозный возврат; инфузионная терапия; мониторинг гемодинамики; положение тела; сердечный выброс; ударный объем



Introduction

Hypotension remains a serious problem in anesthesiology and intensive care, as it often leads to life-threatening hypoperfusion of organs and tissues [1; 2]. Although there is currently no universally accepted definition of hypotension [3], it is generally accepted to distinguish three main causes of its occurrence: hypovolemia, decreased cardiac output, and vasoplegia [4; 5]. Clinical guidelines for the management of cardiac patients in non-cardiac surgery emphasize the key role of assessing fluid responsiveness as the first step in the treatment of hypotension [5]. This approach is increasingly considered more preferable for choosing the optimal strategy.

There are many tests for assessing fluid responsiveness, but many of them have significant limitations [6]. For example, accurate assessment of cardiac output variability often requires the use of invasive hemodynamic monitoring methods [7]. Furthermore, tests based on fluid infusion carry the risk of fluid overload in patients, as they are irreversible [8].

In this context, the passive leg raising (PLR) test is considered a significant alternative [9]. This non-invasive and reversible method simulates autotransfusion, in which gravity redistributes blood from the lower extremities to the heart [10]. Thus, the PLR test represents a practical and safer option for assessing fluid responsiveness [11]. However, currently there is no single universally accepted indicator whose changes need to be monitored during the PLR test to assess fluid responsiveness.

The aim of our study was to evaluate the prognostic significance of various indicators recorded during the PLR test for assessing fluid responsiveness.

Methods

This study was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension statement for network meta-analyses (PRISMA-NMA) [12] and the Cochrane Handbook [13]. The study protocol was registered on the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) under registration number INPLASY 202460038 (doi: 10.37766/inplasy2024.6.0038). The PRISMA-NMA checklist is presented in Supplementary Material, in Appendix 1.

Search strategy

To identify relevant studies, a systematic search was performed covering all available publications from their inception to March 18, 2024. The search strategy included PubMed, Medline, and the Cochrane Central Register of

Controlled Trials (CENTRAL). The search was performed independently by two researchers. Additionally, forward and backward snowballing methods were applied using the Litmaps service [14] to identify additional relevant publications. We did not apply language restrictions. The detailed search strategy, including specific queries and parameters, is presented in Supplementary Material, Appendix 2.

Eligibility criteria and study selection

After automatic duplicate removal, two researchers independently screened the remaining studies based on titles and abstracts using the PICOS criteria: (P) adult patients, (I) bilateral passive leg raising (PLR) test, (C) fluid challenge (FC) method for assessing fluid responsiveness ("gold standard"), (O) area under the ROC curve (AUROC), (S) prospective cohort studies (detailed in Supplementary Material, in Appendix 2). Studies were excluded if they met one of the following criteria: 1) were review articles, case reports, or letters to the editor; 2) did not contain relevant data for network meta-analysis (NMA) (required at least two tested parameters with reported AUROC data); 3) used veno-venous extracorporeal membrane oxygenation (VV-ECMO).

Any disagreements in the study selection process were resolved by discussion with an additional expert until consensus was reached.

Data extraction and endpoints

A specialized data collection form was developed for this review. The primary outcome in this network meta-analysis is the area under the ROC curve (AUROC) for the PLR test.

Three authors independently evaluated the full texts of articles, as well as all additional materials of the included studies, to extract the following data:

1) general information and patient characteristics: first author, cohort, sample size, mean age, sex, APACHE II score, baseline values of cardiac output (CO), cardiac index (CI), stroke volume (SV), type of infusion solution used, initial position during PLR test (angle of head of bed elevation), and time interval for PLR assessment;

2) information about the PLR test and reference method: technique, parameter (Δ SVV – change in stroke volume variation; Δ PPV – change in pulse pressure variation; Δ CI – change in cardiac index; Δ SVI – change in stroke volume index; Δ SV – change in stroke volume; Δ Vpeak – change in peak arterial flow velocity; Δ CO – change in cardiac output; Δ PP – change in pulse pressure; Δ EtCO₂ – change in end-tidal carbon dioxide; Δ VF – change in volume flow; Δ ABF – change in aortic blood flow; Δ CPI – change in cardiac power index;

Δ MAP – change in mean arterial pressure; Δ PtcO₂ – change in transcutaneous partial pressure of oxygen; Δ SBP – change in systolic arterial pressure; Δ HR – change in heart rate) and criterion (threshold value);

3) outcome data: number of responders and non-responders, AUROC values (indicating the maximum AUROC value when multiple were present), sensitivity and specificity.

Additionally, individual parameters were grouped as follows:

1) cardiac output indicators: Δ CI (%), Δ SVI (%) (stroke volume index), Δ SV (%), Δ CO (%), Δ ABF (aortic blood flow) (%);

2) arterial blood flow indicators: Δ V_{peak} in artery (%), Δ VF (volume flow) in artery (%), Δ carotid artery blood flow (%);

3) arterial pressure indicators: Δ PP (pulse pressure) (%), Δ MAP (%), Δ SBP (%).

In studies where data were presented as medians, interquartile ranges, or 95% confidence intervals, well-established statistical methods were used to convert them

to mean $\pm$ standard deviation (SD). These approaches are based on techniques proposed by Luo et al. [15] and Wan et al. [16], as well as the recommendations of the Cochrane Handbook [13]. In cases where AUROC data were not presented, this indicator was estimated using the formula

$$\text{AUROC} \approx (\text{Se} + \text{Sp})/2,$$

where Se is sensitivity; Sp is specificity.

Missing SD data were imputed using multiple imputation in IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA).

Data analysis

We performed a frequentist network meta-analysis (NMA) using a random-effects model, applying the CINeMA (Confidence in Network Meta-Analysis) methodology and software (University of Bern, Bern, Switzerland) [17; 18]. Additionally, a Bayesian random-effects network meta-analysis was performed using the web applications ROB-MEN and MetaInsight [19; 20]. Articles that compared two or more test parameters were included in the NMA.

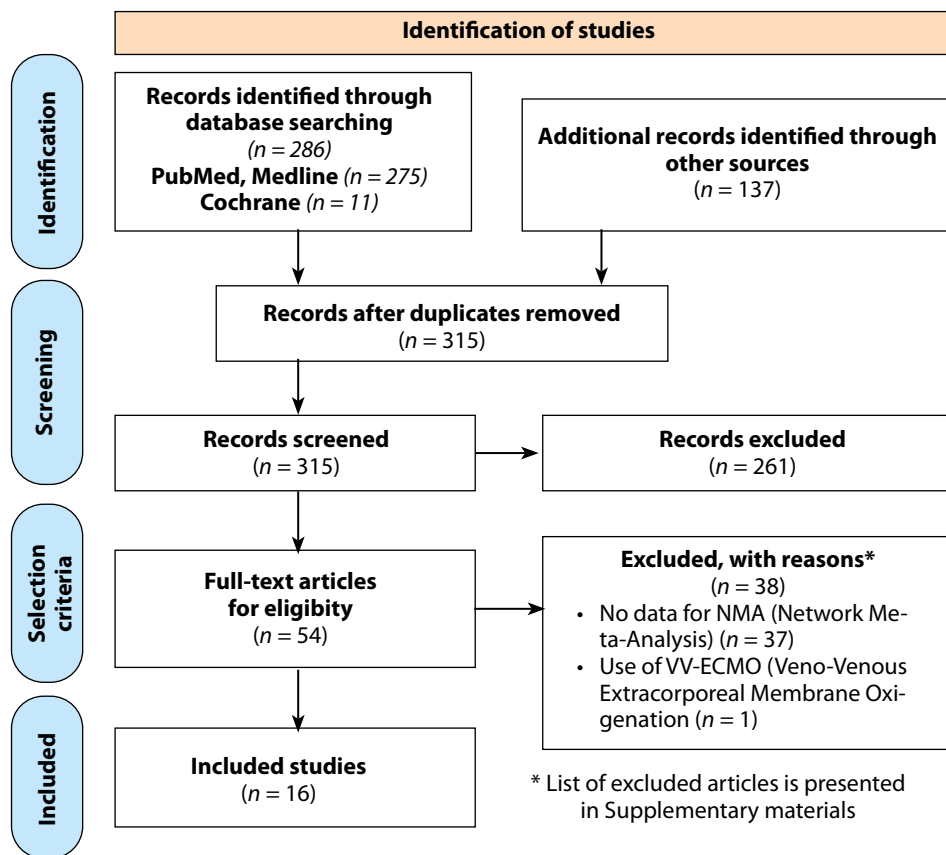


Fig. 1. Study selection flow chart

For the AUROC indicator, the mean difference (MD) with corresponding 95% confidence interval (CI) was calculated. The NMA results were presented using network diagrams, league tables, contribution tables, and NMA forest plots. To calculate the probability that each of the parameters would be the most effective in predicting fluid responsiveness, SUCRA (surface under the cumulative ranking curve) values were obtained [21]. To assess inter-study heterogeneity, a Bayesian NMA was applied with calculation of τ^2 . A τ^2 value exceeding a clinically significant

effect size ($MD \geq 0.1$) was interpreted as an indicator of substantial heterogeneity. Furthermore, we assessed inconsistency using the CINeMA approach.

Internal validity and risk of bias assessment

The internal validity and risk of bias of the included studies were assessed by two independent researchers using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool [22]. An explanation of the risk of bias assessment is provided in Supplementary Material,

Table 1. General characteristics and description of the 16 studies included in the meta-analysis

No.	Study	Cohort	Test method	Test parameters	Gold standard method	Gold standard parameter	Type of fluid used	Volume of fluid administered	Sample size
1	Taccheri T. (2021) [30]	Other ICU patients	PLR	Δ Inferior vena cava respiratory index (absolute change), Δ VTI (%)	FC	Δ CI (%)	Crystalloids	500 ml	30
2	Zhao Z. (2022) [29]	Other ICU patients	PLR	Δ Vpeak (%), Δ VTI (%), Δ CI (%), Δ SVI (%)	FC	Δ CI (%)	Crystalloids	500 ml	40
3	Wu J. (2018) [28]	Shock	PLR	Δ SV (%), Δ Vpeak (%)	FC	Δ SV (%)	Crystalloids	250 ml	62
4	Lakhal K. (2010) [27]	Shock	PLR	Δ CO (%), Δ PP (%)	FC	Δ CO (%)	Colloids	500 ml	102
5	Monnet X. (2013) [26]	Shock	PLR	Δ PP (%), Δ CI (%), Δ EtCO ₂ (%)	FC	Δ CI (%)	Crystalloids	500 ml	40
6	Monge García M.I. (2012) [25]	Shock	PLR	Δ CO (%), Δ EtCO ₂ (%), Δ PP (%)	FC	Δ CO (%)	Colloids	500 ml	37
7	Ma G. (2020) [38]	Cardiac surgery ICU	PLR	Δ SV (%), Δ VTI (%)	FC	Δ SV (%)	Colloids	500 ml	123
8	Krige A. (2016) [37]	Shock	PLR	Δ VTI (%), Δ CO (%)	FC	Δ CO (%)	Colloids	250 ml	33
9	Préau S. (2010) [36]	Shock	PLR	Δ SV (%), Δ VF (%), Δ PP (%)	FC	Δ SV (%)	Colloids	500 ml	34
10	Monnet X. (2006) [35]	Shock	PLR	Δ ABF (%), Δ PP (%)	FC	Δ CI (%)	Crystalloids	500 ml	71
11	Monnet X. (2009) [34]	Shock	PLR	Δ CI (%), Δ PP (%)	FC	Δ SVI (%)	Crystalloids	500 ml	34
12	Saugel B. (2013) [33]	Other ICU patients	PLR	Δ CPI (%), Δ MAP (%), Δ CI (%)	FC	Δ SV (%)	Crystalloids	7 ml/kg	24
13	Marik P.E. (2013) [32]	Other ICU patients	PLR	Δ SVI (%), Δ Carotid artery blood flow (%)	FC	Δ SV (%)	Crystalloids	500 ml	34
14	Xu J. (2017) [31]	Shock	PLR	Δ PtcO ₂ (%), Δ SV (%)	FC	Δ CO (%)	Crystalloids	250 ml	34
15	Si X. (2018) [24]	Other ICU patients	PLR	Δ SV (%), Δ CO (%), Δ SBP (%), Δ MAP (%), Δ HR (%), Δ PP (%)	FC	Δ CI (%)	Colloids	250 ml	40
16	Elsayed A.I. (2021) [23]	Shock	PLR	Δ CO (%), Δ Vpeak (%)	FC	Δ CI (%)	Crystalloids	4 ml/kg	46

Note. FC – fluid challenge; CI – cardiac index; CO – cardiac output; SV – stroke volume; SVI – stroke volume index; VTI – velocitytime integral; Vpeak – peak velocity; PP – pulse pressure; MAP – mean arterial pressure; SBP – systolic blood pressure; HR – heart rate; EtCO₂ – endtidal carbon dioxide; PtcO₂ – transcutaneous oxygen pressure; ABF – aortic blood flow; CPI – cardiac power index; VF – (as in original, possibly velocity flow).

in Appendix 3. Publication bias and small-study effects were assessed using Bayesian NMA meta-regression. The certainty of evidence was determined using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology integrated into the CINeMA approach.

Additionally, a sensitivity analysis was performed using studies with low and moderate risk of bias.

Results

Study characteristics

The initial research identified 423 articles. After the abstract screening stage, 54 articles were selected for full-text evaluation. Following full-text analysis, 38 studies were excluded (details provided in Supplementary Material, Table P2). Thus, 16 prospective cohort studies published between 2006 and 2022 were included in this network meta-analysis [23–38]. A flow diagram reflecting the study selection process is presented in Fig. 1.

Data from 784 patients were included in the network meta-analysis. Among the included studies, 10 focused on patients with shock [23; 25–28; 31; 34–37]. The mean age of participants ranged from 53 to 71 years. In ten studies, crystalloid solutions were used for the fluid challenge as the “gold standard” [23; 26; 28–35]. Nineteen different parameters were used to assess fluid responsiveness (Supplementary Material, Table P3). The volume of solutions administered during the fluid challenge test varied and included 250 mL, 500 mL, and 4–7 mL/kg. The time interval from the start of the PLR to the assessment of hemodynamic parameters ranged from 1 to 5 minutes. The proportion of patients who responded to fluid administration varied from 29 to 68%. A summary of the characteristics of the studies included in the meta-analysis is presented in Table 1 and Supplementary Material, Table P3.

Risk of bias assessment

The risk of bias assessment for the nine included studies showed low risk in six studies, moderate risk in seven, and high risk in three studies (Table 2, Supplementary Material, Table P4). The main sources of bias were factors related to patient selection, conduct and interpretation of PLR and FC. A bar chart of risk distribution is shown in Supplementary Material, Fig. P4. No publication bias or small-study effect was detected in this NMA. Although the inter-study variance was statistically non-significant, substantial inconsistency in results was identified ($\chi^2 = 41.032$; 8 degrees of freedom; $p < 0.001$).

Network meta-analysis

The network graph is presented in Fig. 2.

The data used in the network meta-analysis, including NMA characteristics, league tables, and contribution matrices, are detailed in Supplementary Material, Tables P4–P9.

Cardiac output indicators demonstrated a significant advantage in effectiveness compared to changes in the respiratory index of the inferior vena cava, arterial pressure parameters, pulse pressure variation, and stroke volume variation (mean differences ranging from 0.15 to 0.54; Fig. 3, Supplementary Material, Table P6).

SUCRA analysis showed that cardiac output indicators have the greatest potential for predicting fluid responsiveness (score 88.3). Following in descending order of prognostic ability were $\Delta EtCO_2$ (%) (score 84.8), arterial blood flow indicators (score 72.0), change in cardiac power index (score 71.4), and $\Delta PtcO_2$ (%) (score 58.8). For the remaining parameters, the SUCRA value did not exceed 50 (Fig. 3, Supplementary Material, Fig. P1).

Sensitivity analysis

The main results were confirmed when analyzing studies with low and moderate risk of bias (Supplementary Material, Table P7, Fig. P2).

GRADE assessment

CINeMA ratings are presented in Supplementary Material, Fig. P3. The certainty of evidence for the studied comparisons ranged from very low to high. The level of evidence supporting the superiority of cardiac output indicators over arterial pressure parameters for predicting fluid responsiveness was rated as high.

Discussion

Key results

The network meta-analysis showed that the most reliable indicators for assessing fluid responsiveness during the PLR test are parameters reflecting left ventricular ejection. In contrast, indicators related to the variability of cardiovascular system characteristics – such as heart rate, pulse pressure variation, and stroke volume variation – demonstrated significantly lower effectiveness. Furthermore, arterial pressure parameters were inferior to cardiac output parameters (high level of evidence), indicating their limited value during the PLR test, despite the ease of measurement and widespread availability in intensive care units. Moreover, the notable difference found between the prognostic significance of cardiac

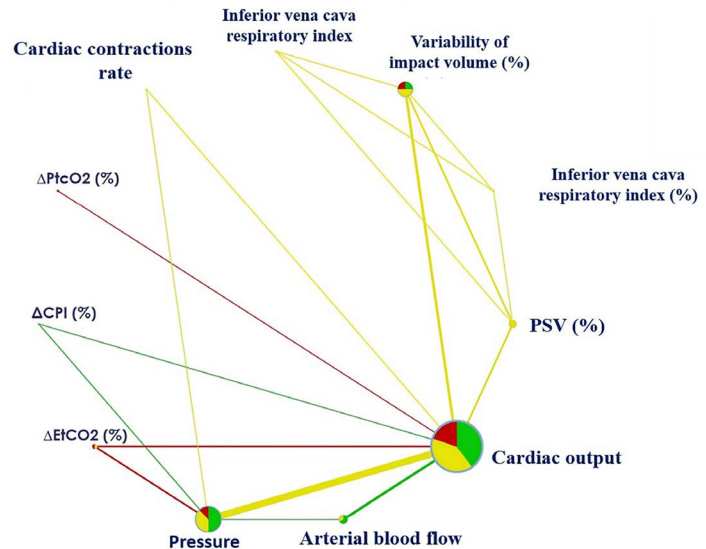
Table 2. Risk of bias analysis

No.	Study	Test parameter	Cutoff value	Risk of bias (QUADAS2)				Overall bias	Applicability concerns (QUADAS2)		
				P	I	R	FT		P	I	R
1	Taccheri T. (2021)	ΔInferior vena cava respiratory index (absolute change)	ND	✓	✗	✓	✓	Moderate	✓	✓	✓
2	Taccheri T. (2021)	ΔVTI (%)	-19.0	✓	✓	✓	✓	Low	✓	✓	✓
3	Taccheri T. (2021)	ΔInferior vena cava respiratory index (%)	-24.0	✓	✓	✓	✓	Low	✓	✓	✓
4	Taccheri T. (2021)	ΔVpeak (%)	-20.0	✓	✓	✓	✓	Low	✓	✓	✓
5	Zhao Z. (2022)	ΔVpeak (%)	ND	✓	✗	✓	✓	Moderate	✓	✓	✓
6	Zhao Z. (2022)	ΔVTI (%)	ND	✓	✗	✓	✓	Moderate	✓	✓	✓
7	Zhao Z. (2022)	ΔCI (%)	9.8	✓	✓	✓	✓	Low	✓	✓	✓
8	Zhao Z. (2022)	ΔSVI (%)	11.0	✓	✓	✓	✓	Low	✓	✓	✓
9	Wu J. (2018)	ΔSV (%)	12.45	✓	✓	✗	✓	Moderate	✓	✓	✓
10	Wu J. (2018)	ΔVpeak (%)	10.6	✓	✓	✗	✓	Moderate	✓	✓	✓
11	Lakhal K. (2010)	ΔCO (%)	7.0	✓	✓	✓	✓	Low	✓	✓	✓
12	Lakhal K. (2010)	ΔPP (%)	9.0	✓	✓	✓	✓	Low	✓	✓	✓
13	Monnet X. (2013)	ΔPP (%)	ND	✗	✗	✓	✗	High	✓	✓	✓
14	Monnet X. (2013)	ΔCI (%)	10.0	✗	✓	✓	✗	High	✓	✓	✓
15	Monnet X. (2013)	ΔEtCO ₂ (%)	5.0	✗	✓	✓	✗	High	✓	✓	✓
16	Monge García M.I. (2012)	ΔCO (%)	12.0	✓	✗	✓	✓	Moderate	✓	✓	✓
17	Monge García M.I. (2012)	ΔEtCO ₂ (%)	5.0	✓	✗	✓	✓	Moderate	✓	✓	✓
18	Monge García M.I. (2012)	ΔPP (%)	11.0	✓	✗	✓	✓	Moderate	✓	✓	✓
19	Ma G. (2020)	ΔSV (%)	13.0	✓	✓	✓	✓	Low	✓	✓	✓
20	Ma G. (2020)	ΔVTI (%)	-4.0	✓	✓	✓	✓	Low	✓	✓	✓
21	Krige A. (2016)	ΔVTI (%)	ND	✓	✗	✗	✓	High	✓	✓	✓
22	Krige A. (2016)	ΔCO (%)	9.0	✓	✓	✗	✓	Moderate	✓	✓	✓
23	Préau S. (2010)	ΔSV (%)	10.0	✓	✓	✓	✓	Low	✓	✓	✓
24	Préau S. (2010)	ΔVF (%)	8.0	✓	✓	✓	✓	Low	✓	✓	✓
25	Préau S. (2010)	ΔPP (%)	9.0	✓	✓	✓	✓	Low	✓	✓	✓
26	Monnet X. (2006)	ΔABF (%)	10.0	✓	✓	✓	✓	Low	✓	✓	✓
27	Monnet X. (2006)	ΔPP (%)	12.0	✓	✓	✓	✓	Low	✓	✓	✓
28	Monnet X. (2009)	ΔCI (%)	10.0	✗	✓	✓	✓	Moderate	✓	✓	✓
29	Monnet X. (2009)	ΔPP (%)	11.0	✗	✓	✓	✓	Moderate	✓	✓	✓
30	Saugel B. (2013)	ΔCPI (%)	15.0	✓	✓	✓	✓	Low	✓	✓	✓
31	Saugel B. (2013)	ΔMAP (%)	15.0	✓	✓	✓	✓	Low	✓	✓	✓
32	Saugel B. (2013)	ΔCI (%)	15.0	✓	✓	✓	✓	Low	✓	✓	✓
33	Marik P.E. (2013)	ΔSVI (%)	10.0	✓	✓	✓	✓	Low	✓	✓	✓
34	Marik P.E. (2013)	ΔCarotid artery blood flow (%)	20.0	✓	✓	✓	✓	Low	✓	✓	✓
35	Xu J. (2017)	ΔPtcO ₂ (%)	13.0	✓	✗	✗	✓	High	✓	✓	✓
36	Xu J. (2017)	ΔSV (%)	10.0	✓	✗	✗	✓	High	✓	✓	✓
37	Si X. (2018)	ΔSV (%)	12.0	✓	✓	✗	✓	Moderate	✓	✓	✓
38	Si X. (2018)	ΔCO (%)	7.0	✓	✓	✗	✓	Moderate	✓	✓	✓
39	Si X. (2018)	ΔSBP (%)	5.0	✓	✓	✗	✓	Moderate	✓	✓	✓
40	Si X. (2018)	ΔMAP (%)	7.0	✓	✓	✗	✓	Moderate	✓	✓	✓
41	Si X. (2018)	ΔHR (%)	-5.0	✓	✓	✗	✓	Moderate	✓	✓	✓
42	Si X. (2018)	ΔPP (%)	5.0	✓	✓	✗	✓	Moderate	✓	✓	✓
43	Elsayed A.I. (2021)	ΔCO (%)	6.5	✓	✓	✗	✓	Moderate	✓	✓	✓
44	Elsayed A.I. (2021)	ΔVpeak (%)	2.5	✓	✓	✗	✓	Moderate	✓	✓	✓

Note. ΔSBP – change in systolic blood pressure; ΔMAP – change in mean arterial pressure; ΔPPV – change in pulse pressure variation; ΔSVV – change in stroke volume variation; ΔSVI – change in stroke volume index; ND – no data; ICU – intensive care unit; ΔPP – change in pulse pressure; ΔCO – change in cardiac output; ΔCI – change in cardiac index; ΔSV – change in stroke volume; ΔHR – change in heart rate; ΔABF – change in aortic blood flow; ΔCPI – change in cardiac power index; ΔEtCO₂ – change in end-tidal carbon dioxide concentration; FC – fluid challenge; FT – process and timing; I – index test; P – patient selection; PLR – passive leg raising; ΔPtcO₂ – change in transcutaneous partial pressure of oxygen; R – reference standard; ΔVF – change in volume flow; ΔVpeak – change in peak arterial flow velocity; ✓ – low risk; ✗ – high risk; ? – unclear risk.

Fig. 2. Network plot for PLR test parameters used for fluid responsiveness prediction

Note. Δ PPV – change in pulse pressure variation; PSV – Pressure Support Ventilation; Δ SVV – change in stroke volume variation; Δ HR – change in heart rate; Δ CPI – change in cardiac power index; Δ EtCO₂ – change in end-tidal carbon dioxide concentration; Δ PtcO₂ – change in transcutaneous partial pressure of oxygen.



output parameters and inferior vena cava assessment was unexpected and indicates the unsuitability of inferior vena cava assessment in the context of the PLR test.

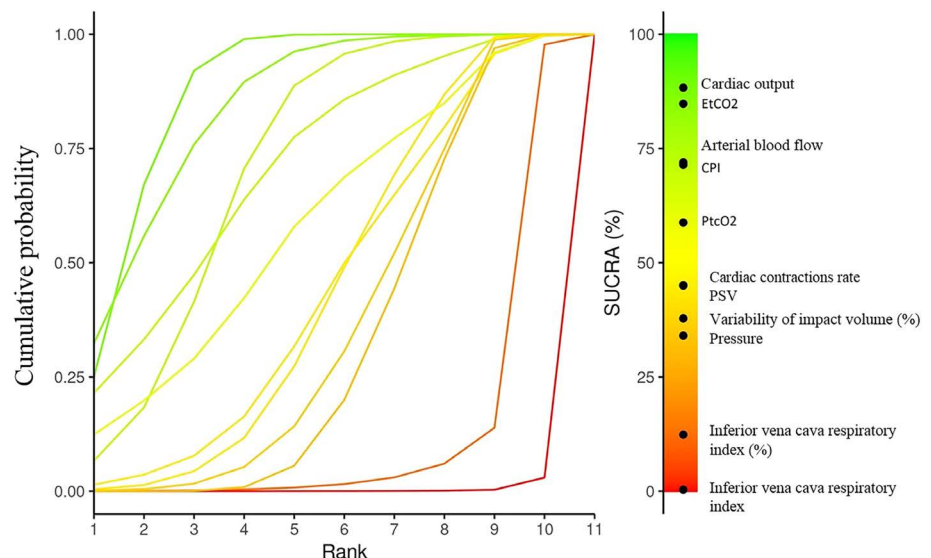
Relationship with previous studies

Alvarado Sánchez et al. arrived at a similar conclusion, showing that the choice of hemodynamic variables significantly influences the diagnostic accuracy of the PLR test. Their work demonstrated that measuring aortic blood flow, cardiac output, stroke volume, or their indices increases diagnostic accuracy. Conversely, the use of surrogate indicators of cardiac output led to a decrease in the prognostic value of the PLR test [39].

In a study by Cherpanath et al., which included a total of 1013 patients, it was shown that changes in pulse pressure during the PLR test have a lower prognostic significance than changes in flow indicators [40]. Monnet et al., performing a subgroup analysis, reached a similar conclusion: the PLR test less accurately predicted the response to fluid challenge if its effects were assessed by arterial pulse pressure rather than by cardiac output [41]. Our network meta-analysis demonstrated that changes in arterial pressure during PLR predict fluid responsiveness significantly worse than cardiac output parameters, which is consistent with the results of the aforementioned studies. This may be explained by the fact

Fig. 3. Litmus Rank-O-Gram. Higher SUCRA values, as well as curves located closer to the upper left corner, indicate higher effectiveness in predicting fluid responsiveness

Note. PPV – pulse pressure variation; SVV – stroke volume variation; IVC – inferior vena cava; HR – heart rate; CPI – cardiac power index; EtCO₂ – end-tidal carbon dioxide; PtcO₂ – transcutaneous partial pressure of oxygen.



that these parameters depend not only on stroke volume/ cardiac output but also on vascular tone and arterial elasticity [42]. However, Lakhal et al., in a study including 112 patients, concluded that changes in systolic arterial pressure during PLR reliably identify patients responding to fluid challenge [43], which contradicts the results of our network meta-analysis.

Taccheri et al. showed that percentage changes in inferior vena cava diameter variability induced by PLR, expressed as a percentage deviation from baseline, reliably predicted the response to a presumed fluid infusion [30]. In contrast, our network meta-analysis showed that inferior vena cava assessment parameters during PLR are significantly inferior to cardiac output parameters and are unsuitable for determining fluid responsiveness.

Significance of the study results

The significance of this network meta-analysis lies in the following aspects.

First, this study is the first network meta-analysis to evaluate various parameters used during the PLR test, with their direct comparison and ranking by prognostic accuracy. This approach allowed for an informed conclusion regarding the optimal parameter for measurement.

Second, the network meta-analysis showed that intracardiac hemodynamic indicators significantly outperform all other methods in predicting fluid responsiveness during the PLR test. In contrast, parameters that seem convenient and reliable, such as arterial pressure or inferior vena cava assessment, are significantly inferior to cardiac output indicators.

Furthermore, this study confirms the higher informativeness of criteria assessing changes in left ventricular ejection during the PLR test over other hemodynamic parameters.

Strengths and limitations

Our study employed advanced statistical methods, including the use of network meta-analysis, standard risk of bias assessment tools, and the application of the GRADE framework, which strengthened the reliability of the results obtained. The deliberate restriction of the analysis to prospective studies only increased the quality of the included data. Among these works, a significant

proportion (37.5%) were classified as having a low risk of bias, while the remaining studies were classified as having moderate (43.8%) or high (18.7%) risk. This network meta-analysis has several limitations, such as differences in patient characteristics and the timing of assessments. In 10 studies, the PLR test was performed in patients in shock, whereas in 6 studies it was performed in patients without shock. Additionally, the type of infusion solutions (colloids or crystalloids) used as the “gold standard” differed between studies, which could potentially affect the results. Another limitation of network meta-analysis is transitivity, as the analysis included indirect comparisons of different test parameters across studies. Nevertheless, based on the SUCRA analysis, it can be argued that the use of cardiac output parameters is the best choice when performing the PLR test to assess fluid responsiveness.

Future research

This network meta-analysis provides valuable data, highlighting the need for scientific research in two directions:

1. Standardization of the PLR test. The lack of uniform recommendations indicates the need for prospective cohort studies aimed at developing standards for performing the PLR test, including measurement timing, initial head-of-bed angle, leg elevation angle, and other related parameters.

2. Standardization of cardiac output assessment. Currently, there is no single method for assessing cardiac output during the PLR test, allowing clinicians to use different approaches – echocardiography, transpulmonary thermodilution, arterial pressure pulse wave analysis, and thoracic impedance cardiography. Since these methods may differ in their prognostic significance for assessing the response to presumed fluid infusion during the PLR test, further studies are needed to determine the optimal method for assessing intracardiac hemodynamic parameters.

Conclusion

This network meta-analysis showed that cardiac output parameters significantly outperform all other indicators in assessing fluid responsiveness during passive leg raising test. Therefore, the use of parameters such as arterial pressure and inferior vena cava diameter is not recommended for this purpose.

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