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ORIGINAL ARTICLE

End Expiratory Occlusion Test for Evaluation of Fluid Responsiveness in Comparison to Passive Leg Raising Test in Mechanically Ventilated Post Cardiac Surgery Patients: A Randomized Clinical Trial

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Background Fluid responsiveness evaluation is critical for hemodynamic optimization in patients receiving ventilator support following cardiac surgery. The end-expiratory occlusion test (EEOT) and passive leg raising (PLR) tests are dynamic methods used for this purpose, but their comparative efficacy remains debated.

Methodology 46 adult patients after heart surgery were recruited in this sequential clinical research. Prior to and following the EEOT and the PLR test, hemodynamic measures such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure variation (PPV), and central venous pressure (CVP) were measured. Responders defined by PPV decrease with cut off 5% in EEO test and cut off at least 10% in PLR test.

Results In the end-expiratory occlusion test, 24 individuals (52.2%) responded. While 27 patients (58.7%) responded to the PLR test. Both tests showed significant increase in SBP, DBP, MAP (P<0.05), and decrease in PPV% (P<0.05). ROC analysis revealed AUCs of 0.875 (SBP, EEOT) and 0.895 (SBP, PLRT) indicating good predictive performance.

Conclusion While both tests reliably predict fluid responsiveness, PLR test demonstrated numerically higher responder rates and greater hemodynamic changes than EEOT, though not statistically significant between both tools in evaluating fluid responsiveness. PPV remains the strongest predictor.

Keywords Cardiac surgery; End expiratory; Fluid responsiveness; Passive leg raising; Pulse pressure variation.
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INTRODUCTION

Fluid therapy is designed to enhance systolic volume, thereby improving cardiac output (COP) and facilitating oxygen delivery to tissues. However, the responsiveness to fluid administration in patients experiencing shock is not linear, as it is influenced by the myocardial contractility. In some cases, excessive fluid administration can be harmful, leading to diastolic dysfunction with elevated filling pressures and subsequent edema which are associated with higher mortality rates and prolonged use of invasive mechanical ventilation (IMV)[1]. In the context of cardiac surgery, optimizing preload, alongside the use of inotropes, is critical. Both fluids and medications must be carefully balanced to achieve the desired therapeutic effects[2].

Among hypotensive unstable patients, the use of fluid, vasopressors, or inotropes, when indicated, must be evaluated and closely monitored to ensure appropriate management[3]. The intensive care unit (ICU) frequently sees cases with acute circulatory collapse and Signs of impaired perfusion and oxygenation. Initial fluid resuscitation in hypotensive patients has been shown to reduce mortality[4]. However, after the initial resuscitation phase, continued fluid administration can be risky[5].

The diversity in clinical practices and the difficulties in anticipating fluid responsiveness prior to volume augmentation have been emphasized in earlier research[6,7]. In intensive care units, dynamic measures including changes in stroke volume and pulse pressure are frequently utilized to evaluate volumestatus[8]. To more accurately estimate fluid responsiveness, new methods have been devised, such as the EEOT[9]. In this test, a clamp is used to stop mechanical ventilation at end-expiration for 15 seconds. The inspiratory phase of positive pressure ventilation raises intrathoracic pressure in sedated, mechanically ventilated patients who are not exerting any effort to breathe. This lowers venous return, which in turn lowers right atrial pressure and right ventricular preload. When ventilation is temporarily halted, at the positive end-expiratory pressure (PEEP) level, right cardiac preload increases, indicating preload responsiveness for both ventricles.

The capacity of the EEOT to forecast fluid responsiveness was investigated by Monnet *et al.*,[10]. They discovered that intra-thoracic pressure rises during inspiration in patients on mechanical ventilation, which lowers venous return. Because EEO stops these pressure changes, preload-responsive individuals have higher venous return, cardiac preload, and stroke volume. During an end-expiratory occlusion, an increase in cardiac index is thought to be a sign of fluid responsiveness. In the ICU, it is crucial to continuously monitor the cardiac index using techniques like pulse contour analysis in order to identify this brief rise.

The Passive Leg Raise (PLR) test is another method to assess fluid responsiveness. This test involves elevating the legs of the patient for approximately 5 minutes, causing about 500mL of blood to be redistributed to the central circulation. Cardiac output is evaluated prior and post the test, with an increase of at least 10% suggesting fluid responsiveness. Some studies have also proposed using changes in pulse pressure, rather than cardiac output, as a marker of fluid responsiveness[11,12].

We compared the EEOT and the PLR test as indicators of fluid responsiveness in the intensive care unit following elective heart surgery.

OBJECTIVES

The primary objective of this study is to compare between the end expiratory occlusion test versus passive leg raising test as predictors of fluid responsiveness in post cardiac surgery mechanically ventilated patients in intensive care units. The secondary objective is to analyze the association between measured hemodynamic variables, vital sign fluctuations, and response to resuscitative interventions for the patients.

PATIENTS AND METHODS

The research was a prospective comparative sequential clinical trial that was randomized. It was registered with the at ClinicalTrials.gov and carried out at Ain Shams University Hospitals in Cairo, Egypt, with approval from the Medical Ethical Committee (FMASU MD 220/2022). Patients undergoing elective heart surgery were included in the registry (identifier: NCT06583200). Both sexes of patients between the ages of 21 and 60 are covered. For the gathering of data, written informed consent was acquired. The trial lasted for a year, beginning in January 2023. The study excluded patients with severe peripheral arterial occlusive disease, interventricular shunt, arrhythmias, lower limb deep vein thrombosis, open chest conditions with an unstitched sternum or impaired left ventricular ejection fraction (<45%), the need for intra-aortic balloon counterpulsation, pregnancy, or any other medical condition that could affect intra-abdominal pressure.

It is estimated that 40 post-cardiac surgery, mechanically ventilated patients were required to detect an expected area under the ROC curve of 0.75 for the predictive value of pulse pressure variation "PPV" for fluid responsiveness by end expiratory occlusion test[9] using PASS© version 11 for sample size calculation, setting power at 80% and α error at 5%. And this sample size would be enough to detect an expected AUC= 0.84 for predictive ability of pulse pressure variation by passive leg raising test[13]. Assuming a drop out rate of approximately 10%. at least 45 post cardiac surgery mechanically ventilated patients should be included. Thus 48 patients were enrolled in the study with random sampling by computer generated program, two patients were excluded due to post operative open chest conditions so 46 patients were included (Figure 1).

Study Procedures:

Immediately following the procedure, the subjects were moved to the ICU.

Measurements such as ECG, pulse oximetry, invasive arterial pressure, central venous pressure, and pulse pressure variation were taken while the patients were sedated and

ventilated on a Philips IntelliVue MX700 monitor. Prior to the end expiratory occlusion test, baseline measurements were taken, including heart rate, pulse pressure variation, arterial systolic and diastolic blood pressure, and central venous pressure. Each patient had a supine end expiratory occlusion test, which involved holding their breath for 15 seconds at the end of expiration while utilizing a GE CARESCAPE R860 ventilator. Measurements were taken at the conclusion of the expiratory occlusion test.

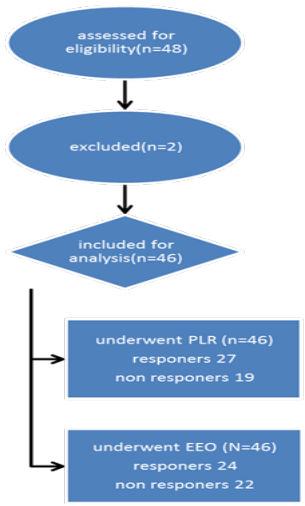

Fig. 1: Consort flow diagram of the study.

A baseline measurements before PLR test were recorded; arterial systolic blood pressure, diastolic blood pressure, heart rate, cntral venous pressure and pulse pressure variation. PLR test was applied starting from 45 semi-recumbent position then transferred to supine position followed by elevating lower limbs 45 for duration of 2 minutes. At the end of PLR test measurements were recorded.

End Expiratory Occlusion test was applied to distinguish the patients into probable responder and probable non-responder according to pulse pressure variation in accordance to previous study where the response to resuscitation defined as decrease in pulse pressure with cut off 5%[14,15]. Passive leg raising test was applied to distnguish the patients into probable responder and probable non-responder according to the pulse pressure variation in accordance to previous study where the response to resuscitation defined as decrease in pulse pressure with cut off at least 10%[15,16].

Statistical analysis:

The statistical software for social sciences, version 26.0 (SPSS Inc., Chicago, Illinois, USA), was implemented to evaluate the data. In the case of parametric (normal) distribution, the quantitative data were displayed as mean±standard deviation and ranges, whereas non-parametric data was displayed as median with inter-quartile range (IQR). Qualitative parameters were also displayed as frequency and percentage. Using the Shapiro-Wilk and Kolmogorov-Smirnov tests, the data were applied to test normality. The statistical tests used included the receiver operating characteristic (ROC) curve analysis and the paired sample *T*-test. A *P*-value <0.05 was deemed significant.

RESULTS

Table (1) shows statistically significant increase mean of SBP, DBP, MAP and CVP in after intervention compared to baseline end expiratory occlusion, with *p*-value ($p<0.05$).

Table 1: Compares baseline and after end expiratory occlusion based on SBP, DBP, MAP, HR, PPV%, and CVP:

Parameters	End expiratory occlusion		Paired Sample *T*-test			
	Baseline	After	MD±SD	*T*-test	*p*-value	Sig.
SBP (mmHg)	107.68±24.10	122.21±22.32	14.53±2.76	4.162	0.006	S
DBP (mmHg)	62.40±8.89	68.92±7.76	6.52±1.30	2.762	0.026	S
MAP (mmHg)	77.33±12.98	86.68±11.52	9.35±1.96	3.469	0.017	S
HR (beat/min)	99.02±13.42	96.85±14.89	-2.17±1.36	1.702	0.134	NS
PPV%	22.75±5.60	17.70±5.34	-5.05±0.96	4.163	0.006	S
CVP (mmHg)	7.87±3.21	8.53±3.06	-0.66±0.42	0.963	0.375	NS

Data presented as mean±SD; MD: Mean difference; SD: Standard deviation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; HR: Heart rate; PPV: Pulse pressure pressure; CVP: Central venous pressure; NS: Non significant; S: Significant; $p>0.05$ is insignificant; *: $p<0.05$ is significant.

While, there was a statistically significant decrease mean of PPV% in after intervention compared to baseline end expiratory occlusion, with *p*-value ($p<0.05$). However, based on HR (beat/min), there is no considerable difference between the baseline and post-intervention periods ($p>0.05$).

Table (2) shows statistically significant increase mean of SBP, DBP, MAP and CVP in after intervention compared to baseline PLR, with *p*-value ($p<0.05$). While, there was a statistically significant decrease mean of PPV% in after intervention compared to baseline PLR, with *p*-value ($p<0.05$). While, there is no statistically significant difference between baseline and after intervention, according to HR (beat/min), with *p*-value ($p>0.05$).

Table (3) shows the diagnostic performance of SBP, DBP, MAP, HR, PPV% and CVP in predicting of fluid response in end expiratory occlusion and PLR. It was also shown that the statistical significance of these results is related to the *p*-value ($p<0.05$).

Table 2: Comparison between Baseline and After according to SBP, DBP, MAP, HR, PPV%, CVP in PLR:

Parameters	PLR		Paired Sample *T*-test			
	Baseline	After	MD±SD	*T*-test	*p*-value	Sig.
SBP (mmHg)	106.89±18.59	124.54±19.42	17.65±3.35	3.614	0.009	S
DBP (mmHg)	58.76±5.83	71.72±7.52	12.96±2.46	3.641	0.008	S
MAP (mmHg)	74.69±8.87	89.33±10.24	14.64±2.78	3.529	0.007	S
HR (beat/min)	98.19±8.22	93.87±13.66	-4.32±1.77	1.585	0.131	NS
PPV%	21.21±4.15	15.87±3.45	-5.34±1.01	4.333	0.003	S
CVP (mmHg)	8.27±2.55	8.68±2.97	0.41±0.26	1.583	0.289	NS

Data expressed as mean±SD; MD: Mean difference; SD: Standard deviation; NS: Non significant; S: Significant; *p*-value >0.05 is insignificant; *: *p*-value <0.05 is significant.

Table 3: Diagnostic Performance of SBP, DBP, MAP, HR, PPV% and CVP in discrimination between fluid responsiveness and non-responsiveness:

Items	Cut-off	Sen.	Spe.	PPV	NPV	AUC (C.I.95%)	*P*-value
EEO							
SBP (mmHg)	>12.64	87.00	88.0	87.9	87.1	0.875(0.821-0.917)	<0.05*
DBP (mmHg)	>5.67	77.0	75.0	75.0	76.0	0.760(0.695-0.817)	<0.05*
MAP (mmHg)	>8.13	82.0	83.0	82.8	82.2	0.825(0.765-0.875)	<0.05*
HR (beat/ min)	>-1.89	48.0	53.0	50.5	50.5	0.505(0.434-0.576)	>0.05
PPV%	>-4.39	82.0	83.0	82.8	82.2	0.825(0.765-0.875)	<0.05*
CVP (mmHg)	>0.65	58.0	52.0	54.7	55.3	0.550(0.478-0.620)	>0.05
PLR							
SBP (mmHg)	>15.36	89.0	90.0	89.9	89.1	0.895(0.844-0.934)	<0.05*
DBP (mmHg)	>11.28	79.0	79.0	79.0	79.0	0.790(0.727-0.844)	<0.05*
MAP (mmHg)	>12.74	84.0	85.0	84.8	84.2	0.845(0.787-0.892)	<0.05*
HR (beat/ min)	>-3.76	49.0	54.0	51.6	51.4	0.515(0.443-0.586)	>0.05
PPV%	>-4.65	85.0	86.0	85.9	85.1	0.855(0.798-0.901)	<0.05*
CVP (mmHg)	>0.40	60.0	53.0	56.1	57.0	0.565(0.493-0.635)	>0.05

Sens.: Sensitivity; Spec.: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area Under the Curve; 95% C.I. Confidence interval; *p*-value >0.05 is insignificant; *p*-value <0.05 is significant.

Figure (2) Receiver-operating characteristic (ROC) curve for prediction of fluid responsiveness for end expiratory occlusion, using the SBP, DBP, MAP, HR, PPV% and CVP.

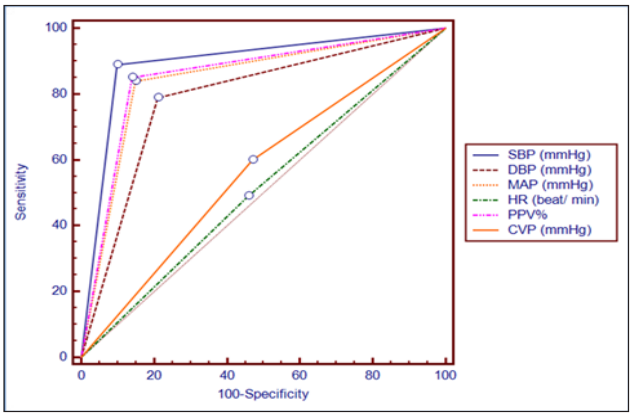

Fig. 2: (ROC) curve for prediction of fluid responsiveness for end expiratory occlusion as regarding to SBP, DBP, MAP, HR.

Figure (3) Fluid responsiveness prediction utilizing receiver-operating characteristic (ROC) curve for PLR based on SBP, DBP, MAP, HR, PPV%, and CVP.

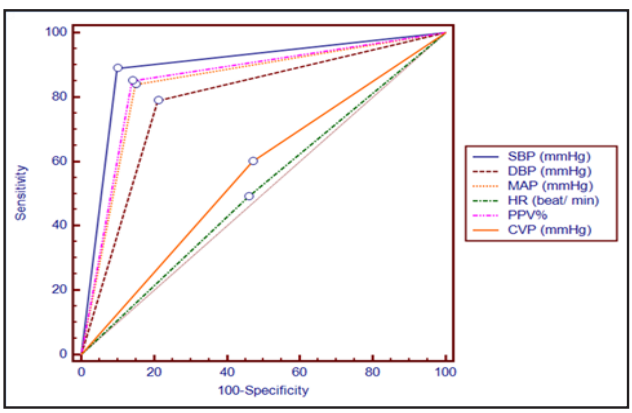

Fig. 3: (ROC) curve for fluid responsiveness prediction for PLR as regarding to SBP, DBP, MAP, HR, PPV% and CVP.

DISCUSSION

Assessing the patient's volume status is essential in peri-operative care. The primary objective is to maintain fluid balance, ensuring stability while avoiding conditions like hypervolemia or hypovolemia. Insufficient hydration is linked to adverse outcomes. Fluids should only be administered based on clearly defined protocols tailored to individual needs, ensuring proper dosing[17].

Before administering fluids, patients must undergo clinical evaluation. In cases of acute circulatory failure, obvious fluid deficits should be addressed immediately, without first assessing preload responsiveness. In other clinical situations, fluids should be administered if a positive impact is expected, necessitating patient examination prior to fluid administration[14].

Current studies draw attention to the disparity in procedures and the unusual foresight of fluid response prior to volume augmentation[7]. Although their limits are well-documented in the intensive care unit, dynamic measures such as changes in stroke volume and pulse pressure are reliable markers[8]. Novel methods have been devised, including the end-expiratory occlusion test, lung recruitment movements, and the evaluation of temporary increases in tidal volume[9,10].

The end-expiratory occlusion test was tested by Monnet *et al.,*[10] to forecast fluid response. In order to measure hemodynamic changes, mechanical ventilation is stopped for 15–30 seconds at the conclusion of the expiration phase. It raises ventricular preload by stopping the decline in venous return, and in patients on mechanical ventilation, stroke volume (SV) rising may be a sign of fluid responsiveness[15].

Preload response in both ventricles can be reliably evaluated using the PLR test, which elevates cardiac preload. In cases with spontaneous ventilation and cardiac arrhythmias, the "self-transfusion" of around 300mL of blood is dependable since it is reversible and independent of heart rate and breathing[18].

This study aimed to compare EEO and PLR tests for predicting fluid responsiveness in post-cardiac surgery mechanically ventilated subjects. We conducted a clinical trial with 46 patients. The end expiratory occlusion identified 24 responders (52.2%) and 22 non-responders (47.8%), while PLR showed a slightly higher responder rate of 27 patients (58.7%) and 19 non-responders (41.3%).

Both tests resulted in significant blood pressure increases for both responders and non-responders with higher increase in responders across SBP, DBP, MAP, and CVP. Additionally, PPV % decreased in both groups, with a more significant difference in responders, while no potential changes in heart rate were observed after either test.

Our findings align with studies by Mallat *et al.,*[19] and Ma *et al.,*[20] who also observed significant blood pressure increases during PLR in responders. Similarly, Monnet *et al*.,[10] found a significant increase in cardiac index and pulse pressure during PLR in responders. In contrast, non-responders showed no significant changes. Regarding end expiratory occlusion, our results are consistent with Monnet *et al.,*[10] who reported a rise in arterial pulse pressure in volume responders.

We evaluated the diagnostic performance of both tests in predicting fluid responsiveness. In PLR, SBP at a cutoff of >12.64mmHg showed high sensitivity and specificity (89.0% and 90.0%, respectively), with an AUC of 0.895. DBP at >11.28mmHg had sensitivity and specificity of 79.0%, while MAP at >12.74mmHg had sensitivity and specificity of 84.0%. PPV% at >-4.65 had sensitivity and specificity of 85.0% and 86.0%, respectively.

Our findings are inagreement with other studies, such as Mallat *et al*.,[19] which reported similar cutoff values for ΔPPV PLR. Additionally, Taccheri *et al.,*[21] demonstrated that ΔPPV PLR estimated fluid responsiveness with high sensitivity and specificity. Monnet *et al.,*[10] and Hamzaoui *et al*.,[22] supported the reliability of the PLR test.

Regarding end expiratory occlusion, our results revealed good sensitivity and specificity for SBP (>15.36mmHg), DBP (>5.67mmHg), MAP (>8.13mmHg), and PPV% (>-4.39). Monnet *et al.,*[10] reported similar findings for end expiratory occlusion, while Si *et al*.,[23] and Messina *et al.,*[24] highlighted the strong diagnostic performance of end expiratory occlusion in predicting fluid responsiveness.

CONCLUSIONS

In summary, our research revealed that the EEOT and PLR test are equally reliable to forecast fluid responsiveness in patients after heart surgery who are on mechanical ventilation, with good sensitivity and specificity. It is not advised to use hemodynamic measurements such as heart rate and central venous pressure to assess fluid responsiveness. When predicting fluid responsiveness, functional hemodynamic indicators like PPV did well.

LIMITATIONS TO OUR STUDY

It is difficult to generalize our findings as we conducted this study in a single center on a small sample size.

ACKNOWLEDGEMENT

We would like to thank Ain Shams university hospital for supporting this study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the research ethics committee at the faculty of medicine, Ain Shams University (FMASU MD 220/2022) and registered with U.S. National Library of Medicine Clinical Trials.gov. Registry, identifier: NCT06583200. Written informed consent was obtained from all patients.

AVAILABILITY OF DATA AND MATERIAL

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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CONFLICT OF INTERESTS

There are no conflicts of interest.

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