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The Ability of Pulse Oximetry-Derived Peripheral Perfusion Index as a New Predictor of Fluid Responsiveness in Critically Ill Patients

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ABSTRACT

Background: Prediction of fluid responsiveness (FR) is of utmost significance in management of critically-ill patients. Echocardiography is a bedside, feasible tool in assessment of FR. Based on passive leg raising test (PLR), pulse oximetry-derived peripheral perfusion index (PPI) can be utilized in prediction of FR in critical-ill cases.

Aim: This study aimed to investigate the ability of pulse oximetry-derived PPI as a new predictor of FR in critically-ill patients.

Methods: This study included 95 critically-ill patients, after PLR test, 36 of our patients were found to be fluid responsive and 59 patients were fluid non-responsive. FR was defined by increase in ≥ 10% increase in left ventricular outflow tract (LVOT) velocity time integral (VTI) (LVOT-VTI) after PLR test. Bedsides, echocardiography and pulse co-oximetry were used to measure LVOT-VTI and PPI before and after both PLR and 200 mL fluid challenge with Ringer's solution in responders. Sequential Organ Failure Assessment (SOFA) score was calculated.

Results: VTI and PPI increased after PLR test compared to baseline values. ΔPPI showed moderate ability to detect fluid responder [A cutoff value of 0.28 achieved a sensitivity (Sn) of 75.0% and specificity (Sp) of 72.9%, with a positive predictive value (PPV) of 63.4%, a negative predictive value (NPV) of 81.5%, and an accuracy of 73.7%. A significant relationship was recorded between ΔPPI and ΔVTI caused by the fluid challenge.

Conclusion: Using bedside transthoracic echocardiography, PPI maneuver was a feasible, sensitive and highly specific method for prediction of fluid-responsiveness in critically-ill patients.

Keyword: PPI, FR, Critically-Ill cases.

INTRODUCTION

Fluid resuscitation has been considered the keystone of the management of cases having circulatory shock. Even though restoring the volume status of a shocked case is substantial, growing evidence displays that needless fluid administration has a harmful effects [1]. Fluid responsiveness (FR) is the ability of the left ventricle to increase its stroke volume (SV) secondary to fluid administration [2].

Evaluation of patient response to volume expansion presents a daily challenge for acute care physicians. Prediction of FR might include static tests or dynamic tests. [3]. Static measures to assess FR have been used for the last years, including central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), right atrial pressure (RAP) left ventricular end-diastolic area (LVEDA), inferior vena cava (IVC) diameter, right ventricular end-diastolic volume (RVEDV) [4].

Dynamic measures to assess FR include systolic pressure variation (SPV), pulse pressure variation (PPV), SV variation (SVV), IVC respiratory variation, carotid artery peak velocity variation, SVC respiratory variation and aortic velocity variation [5]. Transthoracic Echocardiography is a noninvasive method of assessing FR using dynamic alteration in LVOT VTI [6, 7]. As well, a change in pulse oximetry-derived PPI has been shown in recent studies to be a reliable, more feasible tool of assessing FR using pulse co-oximeter in response to fluid challenge test [8, 9]. PPI represents "the ratio between the pulsatile (AC) and non-pulsatile component (DC) of the light reaching the pulse oximeter" [10].

The plethysmographic signal of the pulse oximetry is composed of a pulsatile component (AC) and a non-pulsatile component (DC). This denotes the change in the volume of blood in the finger throughout the cardiac cycle. As a result, this AC depends on the SV, whereas the DC represents the light absorbed by venous blood, capillary blood, and different tissues. PPI decreases in conditions of hypoperfusion secondary to diminished AC with a constant DC of blood flow. Hence, the PPI value is affected by the alteration in cardiac output (COP), an essential determinant of tissue perfusion [11].

Aim of work: This study aimed to investigate the ability of pulse oximetry-derived PPI to predict FR in critically-ill patients measured by VTI of LVOT.

PATIENTS AND METHODS

This observational cohort (longitudinal) prospective study was held at Mansoura Medical Critical Care Unit in The Specialized Medical Hospital through the period from July 2024 to May 2025. This prospective trial included 95 ICU cases and was divided into two groups: Fluid responders group that included 36 patients and fluid non-responders group that included 59 patients.

Inclusion criteria: Cases aged more than 18 years old with critical illness that needs pharmacological and/or mechanical support of vital organ functions without which death could be imminent.

Exclusion criteria: Patients with head trauma, deep vein thrombosis in lower limbs, amputated leg, peripheral vascular disease, which preclude the application of the pulse oximeter, and those with poor echocardiographic window.

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Methods: All patients were subjected to full medical history taking including urban, rural, special habits as smoking, and history of existing diseases (existing co-morbidities e.g.: DM & HTN). Complete general examination included chest examination, abdomen examination and cardiac examination. Routine laboratory investigations included complete blood count (CBC), arterial blood gases, blood culture, liver and kidney function tests and circulatory system biomarkers which included mixed venous oxygen saturation. Hemodynamic parameters included arterial blood pressure (BP), pulse, capillary refill time (CRT), urine output and CVP. Scoring systems used for patients on admission included SOFA and Glasgow coma scale (GCS) to objectively assess a patient's level of consciousness.

Passive leg raising test (PLR) included transferring a patient from a semi-recumbent position to a position in which the trunk was horizontal and the lower extremities were elevated at 30–45° mobilizes blood from the splanchnic territory and the lower extremities and significantly raises mean systemic pressure and the upstream pressure of systemic venous return [12]. The PLR test increased cardiac preload and allowed the evaluation of preload responsiveness of right and left ventricles. The benefit of this is "self-transfusion" of roughly 300 mL of blood, which was transient [2].

Echocardiographic parameters included IVC diameter (assessed directly caudal to the junction of the hepatic vein with the IVC and about one–two cm caudal to the junction of the IVC and the ostium of the right atrium) and LVOT VTI calculation (chamber apical view was obtained and then pulsed-wave Doppler signal adjusted at the level of aortic annulus, VTI was then measured from the area under the envelope and the VTI was assessed by utilizing a phased array probe with a frequency of 1.5 to 4 MHz by expert physician where 3 readings were acquired for each VTI measurement and their average were measured for assessment [13]).

Regarding pulse-oximetry derived PPI, PPI was measured using pulse co-oximeter of applied to the 3rd or 4th digit. PPI reading was recorded following one–two minutes of application of the probe when a stable reading is settled and maximal PI was recorded. The PPI was a ratio calculated from pulse oximetry data by dividing the AC of the signal by DC and multiplying by 100, expressed as a percentage. The formula was "PI = (AC/ DC) x 100".

Two sets of measurements were performed, the initial set of data included baseline measures LVOT VTI and PPI and the second set was performed after PLR test for 1 min. Patients with a 10% change in LVOT VTI following PLR were classified as "responders," whereas the others were classified as "non-responders".

Another two sets of measurements were conducted in responders, the initial set of data included baseline measures LVOT VTI & PPI and the second set was conducted after infusion of 200 mL lactated Ringer's solution over 60 seconds.

Ethical considerations: Approval was obtained from IRB, Mansoura University, to conduct the study. Informed written consents were taken from all cases. Entire classes were informed about the details of the study. Confidentiality was respected. Throughout its implementation, the study matched with the Helsinki Declaration.

Statistical Analysis

Data presentation and statistical testing were carried out based on the nature and distribution of each variable. The Shapiro-Wilk test was applied to evaluate the normality of distribution for continuous variables. Normally distributed numerical data were expressed as mean ± SD. Non-normally distributed numerical data were presented as median and IQR. Categorical data were described using frequencies and percentages. Student's t test was used to compare the means between two independent groups when the data were normally distributed. U test was used for comparing non-normally distributed variables between two independent groups. Chi-square test (χ^2) was used to examine associations between categorical variables. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Table (1) displayed that mean age of study cases was 62.5 ± 14.0 years. Males constituted 58.9% of the sample, while females accounted for 41.1%. The most common primary diagnosis was septic shock in 34.7% of cases, followed by hypovolemic shock (12.6%) and mixed shock (12.7%). Mean GCS was 11.26 ± 5.24 and the mean heart rate was 92.47 ± 16.60 beats/min with a regular rhythm in 87.4% of patients. Mean arterial BP was 78.85 ± 13.35 mmHg and the mean vasopressor dose was 3.26 ± 3.05 μg/min. The mean respiratory rate was 21.45 ± 4.51 breaths/min and mechanical ventilation was required in 14.7% of cases. Mean oxygen saturation was 93.57 ± 4.84%, and mean capillary refill time was 3.92 ± 2.38 seconds. The mean CVP was 13.32 ± 4.08 cmH_2O, and the mean IVC diameter was 1.79 ± 0.47 cm.

Table (1): Demographic, medical data, clinical data, CVP and IVC Diameter of all patients

Parameter	Category	Study cases (n=95)
Age (years)	Mean ± SD	62.5 ± 14.0
	Median (IQR)	64.00 (19 to 89)
Sex	Male	56 (58.9%)
	Female	39 (41.1%)
Primary diagnosis	Hypovolemic Shock	12 (12.6%)
	Hepatic Encephalopathy	6 (6.3%)
	Cerebral stroke	7 (7.4%)
	Septic Shock	33 (34.7%)
	Cardiogenic Shock	3 (3.3%)
	Mixed Shock	12 (12.7%)
	AKI	7 (7.4%)
	Chest infection	8 (8.4%)
	Gastrointestinal bleeding	1 (1.1%)
	Hypo/Hypernatremia	3 (3.2%)
	Anaphylactic Shock	1 (1.1%)
	Hypokalemia	2 (2.1%)
GCS	Mean ± SD	11.26 ± 5.24
	Median (IQR)	14.00 (8.50–15.00)
HR (beats/min)	Mean ± SD	92.47 ± 16.60
	Median (IQR)	90.00 (80.00–106.50)
Regularity	Regular	83 (87.4%)
	AF	2 (2.1%)
	Irregular	10 (10.5%)
MAP (mmHg)	Mean ± SD	78.85 ± 13.35
	Median (IQR)	80.00 (70.00–85.00)
Vasopressor dose (NA) (µg/min)	n (%)	59(62.1%)
	Mean ± SD	3.26± 3.05
RR (breaths/min)	Mean ± SD	21.45 ± 4.51
	Median (IQR)	22.00 (18.00–24.00)
Mechanical ventilation	No	81 (85.3%)
	Yes	14 (14.7%)
SpO_2 (%)	Mean ± SD	93.57 ± 4.84
	Median (IQR)	95.00 (92.50–96.00)
Capillary refill time (CRT) (sec)	Mean ± SD	3.92 ± 2.38
	Median (IQR)	4.00 (2.00–6.00)
CVP (cmH_2O)	Mean ± SD	13.32 ± 4.08
	Median (IQR)	14.00 (10.00-16.00)
IVC diameter (cm)	Mean ± SD	1.79 ± 0.47
	Median (IQR)	1.80 (1.50-2.00)

Table **(2)** showed that age and gender didn't display significant difference between responders and non-responders. HR and MAP didn't show significant difference between both groups. The vasopressor used was norepinephrine and the difference wasn't significant. On the other hand, the responders had a significantly higher mean CRT compared to non-responders.

Table (2): Comparison studies of age, sex, Clinical data between responder and non-responder groups

Parameter	**Responders (n=36)**		**Non responders (n=59)**		
	Mean	**Standard Deviation**	**Mean**	**Standard Deviation**	**P value**
Age (years)	60.6	14.3	63.5	13.8	0.31
Gender	Count	%	Count	%	
Females	15	45.5%	25	40.3%	0.72
Males	18	54.5%	37	59.7%	
Clinical data					
Heart rate	91.24	12.44	89.70	11.78	0.720
MAP	77.22	8.21	77.60	6.28	0.891
Vasopressor (NA) dose (µg/min)	4.44	4.44	2.65	1.71	0.450
CRT (sec)	4.1	1.1	3.2	1.3	0.018*

Used tests: U test & Chi square test

Table **(3)** displayed that responders had a statistically significantly lower mean CVP compared to non-responders. Additionally, IVC diameter was markedly smaller in responders compared to non-responders. Regarding ABG, responders had a statistically significantly higher mean pH compared to non-responders. HCO^- levels were significantly higher in responders compared to non-responders. Insignificant differences were noticed between the two groups in $PaCO_2$ and $ScvO_2$ levels. Regarding laboratory data, responders had statistically significantly lower mean potassium levels compared to non-responders and lower CRP levels. Also, creatinine and bilirubin levels were significantly lower in responders. Besides, mean hemoglobin was slightly lower in responders and albumin was significantly higher. In addition, there were no significant differences noted in sodium, TLC, platelet count, AST, ALT, or INR. Responders had a statistically significantly lower mean SOFA score and mortality rate compared to non-responders.

Table (3): Comparison studies of CVP, IVC, ABG, laboratory data, SOFA score and mortality rate between responder and non-responder groups

	Category	**Responders (n=36)**	**Non responders (n=59)**	**p-value**	**Significance**
CVP (cmH_2O)	Mean ± SD	9.89 ± 2.90	15.41 ± 3.18	p<0.001	HS
IVC Diameter (cm)	Median (IQR)	1.40 (1.20-1.60)	2.00 (1.80-2.20)	p<0.001	HS
ABG					
pH	Mean ± SD	7.40 ± 0.09	7.33 ± 0.09	p=0.001	HS
$PaCO_2$ (mmHg)	Median (IQR)	35.50 (32.00-39.25)	36.00 (31.00-43.00)	p=0.362	NS
HCO_3^- (mmol/L)	Median (IQR)	20.90 (18.60-24.40)	18.60 (16.00-22.00)	p=0.023	S
$ScvO_2$ (%)	Median (IQR)	71.00 (68.10-75.83)	70.00 (65.00-75.00)	p=0.202	NS
Laboratory data					
Na^+ (mmol/L)	Mean ± SD	136.53 ± 8.88	133.46 ± 6.53	p=0.056	NS
K^+ (mmol/L)	Mean ± SD	3.81 ± 0.66	4.22 ± 0.76	p=0.008	HS
Hb (g/dL)	Mean ± SD	8.89 ± 2.16	9.73 ± 1.87	p=0.049	S
TLC ($\times10^3/\mu L$)	Median (IQR)	13.00 (9.20-17.02)	15.76 (8.75-20.70)	p=0.154	NS
PLT ($\times10^3/\mu L$)	Mean ± SD	228.00 ± 49.85	186.12 ± 18.39	p=0.118	NS
CRP (mg/L)	Median (IQR)	34.50 (8.00-107.25)	112.00 (48.00-183.50)	p=0.001	HS
Creatinine (mg/dL)	Median (IQR)	1.25 (0.90-2.30)	2.20 (1.30-3.95)	p=0.006	HS
Albumin (g/dL)	Mean ± SD	3.16 ± 0.51	2.91 ± 0.62	p=0.047	S
Bilirubin (mg/dL)	Median (IQR)	1.00 (0.80-1.48)	1.50 (0.95-2.90)	p=0.019	S
AST (U/L)	Mean ± SD	64.03 ± 6.34	163.53 ± 40.72	p=0.221	NS
ALT (U/L)	Mean ± SD	38.42 ± 47.75	103.37 ± 289.91	p=0.187	NS
INR	Median (IQR)	1.30 (1.18-1.50)	1.30 (1.12-1.65)	p=0.576	NS
SOFA	Mean ± SD	6.31 ± 1.52	10.41 ± 2.32	p<0.001	HS
Mortality rate	n (%)	12 (26.7%)	33 (73.3%)	p<0.001	HS

Used Tests: Student's t test, U test & Chi square test

Table (4) showed that responders had a statistically significantly higher LVOT VTI post-PLR compared to non-responders, despite no significant difference in LVOT VTI pre-PLR. PPI post-PLR was also significantly higher in responders vs non-responders, while PPI pre-PLR showed insignificant difference between groups. Regarding Δ PPI after PLR, responders exhibited a markedly greater change compared to non-responders.

Table (4): Comparison studies of LVOT VTI and PPI pre and post PLR test between responder and non-responder groups

Parameter	Category	Responder (n=36)	Non responder (n=59)	p-value	Significance
LVOT VTI Pre-PLR (cm)	Median (IQR)	17.69 (14.91-21.41)	19.23 (12.09-24.37)	p=0.053	NS
LVOT VTI Post-PLR (cm)	Median (IQR)	21.38 (18.32-25.27)	17.86 (16.44-22.65)	p=0.002	HS
PPI Pre-PLR	Median (IQR)	1.54 (0.95-2.30)	1.26 (0.81-2.22)	p=0.492	NS
PPI Post-PLR	Median (IQR)	2.11 (1.27-3.13)	1.18 (0.57-2.13)	p=0.004	HS
ΔPPI after PLR	Median (IQR)	0.35 (0.27-0.62)	0.11 (0.06-0.28)	p<0.001	HS

Used Tests: student's t test, U test & Chi square test

Table **(5)** showed that LVOT VTI and PPI significantly increased after second fluid challenge in responders group.

Table (5): Comparison studies of LVOT VTI and PPI pre and post second fluid challenge test between responder groups

Parameter	Category	Responder (n=36)	p-value	Significance
LVOT VTI Pre-200 mL RI (cm)	Median (IQR)	17.88 (15.24-20.53)	p=0.492	NS
LVOT VTI Post-200 mL RI (cm)	Median (IQR)	21.52 (18.24-24.71)	p<0.001	HS
PPI Pre-200 mL RI	Median (IQR)	1.54 (0.87-2.34)	p=0.258	NS
PPI Post-200 mL RI	Median (IQR)	2.00 (1.05-2.59)	p<0.001	HS

Used Tests: student's t test, U test, Chi square test

Table **(6)** showed that validity of Δ PPI and the area under the curve (AUC) was 0.775 (p<0.001), reflecting good discriminative ability between responders and non-responders. A cutoff value of 0.28 achieved sensitivity (Sn) of 75.0% and specificity (Sp) of 72.9%, with a PPV of 63.4%, a NPV of 81.5%, and an accuracy of 73.7%.

Table (6): Validity of Δ PPI in discrimination between responders and non-responders

Variable	AUC	95% CI	p-value	Cut off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
ΔPPI after PLR	**0.775**	**(0.682 – 0.868)**	**<0.001**	**0.28**	**75.0**	**72.9**	**63.4**	**81.5**	**73.7**

DISCUSSION

First line treatment in most of the shock states is intravenous fluid administration. When fluid responsiveness isn't evaluated, a fluid bolus increases COP in 50% of the cases only. Fluid overload is linked to elevated mortality and causes numerous adverse events, which include pulmonary oedema, heart failure, tissue breakdown, and impairment of gut functions. Thus, the assessment of volume condition is important in the initial management of critically-ill cases [14].

Echocardiography is a bedside, non-invasive, readily available approach to predict FR by assessing the change in SV due to various fluid challenge techniques [15].

PPI represents "the ratio between the AC and DC of the light reaching the pulse oximeter". The plethysmographic signal of the pulse oximetry consists of AC and DC. The AC represents the change in the volume of blood in the finger throughout the cardiac cycle; as a result, this AC is mainly reliant on the SV, whereas the DC represents the light absorbed by venous blood, capillary blood and different tissues [8].

The mean age in the current study population was 60.6 ± 14.3 years among responders and 63.5 ± 13.8 years among non-responders. Age didn't show significant difference between both groups (p = 0.12). This age group is comparable to that enrolled in **Jozwiak *et al.*** [16] study where mean age was 62 ± 13 among responders and 66 ± 11 among non-responders with insignificant effect on fluid responsiveness.

Mean value of mean arterial BP was 78.85 ± 13.35 mmHg ranging from 70 to 85 mmHg with insignificant difference between responders and non-responders (P =0.891). Also, **Hasanin *et al.*** [8] study demonstrated that MAP was 83 ± 13 in fluid responders and 81 ± 11 mmHg in fluid non-responders with insignificant difference. Also, **Beurton *et al.*** [11] found that mean arterial pressure was 77 ± 13 in fluid responders and 81 ± 12 mmHg in fluid non- responders with no statistically significant difference.

In our study, the vasopressor used was norepinephrine, and mean vasopressor (NA) dose was 4.44 µg/min in fluid responders vs 2.65 µg/min among non-responders. However, the difference wasn't significant (P=0.45). In agreement with our results, **Hasanin *et al.*** [8] used norepinephrine as a vasopressor with a dose of 16.3 mg/min in fluid responders and 17.7 mg/min in non-responders with insignificant difference between both groups.

In the present study, responders had significantly lower central venous pressure (CVP), with a mean of 9.89 cmH_2O compared to 15.41 cmH_2O in non-responders (p<0.001). Against our results, **Beurton *et al.*** [11] found that mean CVP was 10±5 in fluid responders and 10±5 cmH_2O in fluid non-responders with no statistically significant difference.

Our study demonstrated that the IVC diameter was significantly smaller in responders (median 1.40 cm) than in non-responders (median 2.00 cm) (p<0.001). This comes in agreement with **Vijayaraghavan *et al.*** [17] who highlighted the predictive potential of end-expiratory IVC diameter with high Sp, they found that IVC diameter ≤ 13 mm predicted fluid responsiveness with a Sp of at least 80%, while IVC diameter ≥ 25 mm predicted the absence of fluid responsiveness with a Sp of at least 80%.

In the current study, the mean CRT was significantly higher in responders (mean 4.1 sec) than in non-responders (mean 3.2 sec) (p<0.018). This is consistent with the study of **Raia *et al.*** [18] who determined kinetics of CRT following fluid challenge on 40 critically-ill cases and found that responders had a higher baseline median CRT (3.8 sec) compared to non-responder (2.8 sec) with p=0.02.

In the present study, arterial pH was significantly increased in responders (mean 7.40) compared to non-responders (mean 7.33) (p=0.001). Confirming our results, **Bauer *et al.*** [19] led a study to record correlation of arterial pH with hemodynamic response to antidiuretic hormone in cases with septic shock and found that the reduction in arterial pH was independently accompanied by lower odds of hemodynamic response to antidiuretic hormone. Against our results, **Raia *et al.*** [18] found that median of arterial pH was 7.32 ranged from 7.27 to 7.44 in fluid responders and 7.29 ranged from 7.10 to 7.40 in fluid non- responders with insignificant difference.

In the present study, serum creatinine was significantly lower in responders (median 1.25 mg/dL) versus non-responders (median 2.20 mg/dL) (p=0.006). Against our results, **Raia *et al.*** [18] found that median of serum creatinine level was 131 µmol/L ranged from 84 to 241 in fluid responders and 104 µmol/L ranged from 99 to 117 in fluid non-responders with no statistically significant difference regarding serum creatinine level.

In the present study, serum potassium levels were significantly reduced in responders (mean 3.81 mmol/L) compared to non-responders (mean 4.22 mmol/L) (p=0.008). This may be explained that patients with lower potassium levels had better renal perfusion and a more intact renin-angiotensin-aldosterone system (RAAS), enabling more effective fluid responsiveness (e.g., angiotensin II–dependent Na^+/K^+-ATPase regulation on reduced perfusion) and the responders had better acid-base status reducing cellular potassium shifts. However, **Özkarakaş *et al.*** [19] showed insignificant difference in serum potassium value between responders and non-responders.

In the present study, serum albumin was significantly higher in responders (mean 3.16 g/dL) compared to non-responders (mean 2.91 g/dL) (p=0.047). Confirming our results, **Zhang *et al.*** [20] led

a study to report the correlation between serum albumin level and fluid responsiveness found that non-responders had significantly lower albumin level (median 26 g/L vs. 32 g/L in responders ($p<0.001$) and serum albumin level < 28 g/L predicted poor fluid responsiveness.

In the present study, SOFA scores were significantly diminished in responders (mean 6.31) than in non-responders (mean 10.41) ($p<0.001$). These findings align with **Cordemans *et al.*** [21] who assessed the prognostic value of extravascular lung water index (EVLWI), capillary leak parameters, intra-abdominal pressure and fluid balance in critically-ill cases and found that responders (patients who achieved fluid balance targets) had consistently lower total SOFA scores from day 2 onward compared to non-responders ($p < 0.001$).

Our study delved into the outcome of fluid responders and non-responders, revealing that fluid responsiveness was strongly correlated with mortality with p value<0.001. This is against with the findings of **Kattan *et al.*** [22] who found that fluid resuscitation guided by fluid responsiveness assessment had no negative impact on clinically relevant outcomes in septic shock cases. Also, **Raia *et al.*** [18] found that mortality rate was 7 patients (24% of all patients) and all were from responder group.

In the current study, LVOT VTI after PLR was significantly higher in responders (median 21.38 cm) compared to non-responders (median 17.86 cm) ($p=0.002$). Also, **Beurton *et al.*** [11] found the cardiac index post PLR test was 4.03 ± 1.31 in responders and 3.26 ± 1.32 in non-responders with statistically significant difference between both groups. This significant difference in post-PLR LVOT VTI between the two groups supports the clinical utility of dynamic assessment tools in guiding fluid therapy in critically-ill cases. Unlike static measures, which include CVP, LVOT VTI that directly reflects functional cardiac performance, the PLR maneuver provides a reversible and safe "self-volume challenge," and the observed VTI increase in responders confirms the heart's ability to accommodate preload augmentation effectively. This avoids unnecessary fluid overload, which is particularly important in patients at risk of pulmonary edema or organ dysfunction [23].

In the present study, median of PPI pre-PLR was 1.54 in responders and 1.26 in non-responders (median 1.24) with no statistically significant difference ($p=0.492$). Also, **Hasanin *et al.*** [8] found that median of PPI pre-fluid challenge was 0.81 (0.32–2.00) in responders and 0.72 (0.41–2.5) in non-responders with no statistically significant difference between them. Against our study, **Rauch *et al.*** [24] found that median of PPI pre-PLR test was higher in non-responders (2.6) compared to responders (1.2) with significant difference between them.

In the present study, PPI after PLR was significantly higher in responders (median 2.11) than in non-responders (median 1.18) ($p=0.004$). Similarly, **Beurton *et al.*** [11] study found that mean PPI post PLR test was 4.1 ± 2.3 in responders and 2.0 ± 2.0 in non-responders with statistically significant difference between them. Against our study, **Rauch *et al.*** [24] study found that median of PPI post-PLR test was higher in non-responders (2.8) compared to responders (1.7) with statistically significant difference between them. This may be explained by that the baseline of PPI was higher in non-responders than responders.

The change in PPI (ΔPPI) after PLR was significantly greater in responders (median 0.35) versus non-responders (median 0.11) ($p<0.001$). Similarly, **Rauch *et al.*** [24] assessed whether perfusion index (PI) and pleth variability index (PVI) can predict FR in post-surgical, spontaneously breathing cases throughout a PLR test. The prospective study comprised spontaneously breathing cases following major abdominal surgery in the ICU. The authors found that responders (≥10% SV increase) had a 41.2% increase in PI (perfusion index) during PLR, compared to only 11.3% in non- responders. A PI increase ≥ 23% predicted responsiveness with 70% Sn and 75% Sp (AUC 0.74). This finding is against a study that of **Broch *et al.*** [25] who assessed whether perfusion index (PI) and PVI could predict FR in 81 patients undergoing elective coronary artery surgery. The authors found that PVI and PI couldn't predict FR with p=0.11 and 0.14 respectively. They also found that accuracy of PVI to predict FR was improved on analyzing cases with higher PI value and PI of approximately 4% accomplished statistical significance with p=0.01.

In the present study, the ROC analysis for ΔPPI displayed an AUC of 0.775, with a cutoff value 28% yielding 75.0% sensitivity, 72.9% specificity, and 73.7% overall accuracy ($p<0.001$). Supporting our findings, **Hasanin *et al.*** [8] led a study to investigate whether the alterations in the pulse oximetry-derived PPI, as a noninvasive surrogate of COP, could determine FR by utilizing the fluid challenge test or not. ΔPPI displayed moderate ability to determine fluid responders [AUC 0.82, sensitivity 76%, specificity 80%, PPV 92%, NPV 54%, cutoff value ≥5%].

CONCLUSION

In conclusion, responders to fluid challenge demonstrated significantly more favorable clinical and biochemical profiles compared to non-responders. Responders exhibited lower CVP, smaller IVC diameter, higher arterial pH and bicarbonate levels, as well as lower levels of potassium, CRP, creatinine, and bilirubin. They also had higher serum albumin and significantly lower SOFA scores reflecting less severe organ dysfunction. Hemodynamically, responders showed greater increases in LVOT VTI and PPI

following passive leg raising, with a notable rise in ΔPPI. The ROC analysis further confirmed the diagnostic value of ΔPPI in predicting fluid responsiveness with strong sensitivity and specificity. These results suggested that pulse oximetry-derived PPI, particularly changes observed after PLR, may serve as a practical, non-invasive alternative for identifying fluid responders among critically ill patients.

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