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ORIGINAL ARTICLE

The Ability of Pulse Oximetry-Derived Peripheral Perfusion Index to Detect Fluid Responsiveness in Patients with Septic Shock

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Abstract

Background: ***The fluid challenge test is a prominent method for determining fluid responsiveness in patients with acute circulatory failure. An easy method will be tested to detect the patient's response to the fluorimetry-derived using pa, oximetry-derived peripheral pe, and fusion index.***

Objective: ***To evaluate: whether pulse oximetry-derived peripheral perfusion index may predict fluid responsiveness in septic shock patients.***

Subjects and Methodology: ***A prospective cohort research was conducted on 35 septic shock patients requiring fluid resuscitation to compare LVOT VTI variability and PPI for assessing fluid responsiveness. After baseline measurements, we administered a mini fluid challenge of 200ml crystalloids. Fluid responsiveness was characterized as a greater than 10% increase in LVOT VTI.***

Results: ***From 35 patients who were admitted, 26 (74.3%) were fluid responsive and (25.7%) 9 were not responsive; peripheral perfusion index (PPI) had a statistically significant correlation with Meanleft ventricular outflow tract velocity time integral(LVOT VTI) variability.***

Conclusion: ***PPI measured by pulse oximetry is noninvasive, inexpensive, and extremely reliable for estimating fluid responsiveness in critically ill patients with hypoperfusion symptoms. It outperforms LVOTVTI estimations from transthoracic echocardiography. Dynamic PPI trends enable real-time fluid responsiveness-guided patient-tailored early resuscitation.***

Keywords: Pulse Oximeter; Septic Shock; Fluid Responsiveness

1. Introduction

Fluid balance is one of the most difficult management plans for all patients with acute hemodynamic instability because the Frank-Starling law states that IV fluids within limits improve stroke volume and tissue perfusion. However, excess IV fluids increase hydrostatic pressures in the CVS, which makes patients more likely to have edema and organ failure, in addition to higher mortality rates. [1]

Although septic shock has been associated with relative hypovolemia, just 50% of the cases experiencing hemodynamic instability exhibit fluid responsiveness.[2]

For now, static and dynamic components are employed to forecast fluid response. Some hemodynamic indicators obtained during clinical monitoring or altered have been proven to predict fluid infusion response on cardiac output. [3]

In addition to arterial cannulation, invasive central venous catheterization is a major drawback of dynamic or static measurements. This is one reason why non-invasive ultrasonography is used in critical care; echocardiography is a well-established fluid response test. [4]

Tissue perfusion may be diagnosed non-invasively, quickly, and in real-time using pulse oximetry's peripheral perfusion index (PPI). Recent research suggests that the peripheral perfusion index can replace the cardiac index in passive leg-raising tests and pre-load modifying techniques to determine fluid responsiveness. In cases where cardiac output monitors were not accessible, it was suggested that the PPI be used to identify positive fluid challenge tests. [5,6]

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This study primarily aims to correlate fluid responsiveness and PPI readings and their predictability.

2. Patients and methods

This prospective cohort study included 35 ICU septic shock or sepsis patients using a sepsis campaign (admitted to the Critical Care department, Faculty of Medicine, Al-Azhar University, and Cairo University hospitals from November 2022 to August 2023) requiring fluid resuscitation to compare LVOT VTI variability and PPI for assessing fluid responsiveness. After baseline measurements, we administered a mini fluid challenge of 200ml crystalloids. Fluid responsiveness was characterized as a greater than 10% increase in LVOT VTI.

In the study, we included patients who fulfilled these criteria: Patients≥ 18 years old, in Septic shock, Breathing spontaneously, requiring vasopressor medications to keep their mean arterial pressure (MAP) at or above 65 mm Hg. After adequate volume resuscitation, the serum lactate level is over two mmol/L (18mg/dL). Patients with hypoperfusion symptoms (skin mottling, capillary refill beyond 3 seconds).

Exclusion criteria are structural heart disease, poor transthoracic echocardiographic window, impaired left ventricular systolic function, and advanced diastolic dysfunction.

We gave the patient 200 ml crystalloid as a mini fluid challenge. LVOT VTI was measured by pulsed wave Doppler before and after the fluid challenge, with an increase of>10% defining fluid responsiveness. PPI was measured by a pulse co-oximeter before and after the fluid challenge. The accuracy of LVOT VTI and PPI for assessing fluid responsiveness was then compared.

All patients were subjected to the following: Routine Echocardiography study, including dimensions and ejection fraction: Either Simpson's approach or M-mode is used to analyze ejection fraction to rule out heart failure with a lower ejection fraction. Valvular assessment to exclude significant valvular affection. All patients were assessed before and after the administration of the mini-fluid challenge.

To obtain LVOT-VTI, Place the probe in the midaxillary line, namely in the fifth intercostal space, ensuring that the indicator of the probe is directed towards the 3 o'clock position. Orient the probe in an upward direction to enhance the visibility of the left ventricular aortic outflow system.

The Doppler cursor is placed close to the aortic valve annulus, within a range of 15 degrees from the left ventricular outflow tract (LVOT), utilizing the pulsed wave (PW) Doppler sample volume. A method for measuring aortic blood flow involves using PW Doppler across the left ventricular outflow tract (LVOT) in the apical 5-chamber (A5C) view. The VTI is obtained by recording the aortic blood flow using a PW Doppler trace across the LVOT. This trace can be manually traced in the LVOT, and the VTI is determined by measuring the area under the trace. The VTI represents the stroke distance or the displacement of red blood cells during systole. The VTI is calculated by measuring each heartbeat's area under the curve. LVOT-VTI is measured both before and after a mini-fluid challenge of 200ml crystalloids.

The peripheral perfusion index and its variability were obtained using a pulse co-oximeter with the third or fourth digit. The reading was recorded once the probe had been applied for 1-2 minutes, and a stable reading had been obtained.

Pre and post-fluid administration, the Peripheral perfusion index was obtained, and the ΔPPI was calculated.We use trismed co., LTD VITAPIA 7200T Screen machine- Using its pulse oximeter.Two readings of the Peripheral perfusion index and its variability were recorded in two cycles, and the average of the two measurements was calculated. LVOT VTI and Peripheral perfusion index measurements were taken in the same study session.

Sample size calculation

This study was based on a study carried out by Hasaninet et al.,[5] Epi Info STATCALC was used to calculate the sample size by considering the following assumptions: 95% two-sided confidence level, with a power of 80%. & An error of 5% odds ratio calculated = 1.45. The final maximum sample size taken from the Epi—Info output was 35.

Statistical Analysis

Utilizing Statistics, The data was coded and entered using SPSS version 28 by IBM Corp. Quantitative data is described by the mean, standard deviation, median, minimum, and maximum. The data was analyzed using frequency count and percentage. We compared two numeric variables using the non-parametric Mann-Whitney test. Data from the same individual was analyzed using the non-parametric Wilcoxon signed-rank test. Category data was analyzed using the Chi-square test. We used the exact test when the number of projected times was less than 5. We used the Spearman correlation value to correlate quantitative components. A p-value below 0.05 was used to determine statistical significance.[7,8,9]

3. Results

Patients diagnosed with sepsis or septic shockaccording to the latest sepsis campaign guidelines, received a small fluid challenge of 200 ml crystalloid. The LVOT VTI was measured before and after the fluid challenge. Fluid responsiveness is determined by the increase in LVOT VTi after the mini fluid challenge. There were 26 patients who responded to the fluid and 9 patients who did not respond.

Demographic data:patient's ages 61.71 ± 14.31 years. Of the total patients, 51.4% were female.

Comorbidities and clinical data: From total studied population, 22.9% were found to be smoker, HTN was found in 54.3% of the patients, diabetes mellitus was found in 68.6% of patients, 25.7% had chronic kidney disease, 20 % had hepatic disease and lung diseases were found in 20 % of whole study populationas shown in Table1.

Table 1. Comorbidities.

COMORBIDITIES	NO OF PATIENT'S	PERCENTAGE
HTN	19	[54.3%]
DIABETES	24	[68.6%]
CKD	17	[25.7%]
HEPATIC	7	[20%]
PULMONARY	7	[20%]
SMOKER	8	[22.9%]

Hemodynamics: Mean arterial blood pressure measured was [66.31±10.04 mmHg], heart rate was [102.86±15.09 ranging from 79 to 136 beat/:min], UOP was [78.48±37.74 ml/hr.], CVP was [8.91±3.95mmHg], Capillary refill time was [3.37±0.84 sec].

Correlative data: Fluid responsiveness and comorbidities; There was no statistically significant difference between responder and non-responder regarding sex with p value =0.443as shown in Table2

Table 2.Fluid responsiveness and sex

		FLUID RESPONSIVENESS BY LVOT VTI				P VALUE
		Responder		Non responder		
		Count	%	Count	%	
SEX	Male	14	53.8%	3	33.3%	0.443
	Female	12	46.2%	6	66.7%	

Among the studied population, 8 patients were found to be smoker, 6 patients of them (75%) were found to be fluid responder, while 2 patients (25%) of them were found to be fluid non-responder, with no statistically significant regarding p value=1

Considering Hypertension was found in 19 patients of total studied populations, there was 13 (68.4%) of the patients were found to be fluid responder, while 6 (31.6%) of them were found to be fluid non-responder, with no statistically significant regarding p value =0.460

Diabetes was found in 24 patients from whole studied population, 19 patients (79.2%) were found to be responder, whereas 5 patients (20.8%) were found to be non-responder, there is no statistically significance regarding diabetic patient with p value=0.416

Chronic kidney disease patients who were found in whole population was 9 patients, fluid responders account for 8 (88.9%) of the patients, while non-responder account for 1 (11.1%) of the patients, with no statistically significant with p value = 0.391

regarding Hepatic disease there was 7 patients found in whole studied population, 3 patients of them (42.9%) were fluid responder, while 4 patients (57.1%) of them were non-responder, there is statistically significant with p value= 0.055

Concerning patients with Lung disease there was 7 patients from total studied population, 5 (71.4%) of them were responder, while 2 patients (28.6%) of them were found to be non-responder, there is no statistically significance with p value =0.638 as shown in Table 3.

Table 3. Fluid responsiveness and comorbidities

		FLUID RESPONSIVENESS BY LVOT VTI				P VALUE
		Yes		No		
		Count	%	Count	%	
SMOKER	YES	6	75%	2	25%	1
	NO	20	74.1%	7	25.9%	
HTN	YES	13	68.4%	6	31.6%	0.460
	NO	13	81.2%	3	18.8%	
DM	YES	19	79.2%	5	20.8%	0.416
	NO	7	63.6%	4	36.4%	
CKD	YES	8	88.9%	1	11.1%	0.391
	NO	18	69.2%	8	30.8%	
HEPATIC DISEASE	YES	3	42.9%	4	57.1%	0.055
	NO	23	82.1%	5	17.9%	
LUNG DISEASE	YES	5	71.4%	2	28.6%	0.638
	NO	21	75%	7	25%	

Fluid responsiveness by PPI:PPI in fluid responder patients before fluid in the studied population showed a mean value of 1.96 ± 1.20 and after fluids showed a mean value of 8.06 ± 2.62, It was statistically significant difference in fluid responders (26 patients) with P value (0.001)as shown in Table 4.

Table 4. Comparison between before and after fluids in responder's patients

	BEFORE FLUIDS					AFTER FLUIDS					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	P value
PPI IN FLUID RESPONDER	1.96	1.20	1.95	0.18	6.00	8.06	2.62	8.00	3.00	14.80	<0.001

While PPI in fluid non-responder patients before fluids in the studied population showed a mean value of 1.87 ± 1.05 and after fluids showed a mean value of 2.98 ± 1.52, It was statistically significant in fluid non-responders (9 patients) with P value (0.008)as shown in *Table 5*.

Table 5. Comparison between before and after fluids in non-responder's patients

	BEFORE FLUIDS					AFTER FLUIDS					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	P value
PPI IN FLUID NON-RESPONDER	1.87	1.05	2.00	0.30	3.00	2.98	1.52	3.00	0.60	5.00	0.008

Correlation between Mean LVOT VTI variability and Mean peripheral perfusion index variability: Meanperipheral perfusion index influidresponsivepatients was found to be 7.87 % and in fluid non-responsive patients was2.41%, there was statistically significant difference between responders and non-responders showing P value < 0.001 as shown in Table 6.

Table 6. Mean peripheral perfusion index in fluid responsive and non-responsivepatients:

	FLUID RESPONSIVENESS BY LVOTVTI		P VALUE
	Mean ± SD		
	Responder	Non responder	
MEAN PERIPHERAL PERFUSION INDEX VARIABILITY %	7.87± 3.12	2.41± 1.34	< 0.001

Measurementsin2cycles were taken and the mean was calculated

Astatisticallysignificantcorrelationwasfoundbetween MeanLVOTVTIvariability with peripheral perfusion index variability [r=0.573,p<0.001] as shown in Table 7 and Figure 1.

Table 7. Correlation between mean LVOTVTI variability and mean PPI variability

		D.PPI
D.VTI [%]	Correlation Coefficient	0.573
	P value	0.001

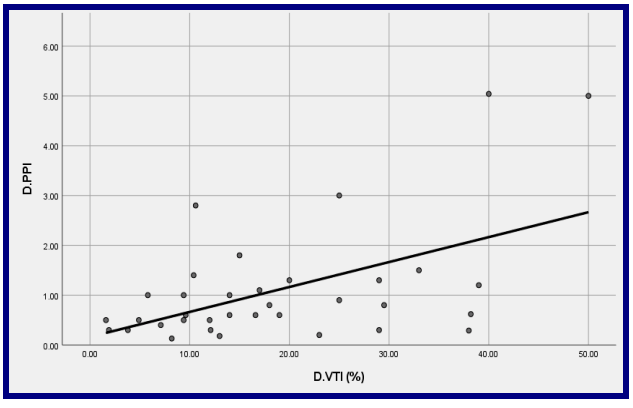

Figure1.Correlation between mean LVOTVTI variability and mean PPI variability

Area under the ROC curve of mean peripheral perfusion index variability was 0.976 (95% confidence interval 0.928-1.025, p < 0.001) corresponding to a cut-off value of >4.5% to predict fluid responsiveness in patients with septic shock was96.2% sensitivity and specificity100%as shown in Table 8, Figure 2.

Table 8. Sensitivity analysis showing predictability of PPI for fluid responsiveness

TEST RESULT VARIABLE(S)	AREA UNDER CURVE	P VALUE	95% CONFIDENCE INTERVAL				
			Lower Bound	Upper Bound	Cutoff value	Sensitivity %	Specificity %
D.PPI	0.976	<0.001	0.928	1.025	>4.5	96.2%	100%

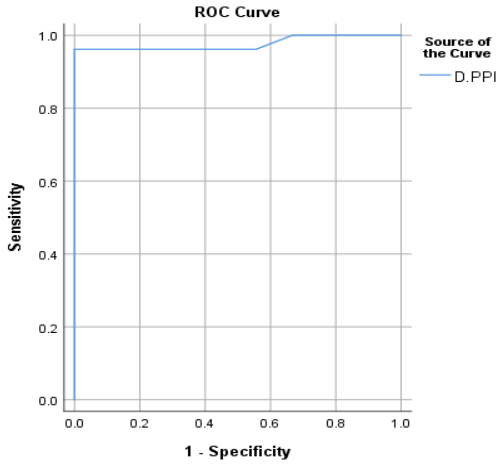

Figure 2. Roc curve using PPI to detect fluid responsiveness

4. Discussion

Administering intravenous fluids is crucial for resuscitating patients with septic shock. Fluid resuscitation has been found to hurt septic patients, leading to increased mortality rates. Given the high occurrence of fluid non-responders in septic shock patients, there is an increased chance of fluid overload in case of failure to assess fluid responsiveness.[10]

Patients with circulatory insufficiencies or poor tissue perfusion undergo fluid responsiveness evaluations by fluid responsiveness testing to guide their fluid resuscitation. Fluid responsiveness evaluations improve patient outcomes by targeting and individualizing fluid treatment, decreasing complications, and improving hemodynamics. This method supports patient-centered treatment in numerous therapeutic settings. [11]

Peripheral perfusion measures as cardiac output surrogates during fluid responsiveness assessment are intriguing. Perfusion indices like transcutaneous partial pressure of oxygen monitoring, capillary refill time, skin reflectance spectroscopy, near-infrared spectroscopy, and central venous oxygen saturation can detect fluid responsiveness.[12] Nevertheless, many of these methods necessitate specialized probes or multiple blood samples, which can be costly for routine examinations. PPI is a simple way to monitor in real-time without disturbance. It can be seen with a long probe. Therefore, it may be used in many contexts, including limited resources.[5]

Our study's major findings were that ΔPPI can accurately estimate the volume status of patients in the ICU with high sensitivity and specificity and is easy to perform in the ICU. It can also detect fluid responsiveness in patients with sepsis and septic shock.

The fluid responder's lVOT VTI showed significant increases after fluid challenge compared to baseline (14.54 ± 3.67 vs. 17.84 ± 3.88 cm, p<0.001). The mean improvement in LVOT VTI after fluid was 23.02 ± 11.27%. Similarly, in responders, PPI improved significantly from 1.96 ± 1.20% at baseline to 8.06± 2.62% post-fluid challenge (p<0.001). On correlation analysis, the LVOT VTI and PPI variability showed a moderate positive relationship, with a correlation coefficient of 0.423 (p=0.011).

The area under the ROC curve of mean peripheral perfusion index variability was 0.976 (95% confidence interval 0.928-1.025, p < 0.001), corresponding to a cutoff value of >4.5% to predict fluid responsiveness in patients with sepsis and septic shock there was 96.2% sensitivity and specificity100%.

Burton et al. [13] discovered a correlation between positive leg-raising tests and an increase in PPI, which aligns with the current findings. Unlike Beurton et al., our findings demonstrated higher accuracy (AUC 0.89) and a lower threshold (9%) than their study. The disparities in outcomes between our results and the study conducted by Beurton et al. might be attributed to significant dissimilarities: Beurton et al. applied the passive leg raising test, while we employed a fluid challenge. The passive leg-raising test enhances the transfer of blood from the lower extremities to the central circulation with greater efficacy than the fluid challenge test. This can increase cardiac output and improve PPI. Our study included only septic shock patients, whereas Burton et al. included undifferentiated shocked patients. In a recent study, Beurton et al. examined the effectiveness of the PPI in detecting patient response to the end-expiratory occlusion test, a commonly used measure of fluid responsiveness. Interestingly, they found a cutoff value (2.5% and 5%) close to ours. [14]

the previous study depended on the positive leg-raising test, but in our study, we employed the reaction to a 200 mL crystalloid bolus as an alternative.

In a separate study conducted by De Courson

et al.[15], they utilized a different technique called the lung recruitment maneuver to detect fluid responsiveness by PPI, unlike our fluid challenge test method. However, their results align with our findings in the current study, suggesting that the change in pulse pressure variation (PPI) may serve as a substitute for cardiac output.

A study done by Morakul S et al.,[18] on Mechanically Ventilated Patients using Lung Recruitment Maneuver shows that ΔPI was greater in the Fluid-responder group than in the fluid non-responder group (55.2± 17.8% vs. 35.3 ± 17.3%, p < 0.001, respectively) after leg raising maneuver, which supports the present study.

This study used a 10% increase in the VTI to identify fluid responders. This value has been utilized in various academic studies, including the one conducted by Burton et al.. 13 Many researchers typically utilize a threshold that falls within the range of 10 to 15% for the cardiac output or any of its surrogates. [16, 17]

This study differs from Iizuka et al.[19], which examined the effect of intraoperatively end-expiratory occlusion tests to determine fluid responsiveness in lung-protective ventilation patients in 41 elective surgery patients. Sixteen patients responded, and 25 did not. The area under the receiver operating characteristic curves for ΔPI20 and ΔPI40 for fluid challenge prediction was 0.561 (95% CI 0.374–0.749) and 0.688 (95% CI 0.523–0.852), respectively. In patients receiving lung-protective ventilation (7 ml/kg), intraoperative EEOT perfusion index changes did not predict fluid responsiveness. Due to the patient's mechanical ventilation, intraoperative risk of pneumothorax, and huge sample size, their result differed from ours.

4. Conclusion

PPI measured by pulse oximetry is non-invasive, inexpensive, and extremely Reliable for assessing fluid responsiveness in critically ill patients with hypoperfusion symptoms, outperforming LVOTVTI estimations from transthoracic echocardiography. Dynamic PPI trends enable real-time fluid responsiveness-guided patient-tailored early resuscitation.

Disclosure

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Authorship

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Conflicts of interest

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