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Usefulness of peak flow variation in peripheral arteries for prediction of fluid responsiveness in critically ill patients compared to stroke volume variation

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Abstract:

Background:-The aim of intravenous (IV) fluid load administration is to improve the tissue perfusion through increasing stroke volume (SV) and cardiac output (COP). Patients in whome COP increased by ≥ 15% are called fluid responders and those account only 50% of hypotensive patients. [1]

So it is *very* crucial to assess the fluid status of patients before fluid administration to distinguish between patients who may benefit and those who may not benefit or fluid administration is likely to be harmful in those patients. **Objectives:** to validate the diagnostic value of peak flow velocity in carotid artery by Doppler ultrasound in comparison to stroke volume variation (SVV) by velocity time integral (VTI) in assessment of fluid responsiveness in critically ill patients. **Methods:** This study is a prospective cohort study at the critical care department in Beni-Suef university hospital ,we studied the effect of fluid challenge on 49 critically ill patients with hypotension (MAP<65mmHg). Carotid Doppler peak velocity (CDPV) and VTI measurements were obtained before and after fluid challenge. Fluid challenge responders were defined as patients whose SVV increased more than 10 % after fluid bolus by echocardiography . **Results:** ΔCDPV correlated significantly with an increase in SVV by VTI after fluid bolus. Area under the receiver-operator characteristic curve (AUC) of CDPV was 0.937 [95% confidence interval (CI) 0.858 – 1.00].

The optimal cut-off point of ΔCDPV for fluid responsiveness was 12.25% with a sensitivity and specificity of 90% and 94.7% respectively. **Conclusion**: Doppler assessment of carotid peak velocity seems to be a highly feasible and reliable method to predict fluid responsiveness in critically ill patients with hypotension (MAP <65 mmHg)

Keywords:

Carotid artery Doppler ultrasound, fluid responsiveness ,SVV , VTI

1. Introduction:

The cornerstone of resuscitation of hemodynamically unstable patients with hypotension is often considered fluid loading. However, only roughly half of those patients respond to fluid challenge, defined as an increase in cardiac output upon fluid loading ≥15%. [1, 2]

Although rapid optimization of volume status has shown to improve outcome, extended fluid loading is associated with increased morbidity and mortality [3–6]. There are two types of indices to predict fluid responsiveness , static as central venous pressure (CVP) and pulmonary capillary wedge occlusion pressure and these indices are not recommended [7,8] . And dynamic indices as pulse pressure variation (PPV) and SVV are more likely to be better and accurate indices to predict fluid responsiveness in critically ill patients. [9]

PPV is minimally invasive ,SVV can be obtained by Doppler ultrasound. Carotid blood flow velocity (CBFV) is well correlated with COP. [10] But measuring CBFV is easier than measuring COP by echocardiography because carotid artery is more shallow to obtain a high quality ultrasound image . [11-15]

2. Patient and methods:

a. Study patients and design:

This prospective study was conducted on 49 patients in the critical care department in Beni-Suef university hospital. The period of the study ranged from January 2023 to July 2023.

Inclusion criteria: Adult patients (above 18 years), hypotensive (MAP<65mmHg) with sinus rhythm.

Exclusion criteria: Significant carotid stenosis more than 60% , none sinus rhythm ,cardiogenic shock or co-existing evidence of dilated cardio myopathy (DCM), more than mild atherosclerosis ,significant valvular heart disease ,any contraindication to fluid bolus and cervical spinal cord injury.

b. Methodology:

All patients included in this study were subjected to the following: history taking , full clinical evaluation ,laboratory investigations and required imaging according to the clinical situation.

Intervention:-

1- Baseline evaluation:

A-hemodynamic variables (SBP, DBP, MAP, HR and RR)

B-Common carotid artery data variables by Doppler study: Maximum CDPV (MaxCDPV)& Minimum CDPV (MinCDPV) .

C-Echocardiographic data variables:left ventricular outflow tract velocity time integral (LVOT VTI) and left ventricular outflow tract diameter (LVOTD)

D-ECG: To exclude arrhythmias.

2- Fluid bolus of 250 ml isotonic saline 0.9% was administered over 10 minutes

3- Collecting the same data immediately after fluid bolus.

- **Fluid responsiveness:**

≥10% increase in SV is more likely to be fluid responsive patient , while < 10%increase in stroke volume is less likely to be fluid responsive patient.

Transthoracic echocardiography (TTE):

Bedside echocardiography was performed using a Vivid S5 General Electric® (3.5 MHz).

Measurement of LVOT VTI:

Through the five-chamber view , using pulsed wave Doppler (PWD) , LVOT VTI was obtained before and after fluid bolus.

Measurement of LVOTD:

From the long axis parasternal view, and by the 2D mode (two dimension), LVOTD was measured in cm.Then SV could be obtained from the following equation :-

SV = VTI ×CSA (Cross Sectional Area of (LVOTD))

CSA=3.14× (LVOTD)/2)*2

Carotid Doppler Ultrasonography:

As shown in figure (1) , MaxCDPV and MinCDPV could be measured with a linear array transducer , using PWD , at the center of common carotid artery (CCA) ,through a longitudinal view with some angulation not more than 60 degree , at 2 cm from the bifurcation of CCA. Then ΔCDPV could be obtained from the following equation: (MaxCDPV− MinCDPV) / [(MaxCDPV + MinCDPV) / 2] × 100, expressed as a percentage. Then the fluid bolus was given and measurements were taken again immediately after fluid bolus.

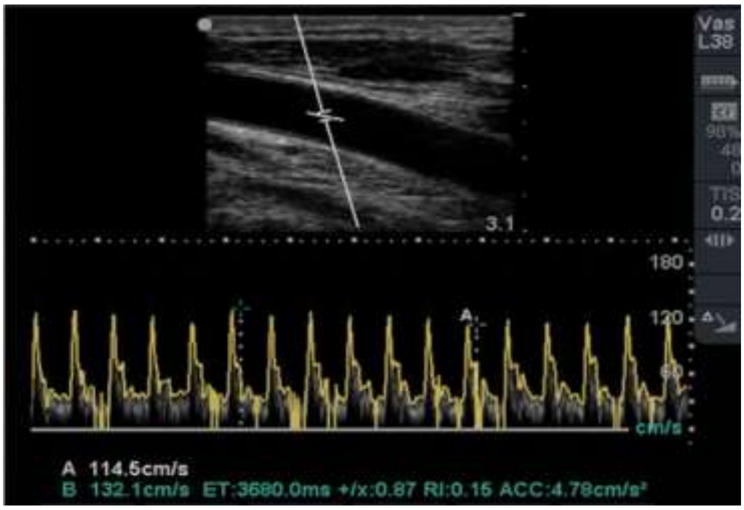

Figure (1): Measurement of variation in carotid peak systolic velocity. [14]

Ethical considerations:

The patients gave their informed written permission. The research protocol obtained clearance by the ethical committee of Beni-Suef university college of medicine No. FMBSUREC/08032022.

***Statistical analysis*:**

SPSS (statistical package for social science) version 26.0 on an IBM compatible PC was used to analyze the data (SPSS Inc., Chicago, IL, USA). The chi squared test was used to examine the qualitative data, which was expressed as a number and a percentage. The Shapiro-Wilks test was used to check the normality of quantitative data, presuming that P>0.05 indicated normalcy. The mean and standard deviation of the quantitative data were reported, and the diagnostic accuracy of the CDPV was evaluated using ROC curve analysis, the t-test, and the Mann Whitney U test. In this paper, $P < 0.05$ was deemed significant, and 0.05 was the starting point for the recognized level of significance.

3. Results:

As shown in table (1): Out of 49 patients, 13 were males (26.5%%) and 36 were females (73.5%).According to the increase in SV, our patients (49) were classified into two groups : fluid responders (30 pts), in whome SV increased ≥10% and fluid non-responders (19 pts) in whome SV increased < 10%. Out of the 30 patients, 8 were males and 22 were females. Out of the 19 patients , 5 were males and 14 were females. The mean ages of responders and non-responders groups were (53.7±18.5 &53.6±16.3 yrs respectively) ,with no significant difference between both groups regarding age or sex (P-value 0.976 &0.978 respectively). There were a number of comorbidities among our studied group, where 20 patients (40.8%) had diabetes mellitus (14 responders & 6 non-responders) and 25 patients (51%) had hypertension (15 responders &10 non-responders). There was no significant difference between responders and non-responders regarding comorbidities (P-value 0.295 &0.444 respectively).

Vital signs were assessed, where there were a statistically significant difference between both groups regarding MAP and SBP after fluid bolus among the responders group (P-value 0.007 & 0.001 respectively).

There was no statistical significant difference between both groups regarding RR,HR and DBP (P-value 0.883,0.290 and 0.064 respectively).

Table (1): Basic demographic , comorbidities and vital signs of the studied group (n=49).

Total (n=49)	Fluid responders (n=30)	Fluid non-responders (n=19)	P-value
Sex **Male** **Female**	8 (26.7%) 22 (73.3%)	5 (26.3%) 14 (73.7%)	0.978
Age(mean ±SD) (years)	53.7±18.5	53.6±16.3	0.976
Comorbidities **DM** **HTN**	14 (70%) 15 (60%)	6 (30%) 10 (40%)	0.295 0.444
MAP(Before **MAP(After)** **(mmHg)**	54.2 ± 8.2 59.4 ± 9.2	49.9 ± 9.6 51.2 ± 11.1	0.101 0.007
RR(Before) **RR(After)** **(breath/min)**	19.3 ± 3.6 18.2 ± 3.5	20.1 ± 3.6 18.4 ±2.4	0.480 0.883
HR(Before) **HR(After)** **(bpm)**	90.1 ± 14.5 84.5 ± 15.7	91.1 ± 15.6 89.4 ± 15.7	0.819 0.290
SBP(Before) **SBP(After)** **(mmHg)**	72.7 ± 11 80.9 ± 12.2	65.3 ± 10.7 65.3 ± 12.1	0.026 <0.001
DBP(Before) **DBP(After)** **(mmHg)**	45.2± 8.1 50 ± 9.7	42.1± 9.9 44.2 ± 11.3	0.239 0.064

As shown in table (2): Out of 49 patients, 30 (61.2%) diagnosed with septic shock, 19 (38.8%) diagnosed with hypovolemic shock.

Table (2): Diagnosis of the studied group

Diagnosis	Number	Percentage
Septic shock	30	61.2%
Hypovolemic shock	19	38.8%

As shown in table (3): There were no significant statistical differences between both groups regarding laboratory investigations (P-value <0.05 for all).

Table (3): Laboratory investigations of the two study groups .

		Responder	**Non-Responde**	**P-value**
CBC	TLC(cell/mm3)	12.7 ± 7.9	15.5 ± 6.2	0.196
	Hb(gm/dl)	10.0 ± 2.1	10.0 ± 1.8	0.996
	PLTs(gm/dl)	217.5 (139 – 308)	227 (140 – 300)	0.735
KFT	Creatinine(gm/dl)	1.6 (0.9 – 3)	1.5 (0.9 – 6.7)	0.564
	Urea(mg/dl)	66.5 (39.8 – 85.5)	60 (45 - 110)	0.579
Electrolytes	Na(mmol/dl)	136.4 ± 8.3	134.3 ± 9.6	0.412
	K(mmol/dl)	4.3 (3.8 – 4.9)	3.9 (3.7 – 4.1)	0.206
ABG	pH	7.33 ± 0.07	7.34 ± 0.05	0.806
	pCO_2(mmHg)	34.1 ± 8.8	33.0 ± 7.8	0.652
	HCO3(mEq/L)	19.0 ± 4.9	18.1 ± 3.9	0.503

As shown in table (4): There was a significant statistical correlation in detection of fluid responsiveness by the CDPV method compared to the standard method (VTI). Table (4), demonstrated that out of 49 patients 25 (51%) were fluid responders by CDPV method and out of the same number (49) , 30 patients (61.2%) were responders by VTI method (P-value <0.001).And regarding non-responders, out of the 49 patients 24 (49%) were non-responders by the CDPV method and out of the same number (49) , 19 (38.8%) were non-responders by VTI method (P-value< 0.001).

Table (4): Comparison between the two modalities regarding fluid responsiveness.

	VTI	**CDPV**	**P value**
Responders	30 (61.2%)	25(51%)	<0.001
non-responders	19 (38.8%)	24(49%)	<0.001

As shown in table (5) and figure (2): At a cut-off point of 12.25%, the sensitivity and specificity of CDPV in the Prediction of fluid responsiveness with reference to the LVOT VTI measurements were (90% & 94.7% respectively), With an AUC:0.937, P-value <0.001 and 95% CI (0.858-1.00).

Table (5): Validity of CDPV in the prediction of fluid responsiveness with reference to the LVOT VTI measurement among the studied group.

	CDPV
AUC	**0.937**
SE	**0.040**
P value	**<0.001**
95% CI	**0.858 – 1.00**
Cutoff point	**12.25%**
Sensitivity	**90.0%**
Specificity	**94.7%**

SE: standard of error

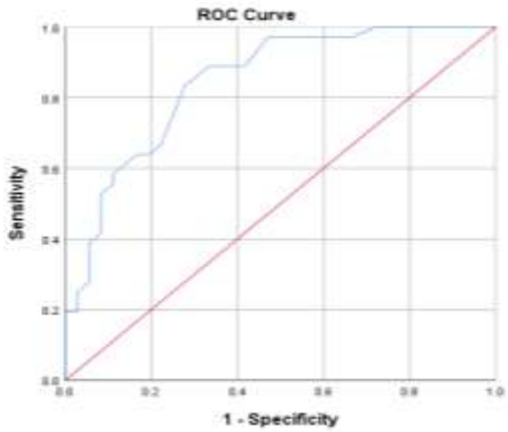

Figure (2): ROC curve for the CDPV accuracy in the prediction of fluid responsiveness with reference to the LVOT VTI measurement.

4. Discussion:

This prospective cohort study was conducted on 49 critically ill patients with hypotension a (MAP < 65 mm Hg)) during the period from January 2023 to July 2023 at the critical care department, Beni-Suef university hospital, to compare between the accuracy of CDPV in predicting fluid responsiveness in critically ill patients in comparison to SVV. The patients were divided into two groups : responders (SVV increased ≥10% after bolus fluid) and non-responders (SVV increased <10%).

Results showed no statistical significant difference between the two groups (responders and non-responders) regarding age, gender, hypertension and diabetes mellitus (P-values 0.976, 0.978, 0.444 and 0.295 respectively).

In our study, The HR and RR decreased significantly after fluid bolus among both groups with a P value <0.05, while DBP and CVP increased significantly after fluid bolus in both groups with (P value <0.001). The SBP and MAP increased significantly after fluid bolus among the responders with a P value <0.001. There was no significant difference between responders and non-responders regarding HR, RR, CVP and DBP measurements after fluid bolus (P-values 0.290, 0.883, 0.256 and 0.064 respectively), however SBP and MAP were significantly higher in the responders group after fluid bolus with a P value <0.05.

Similar to our results to some extent, a prospective cohort study by **Wang et al. in 2020,** was conducted on 44 patients with septic shock who received pulse index continuous cardiac output (PiCCO) monitoring in the ICU, they detected an increase in MAP and CVP significantly in both groups after fluid bolus administration (P-value <0.05), while HR significantly decreased as compared to those before fluid administration (P-value < 0.05). [16]

In contrast to us a randomized controlled trial by **Vos et al. in 2018 ,** was performed on 30 patients undergoing major hepatic resection in whom they investigated the ability of dynamic preload variables to predict fluid responsiveness, they reported that the MAP and HR showed no significant difference in both groups (P-value > 0.05) , while CVP was significantly increased in responders after fluid administration (P-value < 0.05), however there was no significant changes in CVP among non-responders. [17]

These differences between our study and the previously mentioned study by **Vos et al. in 2018**, may be speculated by that adequate and optimal management of shock depends on multiple factors as starting time of resussitation, fluid loading,Vasopressor support, Comorbidities and Severity of the disease which may affect the response of patients to fluid therapy. [18]

We investigated the predictive role of Doppler-acquired respirophasic carotid flow dynamics on fluid responsiveness. In our current study, we detected that out of 49 patients , 25 (51%) were fluid responders by CDPV method and out of the same number (49), 30 patients (61.2%) were responders by VTI method (P-value <0.001).Regarding non-responders, out of the 49 patients 24 (49%) were non-responders by the CDPV method and out of the same number (49), 19 (38.8%) were non-responders by VTI method (P-value< 0.001). At a cut-off point of 12.25%, the sensitivity and specificity of CDPV in the prediction of fluid responsiveness with reference to the LVOT VTI measurement were (90 % & 94.7 % respectively) ,with an AUC 0.937, P-value <0.001 and 95% CI (0.858-1.00).

In agreement with **Song et al. in 2014,** a study was conducted on 40 mechanically ventilated Patients with ischemic heart diseases to detect the usefulness of carotid artery peak velocity variation in prediction of fluid responsiveness. Patients were classified into responders (n=23) and non-responders (n=17), responders defined by increased SVI by ≥ 15% after fluid bolus administration (6 ml/kg).Results revealed at a cut-off value of 11% ,sensitivity and specificity were (83% & 82% respectively) with an AUC of 0.85 and P-value <0.001. [13]

Results of our study also in agreement with **Ibarra-Estrada et al. in 2015,** who studied many dynamic variables to detect fluid responsiveness among 19 mechanically ventilated septic patients . All these variables compared to the changes in SVI before and after fluid bolus.Results revealed that among dynamic variables, ΔCDPV had the highest AUC: 0.88 (P-value < 0.001; 95 % CI 0.77–0.95) with an optimal cut-off point at 14%. [14]

Likewise, **Kim D-H et al. in 2018,** evaluated the respirophasic Carotid artery peak velocity in detection of fluid responsiveness in spontaneously breathing patients and revealed that ΔCDPV was found to predict fluid responsiveness (AUC 0.818, P-value <0.001 & 95% CI:0.701-0.935) with an optimal cut-off value 9.1%. Sensitivity and specificity were (72.7% & 87.1% respectively). [19]

In concordance with our study**, Nianfang Lu et al**. **in 2018,** evaluated variability of peripheral arterial peak velocity to predict fluid responsiveness in 65 patients with septic shock. The increase in cardiac index (ΔCI) after fluid bolus ≥ 10% was defined as fluid responsiveness. The study revealed that the optimal cut-off value of ΔCDPV 13.0% could predict fluid responsiveness (AUC 0.906 & P-value< 0.05), the sensitivity and specificity were (75.2% & 94.9% respectively). [20]

Also in agreement with our results **,Yu Chen et al**. **in 2022,** evaluated correlation between respirophasic carotid artery peak velocity variation and stroke volume variation in 97 patients under general anaesthesia . Fluid responsiveness was defined as an increase in SVV ≥ 13%. 41 patients were fluid responders (42.3%). ΔVpeak was positively correlated with SVV (AUC 0.781, P-value <0.001 and 95% CI 0.686–0.875) with an optimal cut-off point 11.69% ,the sensitivity and specificity were (78% & 67% respectively). [21]

A meta-analysis by **Yao B et al in 2018 ,** in which nine studies with a total of 402 patients were included, showed that ΔVpeak of carotid artery was accurate diagnostic method for assessing fluid responsiveness with a pooled sensitivity and specificity of (85% & 86% respectively), with an AUC:0.9268 and 95% CI: 0.77-0.92 . [22]

Limitations: Our study had some limitations. First, our study was single centered study based on small sample size. Secondly, the results were obtained by one ultrasound operator so it may carry intra-observer variability.

5. Conclusion:

CDPV seemed to be a highly feasible and reliable method for predicting fluid responsiveness in critically ill patients with hypotension (MAP <65mmHg) with reference to the LVOT VTI.

Conflict of interests : None

Funds : None

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