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Original article

Changes in carotid flow time In guiding fluid resuscitation in septic patients

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Abstract

The goal of this study to use carotid ultrasonography to detect changes in carotid flow time in comparison to echocardiography in assessment of changes in heart dynamics to assess changes in volume status before &after passive leg raising in septic patients. We arranged patients into two groups ,Group one: *fluid responder 18 paients (45.5%)*, Group two non-*fluid responder :22 patients(54,5%)* . Increase carotid flow time (CFT) by *7msec* is cosidered fluid responsive, 10% increase in stroke volume to be fluid. The PLR test could assess fluid responsiveness with specificity 100% and sensitivity 95% with cut of 10.6% change in CO to predict fluid responsiveness.the study show a statistically significant moderate positive correlation between CCA flow time (CFT) both after PLR and the percent of change in CO measured by echocardiography. An agreement analyses were formed, we concluded that an overall good agreement between carotid artery blood flow measurement and Doppler echocardiography measurement with **P value < 0.001**, so we can use this parameters to predict fluid responsiveness post PLR perform are promising tool for the evaluation of fluid responsiveness in critically ill septic patients ,The PLR maneuver has demonstrated excellent performance for predicting fluid responsiveness. It is simple to perform, but requires a reliable system of COP monitoring able to quantify the short-term changes.

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1. Introduction:

Accurate estimation of intravascular volume status is important in the resuscitation of patients in intensive care units . Although intensive fluid therapy in patients with life-threatening volume depletion can prevent death and end-organ damage, volume overload is known to result in increased mortality, morbidity, and duration of hospital stay . Ultrasound measurement using the carotid artery is being studied as possible simple, dynamic markers of volume responsiveness. It has the advantage of being a bed-side test. It is superficial, is noninvasive, and has a small learning curve, and the carotid artery is just distal to the aortic outflow tract. The important carotid metrics are carotid blood flow (CBF) and corrected carotid flow time (CFT).[9] CBF has been studied and shown to have a strong correlation with stroke volume index (SVI), measured using echocardiography. SVI is considered a gold standard in determining volume responsiveness. Marik et al. compared the changes in SVI and CBF after a passive leg raising (PLR) test and showed that CBF had a sensitivity and specificity of 94% and 86% respectively, establishing CBF to be a good surrogate measure of SVI. However, CBF is prone to technical errors due to the variations in the angle of insonation.[10]

CFT measures the duration of systole or ejection time of the left ventricle. It is measured on a Doppler tracing from the beginning of the upstroke to the dicrotic notch and is corrected for heart rate by dividing it by the square root of the cycle time. It has been shown to have significant change with change in volume status.[4,9-13]

It is not dependent on the measurements of Doppler tracing and hence more accurate. Its role in determining fluid response in critically ill patients has not been established. This study aimed to determine if CFT could be used as a reliable, simple, and noninvasive metric to determine fluid responsiveness. The objectives are (a) to determine the dynamic changes of CBF and CFT in response to passive leg raising in patient who present to the ED and (b) to determine the correlation between change of CBF and CFT after a PLR.

2. Patients And Methods:

This study is a clinical randomized observational study, was conducted on **40** patients diagnosed as having sepsis and septic shock. Patients were admitted to the critical care department in Beni-Suef university hospital during the period from **:** April 2019 till May 2020.The study , was approved by the ethical committee of faculty of medicine Beni-Suef University.

Inclusion criteria:

sepsis is defined as patient who had 2or more of qSOFA score:

i. Respiratoty rate > 24 breath /min
ii. Altered mentation
iii. systolic blood pressure <90mmHg

septic shock defined as sepsis with persisting hypotention requiring vasopressor to maintain MAP <75 mmHg and having a serum lactate level < 3 mol/L despite adequate resuscitation(28).

3. Excluded from the study:

- patients less than 18 years old
- Arrhythmia
- Disturbed concousness level
- Patients with neurogenic shock,obstructive shock ,cardiogenic shock
- Any abnormlity in carotid artery(carotid stenosis , aneurysm ,kinking)

All 40 patients included in our thesis were subjected to standard study protocol consists of:

A. Carotid flow time before and after passive leg raising

Crotid flow time was measured in a representive beat by meauring time beginning of the current beat to the beginning of the adjacent beat and recorded in seconds

Measurement of Stroke volume,cardiac output before and after passive leg raising:

LVOT-diameter was measured in this parasternal long-axis in in biplane mode at mid-systolic one cm below the aortic valve. Then LVOT measured by using pulsed wave-Doppler at the base of the aortic leaflets, and then moving slowly away towards the LVOT until a typical subvalvular flow profile was (approximately 1 cm below the aortic valve) obtained,A full volume recording of LV during four cardiac cycles was performed.(8)

SV and COP measured from VTI ,LVOT using following equation:

LVOT area =∏ (LVOT diameter)2÷ 4 Stroke Volume =LVOT area x LVOT VTI Cardiac output=Heart Rate x Stroke Volume

B. passive leg raising:

Patient put at 45 degrees head up semi-recumbent position lower patient’s upper body to horizontal and passively raise legs at 45 degrees up maximal effect occurs at 30-90 seconds

- ❖ 10% increase in stroke volume to be fluid responsive
- ❖ Increase carotid flow time (CFT) by ***10msec*** is cosidered fluid responsive

The study population were subdivided into two groups Responder and Non Responder :

Responder Group 1 were defined as those who had increase of 15% in co from baseline measured by echocardiography after fluid challenge

Non Responder Group 2 were defined as those who had increase of less than 15% in co from baseline measured by echocardiography after fluid challenge.

Statistical methodology

- Analysis of data was done by IBM computer using SPSS (statistical program for social science) as follows;

- Description of quantitative variables as mean, SD and range.

- Description of qualitative variables as number and percentage.

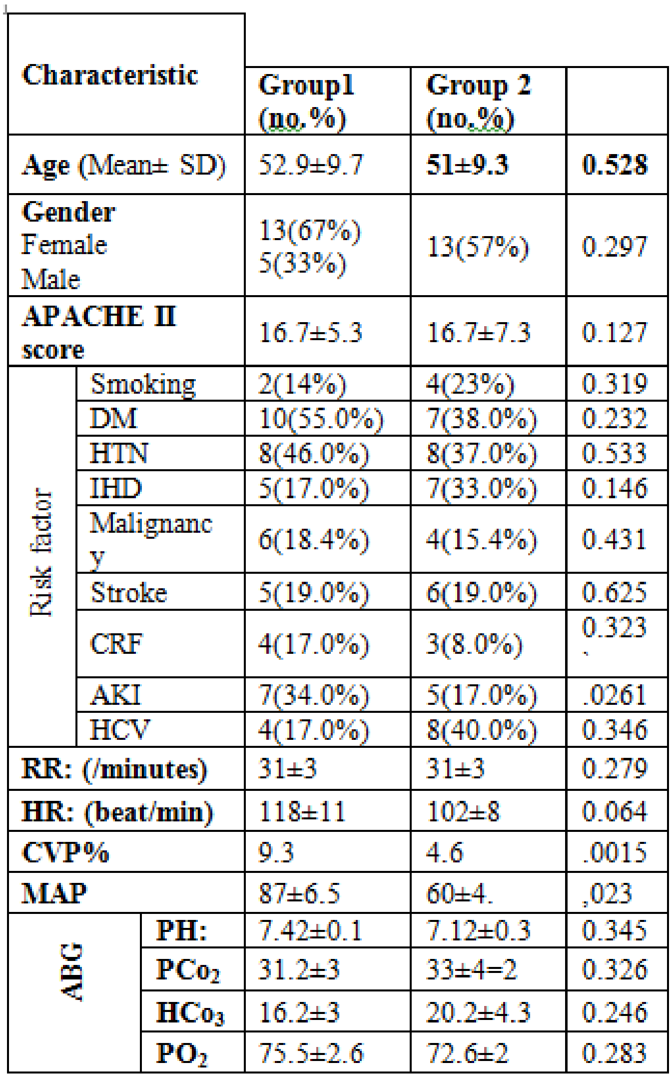
- Unpaired t-test was used to compare quantitative variables, in parametric data (SD < 50 % mean)

- P value > 0.05 insignificant
- P < 0.05 significant
- P < 0.01 highly significant [20].

4. Results:

As summarized in Table 1, baseline characteristics, such as age, gender,co-morbidities and risk factors, , APACHE II score, resoiratory rate,,Heart rate or ABG were not significantly different between both groups (all P>0.05).But **cvp,MAP** significantly different between both groups (P<0.05)

Table (1):



Characteristic		**Group1 (no.%)**	**Group 2 (no.%)**	
Age (Mean± SD)		52.9±9.7	**51±9.3**	**0.528**
Gender Female Male		13(67%) 5(33%)	13(57%)	0.297
APACHE II score		16.7±5.3	16.7±7.3	0.127
Risk factor	Smoking	2(14%)	4(23%)	0.319
	DM	10(55.0%)	7(38.0%)	0.232
	HTN	8(46.0%)	8(37.0%)	0.533
	IHD	5(17.0%)	7(33.0%)	0.146
	Malignancy	6(18.4%)	4(15.4%)	0.431
	Stroke	5(19.0%)	6(19.0%)	0.625
	CRF	4(17.0%)	3(8.0%)	0.323
	AKI	7(34.0%)	5(17.0%)	.0261
	HCV	4(17.0%)	8(40.0%)	0.346
RR: (/minutes)		31±3	31±3	0.279
HR: (beat/min)		118±11	102±8	0.064
CVP%		9.3	4.6	.0015
MAP		87±6.5	60±4.	,023
ABG	**PH:**	7.42±0.1	7.12±0.3	0.345
	PCo$_2$	31.2±3	33±4=2	0.326
	HCo$_3$	16.2±3	20.2±4.3	0.246
	PO$_2$	75.5±2.6	72.6±2	0.283

Table 2: Comparing between 2 study groups rearding SV & sv% by ANOVA

There is statistically significant difference between responders and non responders group regarding sv & increase sv post PLR in the study group by ANOVA test (P.<0.05).

	Group1 **Responder**	**Group2** **NonResponder**	**P value**
SV	82.72	64.75	0.026
SV %	18.7	10.43	0.023

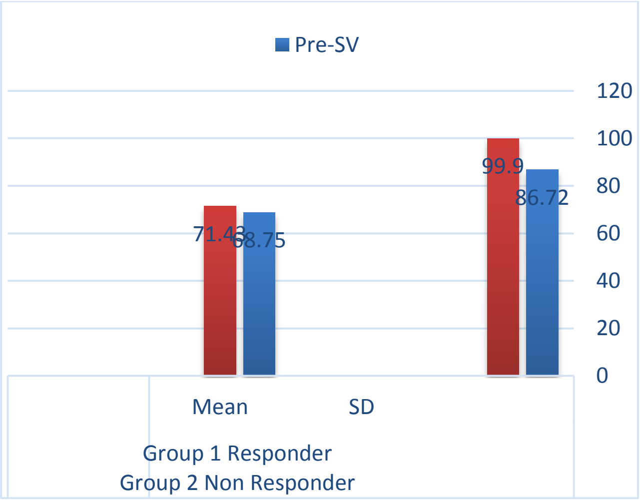


Table 3: Comparing between study groups regarding COP&raising COP POST PLR by ANOVA test in the study group

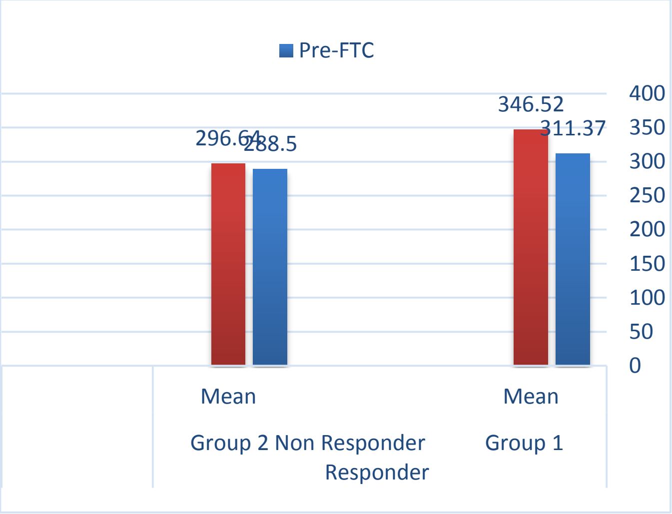
There is statistically significant difference between responders and non responders group regarding COP & increase of mean in the study group by ANOVA test (P.<0.05).

	Group1 Responder	**Group2 NonResponder**	**Pvalue**
COP	5.160	3.69	0.014
COP %	18,14	10,82	0.026

Table 4: Comparing between study groups regarding carotid flow time &increase carotid flow time post leg raising by ANOVA test in the study group

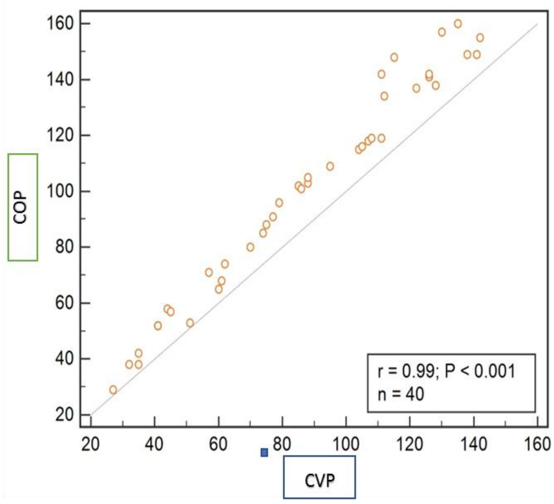
There is statistically significant difference between responders and non responders group regarding CFT& increase of mean CFT post PLR in comparison to pre- CFT in the patient

	Pre-CFT	**Post-CFT**	**pvalue**
Group1Responder	311.37	358.52	0.001
Group2nonResponder	268.5	286.64	0.418



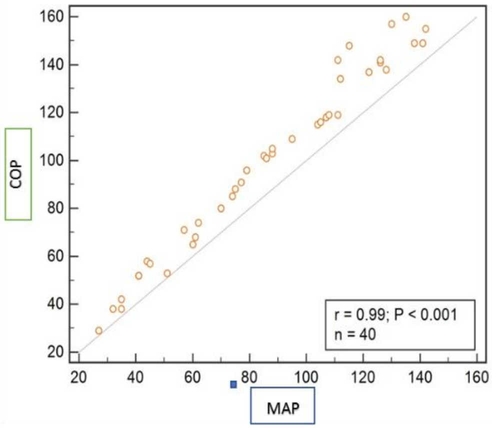
Pearson correlation between % CVP with % Echo COP.

There is statistically significant positive linear correlation between % CVP with % Echo COP post PLR (r 0.517) and p<0.0001. by ANOVA test (P.<0.05).



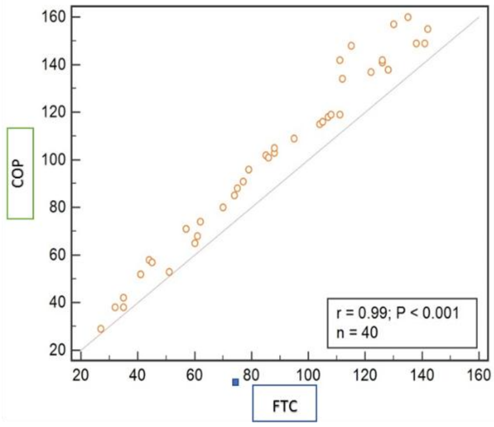
Pearson correlation % MAP and % Echo

There is statistically significant positive linear correlation between % MAP with % Echo COP post PLR with (r 0.517) and p<0.0001. by ANOVA test (P.<0.05).



Pearson correlation Carotid corrected flow time and changes of COP

There is statistically insignificant correlation between FTC% and change COP% POST PLR with (r 0.537) and p<0.0001.



5. Discussion:

Accurate assessment of intravascular fluid status and measurement of fluid responsiveness have become increasingly important in critical care. It is now widely recognized that both inadequate and excessive fluid replacement are deleterious to health, and both can affect recovery during critical illness.Clinical studies have consistently demonstrated that only about 50% of hemodynamically unstable patients are volume responsive , It is therefore essential to have reliable bedside tools to predict the efficacy of volume expansion, and thus distinguishing patients who might benefit from volume expansion from those in whom the treatment is likely to be inefficacious(14) .

This study was a prospective observational study conducted on fifty critically ill septic patients admitted to Critical Care Department of Benisuef University Hospital . The aim of this study was to investigate the accuracy carotid artery flow time measurement in the assessment of fluid responsiveness in critically ill septic patients. We also aimed to investigate the accuracy of PLR maneuver as a simple easy method in hemodynamic evaluation of critically ill septic patient.

Regarding hemodynamic data(SBP,DBP,MAP) This Study demonstrated a statistically significant difference between responders and non-responders regarding % MAP which showed moderate correlation with % CO (r=0.413 and P=0.0028) that used to evaluate fluid responsiveness.

The findings were in agreement with, **Nonnet et al 2012**[13] **and Pakhat et al 2011** [20] the previous studies found a statistically significant correlation between MAP and %PP and percentage cardiac output (%CO) after fiuid challenge but with variable degrees of correlation strength ranging (r =0.14-,52, p=0.004 and r=0.36, p-0.005, respectively).

Our study showed statistically significant difference in CVP post PLR and FC being higher in responders group. This was in alignment **with Pierlakos et al 2012** (13)

Our results showed moderate correlation between baseline CVP and % COP (r=(-0.286, -0.271). This was in agreement with the meta-analysis published **by Mklrik et al 2010** [2581, They found the correlation coefficient between the baseline CVP and the delta SVI/CI (r=0.14 (95% CI, 0.1-0.37), being 0.25 (95% CI, 0.17-0.43) in the ICU patients, and 0.13 (95%CI, 0.03-0.24)

In contrary with our results, **Tkiel et al 2008** [20] found The initial CVP was not different between the groups of responders and non responders, and the change in CVP did not correlate with the change in SV following volume expansion.

In common carotid data discussion**,** Our study results showed that there was a statistically significant difference between responders and non-responders regarding carotid artery flow time (CFT) both after PLR. We also found a significant correlation between %CFTand %COP indicating the ability to use this measures as a surrogate of echocardiography in assessment of fluid responsiveness being non-invasive, repeatable and the structures of interest are superficial in location, thus easy to image.

Our study results demonstrated that fluid responsiveness in critically ill septic patients could be efficiently predicted by %CFT with good sensitivity (85-90%) and specificity 90% when compared to PLR test on cardiac parameters measured by echocardiography

Our results was in agreement with **Mallet al 2007** [26] . They found that carotid flow time measurements correlated moderately with cardiac output regardless a single waveform were used: p=0.44, 95% CI 0.18-0.63.

In addition, **MArrik et al** [29] suggested that changes in corrected carotid flow following a PLR maneuver may be a useful adjunctive method for determining fluid responsiveness in mixed spontaneous and mechanically ventilated patients.

They found a strong correlation between the percent change in SVI by PLR measured by

Bioreactance and the concomitant percent change in corrected carotid flow (r = 0.59, P= 0.0003). Using an increase in corrected carotid flow of 7% for predicting volume responsiveness, they found two false positive results and one false negative result, giving a sensitivity and specificity of 94% and 86%, respectively

Also **RAphrig et al** [22] found a significant correlation between changes in CCA Doppler flow "CCADflow" and COP in cardiac surgery patients following PLR (r=0.69 [0.70-0.791) ,p 0,0003,r2 =0,63) This correlation did not change when only patients on SIMV or PSV were analysed (r = 0.78 [0.58-0.88], P <0.0001, r2 =0.61).

The correlation overall was similar for corresponding changes carotid flow time and CO when analysed before and after PLR compared to absolute values. Furthermore, equivalent correlations in patients with a volume controlled mode of ventilation compared to patients on a pressure support mode suggest that intrathoracic pressure changes did not confound the carotid flow time /CO correlation, as proper active inspiratory efforts were absent during all measurements and PEEP and tidal volumes were comparable [26]. And this results could be in line with our study results regarding whether the patients were spontaneously breathing or mechanically ventilated.

However, in contrast to our results, they couldn't discriminate fluid responders. This could be explained by the different patients population as their study was conducted on post-operative cardiac surgery that have altered pathophysiologic parameters post-surgery.

In echocardiography results discussion,Our study results showed that 73.5% (n-20) of the study population were fluid responders with use of 14% change in COP. This results strengthen the concept that about 63% only of septic patients are fluid responder.

In agreement with our study, [27] **Takall et al** found 64% of his studied population are fluid responders with great similarity of studied population

This was in concordance with a meta-analysis done **by Cavas et al 2016** They concluded that approximately 68% of spontaneously breathing patients were fluid responsive. The studies used different parameters and values to predict fluid responsiveness including SV, COP,CI, VTI and from 11% to 15% cutoff value to define fluid responsiveness

This finding reinforces the importance of assessing fluid responsiveness in critically ill patients prior to intravascular volume expansion, thus avoiding unnecessary exposure to additional fluids. [25

Physiologically, the change in intravascular volume should be reflected as a change in the duration of systole.[16] In our study, the baseline CFT was 321.3 ± 34.3 ms which is consistent with the study done by Hossein-Nejad et al., which showed mean baseline CFT in healthy volunteers to be 325.18 ± 22.15 ms.[17] Blehar et al. in their study in dehydrated patients who received a mean fluid bolus of 1110 ml showed that the mean CFT significantly changed from a baseline of 299–340 ms, which was an increase of 14.9%.[9] In our study, however, the mean baseline CFT increased by only 2.3% from 321.3 ± 34.3 ms to 325.18–328.9 ± 33.9 ms The study found that PLR test could assess fluid responsiveness with specificity 100% and sensitivity 95%% with cut off 10% change in COP to predict fluid responsiveness

Our results are consistent with results of the 2 meta-analyses by **Momet et al 2013 and Coerpaneth et al 2016** [23, 24]. Both reviewed the existing literature in which the ability of the PLR maneuver to predict a significant increase in CO was tested. The pooled sensitivity and specificity in the more than 20 studies, comprising 1000 patients. When seeking for the best threshold of PLR-induced changes in CO for predicting fluid responsiveness, the proposed value was 11 %

Importantly, the diagnostic performance was also maintained independently from the patient being spontaneously breathing or under controlled mechanical ventilation [23-26]

Carotid ultrasound must, of course, be placed in clinical context. It is generally accepted that dynamic methods are preferred measures of fluid responsiveness, but a single ideal test remains elusive. It is foreseeable that in the future, clinicians will determine fluid responsiveness with not a single test but instead a comprehensive set of measurements and clinical assessments, which may include carotid ultrasound. (26)

The limitations of this study were that it was performed in a single center, by convenience sampling of patients. CBF was used as our reference standard which is not the current gold standard. All the measurements were done by single operator, so it is difficult to hypothesize on the interoperator variability that might affect measurements. The operator was also not blinded to the measurements. Our patient population was diverse, so the generalizability of the study is limited(11).

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