Original Article

Evaluation of Carotid Flow Time to Assess Fluid Responsiveness in the Emergency Department

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Abstract

Background: Assessing fluid responsiveness in critically ill patients is challenging. Objective, noninvasive tests that are easy to perform are needed. Doppler measurements of dynamic carotid artery parameters such as carotid blood flow (CBF) and carotid flow time (CFT) are being studied as the potential indicators of volume responsiveness, but the data supporting its use are sparse. **Methods:** This prospective, observational study was conducted in the adult emergency department from June to September 2018. Patients who were prescribed a bolus of 500 ml of crystalloid for any indication were enrolled. Carotid Doppler was performed before and after a fluid bolus to measure the change in CBF and CFT. The aim of our study was to determine if CFT can be used as a marker of fluid responsiveness. **Results:** During the 4-month study period, 209 patients were recruited through convenient sampling after obtaining informed written consent. 29.6% of patients presented with a mean arterial pressure (MAP) <65, among whom 58.1% had septic shock. The baseline CBF was 643.0 ± 212.7 ml/min, and it was 583.9 ± 207.1 ml/min and 668 ± 210.8 ml/min in hypotensive and normotensive patients, respectively. Considering a >10% increase in CBF as fluid response, there were 59% responders and 41% nonresponders. The MAP increased by 9.5% in the responders, while there was no significant change in CFT after the fluid bolus. There was no difference in CFT among the responders as compared to the nonresponders. There was no correlation between the change of CBF and CFT ($r^{[207]} = 0.013$, $P = 0.061$) after the fluid bolus. **Conclusion:** Though easy to perform, CFT is probably not a good indicator of fluid responsiveness.

Keywords: Carotid blood flow, carotid flow time, Doppler, emergency department, fluid responsiveness

Introduction

Fluids are an integral part of treating critically ill patients in the emergency department (ED). They are part of our treatment guidelines and have shown to improve outcomes in patients with sepsis and septic shock.[1,2] The main aim of administering fluid is to increase cardiac output (CO) and organ perfusion. However, literature suggests that only about 50% of patients respond to a fluid bolus.[3-5] Excessive administration of the fluid, on the other hand, has been shown to be associated with an increase in morbidity and mortality.[6-8] The ED is an area of high acuity, and time is of the essence in critical patients. Most methods of determining fluid response are cumbrous, time-consuming, and hence unfeasible to be employed. Hence, fluid therapy is usually empirical. Noninvasive metrics that help determine fluid response speedily and objectively are warranted. 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.[4] 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.[4]

Received: 19-05-2020 **Revised:** 19-07-2020 **Accepted:** 07-08-2020 **Available Online:** 01-10-2020

Access this article online

Quick Response Code:

Website: www.jmuonline.org

DOI: 10.4103/JMU.JMU_77_20

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How to cite this article: Judson PI, Abhilash KP, Pichamuthu K, Chandy GM. Evaluation of carotid flow time to assess fluid responsiveness in the emergency department. J Med Ultrasound 2021;29:99-104.

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 a bolus of 500 ml of crystalloid among patients who present to the ED and (b) to determine the correlation between change of CBF and CFT after a fluid bolus.

Methodology

Study design

This was a prospective, nonrandomized, cross-sectional study.

Study setting

We conducted this study in the ED of a large tertiary care hospital in South India between June 2018 and September 2018. Our ED is a 49-bed department and tends to about 300 patients per day.

Participants

Two hundred and nine patients who were prescribed a fluid bolus of 500 ml of crystalloid for any indication by the treating physician were included in the study after obtaining informed written consent. Due to arduous nature of recruiting consecutive patients in a busy ED like ours, we employed a convenience sampling technique by recruiting patients between 10 a.m. and 4 p.m. on weekdays only. The decision to administer the bolus was at the discretion of the treating physician as part of routine standard of care which included the following: patients with a mean arterial pressure (MAP) <65, systolic blood pressure <100 mmHg with signs of end-organ hypoperfusion such as tachycardia and elevated lactates and patients who were clinically dehydrated. Patients were excluded if patients did not consent, had irregular heart rhythm (e.g., atrial fibrillation), pregnant, on inotropes/vasopressors whose doses were adjusted during the measurements, and were critically ill (on whom urgent resuscitation was being performed).

Ultrasound technique

For the carotid ultrasound, the SonoSite M-Turbo (FUJIFILM SonoSite, Inc., India) ultrasound system was used. The linear array transducer with a frequency of 13–6 MHz was used and the angle of insonation was <60° for all measurements. The patient was placed in a 45° semi-recumbent position, and measurements were performed before and after a bolus of 500 ml of crystalloid. The long-axis view of the carotid artery was obtained, and the carotid diameter was measured 1 cm proximal to the carotid bulb from intima to intima. Doppler tracings were obtained by placing the 0.5 mm sample gate at the center and parallel to the vessel. CBF was measured by time average peak of three waveforms of the Doppler tracings. Systolic time and cycle time measurements were taken obtained from the same tracing, and the corrected flow time was calculated by Bazett's formula. The scan was performed by a single emergency medicine physician, and all measurements were stored and validated by an experienced intensive care unit sonologist.

Outcomes

The main outcome of the study was to determine the correlation of percentage change in CBF and corrected CFT after a fluid bolus and to determine if corrected CFT can be used as a surrogate marker of volume responsiveness. A cutoff of 10% increase in CBF was considered as response to the fluid bolus.[4,11-13] The secondary analysis was to assess if there was a significant change in the mean of CBF and CFT after fluid bolus and to compare the change in CFT in the responders as compared to the nonresponders.

Sample size

Based on the study by Marik *et al*., a sample size of 209 was calculated with an alpha error of 0.05 and a power of 80% to give the new test (CFT) a sensitivity and specificity of 80 and 70 percent respectively.[2]

Statistical analysis

The percentage change of prebolus to postbolus measures of CBF and CFT was compared using Pearson's correlation coefficient. Paired sample *t*-test and histogram distributions were used to determine if there was a statistically significant difference in the mean of CFT in the responders compared to the nonresponders. Analysis of data was done using Statistical Package for the Social Sciences (SPSS) for Windows software released 2015, Version 23.0, Armonk, NY, USA.

Ethical considerations

Before the commencement of the study, approval from the institutional review board ethical committee was obtained (IRB Min No.: 11027). Patient confidentiality was maintained using unique identifiers and by password protected data entry software with restricted users.

Results

Patient demographics

A total of 209 boluses of crystalloid were studied, and complete data set of hemodynamic variables and carotid parameters (CBF and CFT) was recorded before and after each bolus of fluid. The demographic data of the patients of all the 209 patients included in the study are described in Table 1. There was a male predominance with male of 61.2%, the mean age being 42.2 ± 15 years. Patients had comorbidities such as diabetes (22.4%), hypertension (8.1%), and coronary artery disease (2.8%). There were 29.6% of the patients who presented with hypotension, the most common diagnosis among them being septic shock (58.1%) followed by acute

gastroenteritis (14.5%), poisoning (12.9%), trauma (4.8%), anaphylaxis (2.3%), and others (6.5%). The hemodynamic variables and the carotid ultrasound parameters and their changes after a fluid bolus of 500 ml of crystalloid are described in Table 2. A *t*-test was performed to check if the change in these values was significant. There was an 8.6% increase in the MAP from a baseline of 68.3–74.2 which was statistically significant. The mean of CBF saw an increase from 643 to 720 ml/min which was an increase of 12%. The mean of corrected CFT however only saw an increase of 2.3% from 321.3 to 328.9 ms after the bolus of fluid.

Volume response in our study was considered as an increase in CBF by 10% after administering a fluid bolus of 500 ml of crystalloid. According to this definition, 59% of the patients enrolled saw an increase in CBF by 10% and were considered as volume responders while 41% were nonresponders. Table 4 represents the change in hemodynamic variables and carotid ultrasound parameters after a fluid bolus in the responders and nonresponders. The MAP in the responders had an increase of 9.56% from 66.9 to 73.3 mmHg after a fluid bolus. The MAP also increased in the nonresponders by 7.2% from a baseline of 70.4–75.5 mmHg. Corrected CFT in the responder group increased by 3.1% after a fluid bolus from 318.3 to 328.2 ms, and this change was not statistically significant. The nonresponder group however saw a statistically significant change from 325.6 to 329.8 ms.

Table 1: Baseline characteristics (n=209)

Baseline characteristics	*n* (%)
Mean age (SD) in years	42.2 (15.5)
Gender	
Male	128 (61.24)
Female	81 (38.75)
Comorbidities	
Diabetes mellitus	47 (22.4)
Hypertension	17 (8.1)
Coronary artery disease	6 (2.8)
Patients who presented with hypotension (MAP <65 mmHg)	62 (29.6)
Septic shock	36 (58)
Acute gastroenteritis	9 (14.5)
Poisoning	8 (12.9)
Dehydration	4 (6.4)
Trauma	3 (4.8)
Anaphylaxis	2 (3.2)

MAP: Mean arterial pressure, SD: Standard deviation

The changes in CBF after a fluid bolus of 500 ml of crystalloid in the responders and nonresponders studied showed the mean in the responder group increased by 25% after a fluid bolus from 592.2 to 740.6 ml/min. The mean in the nonresponder group decreased by 3.6% from 717.1 to 691.1 ml/min and this change was statistically significant [Table 3].

The distribution of the change in corrected CFT after a fluid bolus in the responders and nonresponders is represented in Figure 1. There is no difference in the change of CFT in the responder's compared to the nonresponder's.

Correlation of carotid blood flow and carotid flow time

A Pearson's correlation examined the relationship between the percentage change (Δ%) of CBF (M = −77.4, standard deviation [SD] = 124.3) and CFT (M = −7.62, SD = 26.0) after fluid bolus administration of 500 ml of crystalloid. CFT did not correlate with CBF ($r^{[207]} = 0.013$, $P = 0.061$) and this is represented by the scatter plot in Figure 2.

Discussion

The results of this study of 209 patients show that (a) there is no correlation between CBF and CFT; (b) though CFT is a technically easier test to perform, it did not predict volume responsiveness. This study is consistent with a recent study which compared CBF and CFT to the gold standard invasive measurements of CO and demonstrated that CFT did not correlate with CO.[14]

Table 2: Changes in hemodynamic parameters and carotid ultrasound metrics in the responders (*n*=85) and nonresponders (*n*=124) before and after a fluid bolus

	Before bolus	After bolus	Difference, mean (%)	95% CI		*P*
				Lower	Higher	
HR (beat/min)						
Responders	103.7 (23.8)	100.4 (21.9)	−3.3 (3.1)	−5.2	−1.3	<0.01
Nonresponders	105.5 (26.3)	101.5 (23.8)	−3.9 (3.7)	−6.0	−1.8	<0.01
MAP (mmHg)						
Responders	66.9 (19.3)	73.3 (16.7)	6.4 (8.7)	3.4	9.4	<0.01
Nonresponders	70.4 (18.7)	75.5 (17.4)	5.1 (6.7)	2.1	8.1	<0.01
CBF (ml/min)						
Responders	592.2 (189)	740.6 (246)	148.3 (20.0)	132.9	163.8	<0.05
Nonresponders	717.1 (24.3)	691.1 (212.2)	26.0 (−3.7)	46.4	5.6	<0.01
CFT (s)						
Responders	318.3 (32.3)	328.2 (33.2)	9.9 (3.01)	5.8	14.0	0.19
Nonresponders	325.6 (36.7)	329.8 (35.1)	4.2 (1.2)	−2.1	10.6	<0.01

MAP: Mean arterial pressure, CBF: Carotid blood flow, CFT: Carotid flow time, CI: Confidence interval, HR: Heart rate

Table 3: Baseline mean hemodynamic variables and mean carotid metrics (carotid blood flow and corrected flow time) before and after fluid bolus

Variable	Before bolus	After bolus	Difference, mean (%)	95% CI for difference		*P*
				Lower	Higher	
Heart rate	104.47±24.8	100.89±22.6	−3.5 (−3.4)	−5.0	−2.1	<0.001
Mean arterial pressure	68.3±19.17	74.2±17.0	5.8 (7.9)	3.7	8.0	<0.001
CBF	643.0±212.7	720.5±233.6	77.4 (10.7)	60.4	94.4	<0.001
Corrected CFT	321.3±34.3	328.9±33.9	7.6 (2.3)	4.0	11.1	<0.001

Data are presented as mean±SD. SD: Standard deviation, CI: Confidence interval, CBF: Carotid blood flow, CFT: Carotid flow time

Table 4: Baseline hemodynamic variables and carotid parameters in patients with hypotension (mean arterial pressure <65 mmHg) (*n*=62) and those without hypotension (mean arterial pressure >65 mmHg) (*n*=147)

	Before bolus	After bolus	Difference, mean (%)	95% CI for difference		*P*
				Lower	Higher	
Pulse rate						
MAP <65	101.4 (26.0)	98.6 (23.2)	−2.74 (2.7)	−4.51	0.97	0.003
MAP >65	105.7 (24.3)	101.8 (22.4)	−3.93 (3.6)	−5.82	−2.05	<0.01
CBF						
MAP <65	583.9 (207.1)	638.3 (183.3)	54.38 (8.5)	20.97	87.79	0.002
MAP >65	668 (210.8)	755.1 (244.2)	87.18 (11.5)	67.56	106.80	<0.01
CFT						
MAP <65	324.4 (40.2)	329.5 (40.1)	5.09 (1.5)	0.92	11.10	0.09
MAP >65	319.9 (31.5)	328.6 (31.1)	8.69 (2.6)	4.28	13.10	0.001

MAP: Mean arterial pressure, CBF: Carotid blood flow, CFT: Carotid flow time

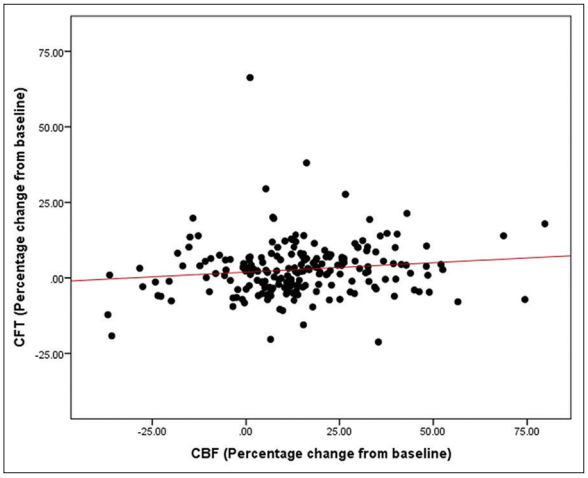

Figure 1: Scatter plot representing the correlation between percentage change carotid blood flow and percentage change carotid flow time

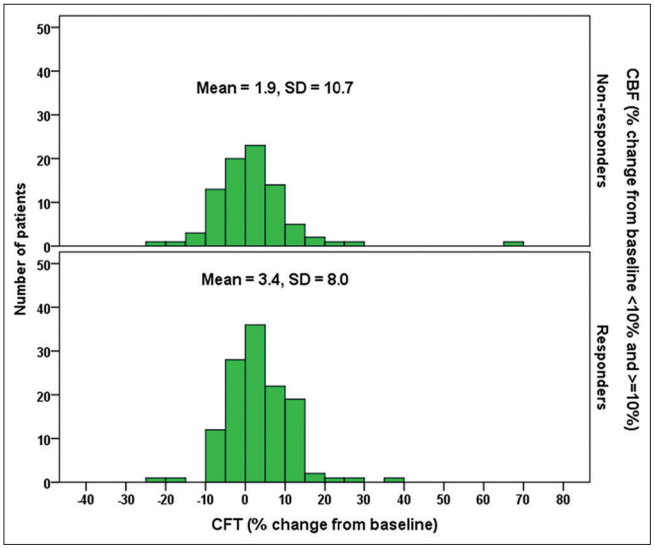

Figure 2: Percentage change in carotid flow time after a fluid bolus among the responders and nonresponders

The assessment of fluid responsiveness in the ED is challenging since most methods lack practicality. Carotid ultrasound has the potential to be a very useful tool since it is noninvasive, provides a great sonographic window, and is easy to perform. Stolz *et al*. in a recent study demonstrated the ability of emergency physicians to obtain carotid artery measurements after viewing an instructional video and found the average time required was only 2.9 min, and there was no difference between among novice and experienced groups.[15]

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

after a fluid bolus of 500 ml of crystalloid.[17] This is probably because this study was conducted in the ED, among patients with varied diagnosis and volume status, which is usually the general scenario in this population of patients. Surprisingly, in this study, even though blood flow measured using CBF in the responders group showed an increase of more than 25%, CFT saw a statistically insignificant trivial change with a fluid bolus. The change in CFT in the responder group versus the nonresponders after a fluid bolus did not show any difference in their response to volume expansion.

Changes in the CBF after a fluid bolus have also been studied and have shown to have a strong correlation to SVI measured by echocardiography.[4] It has also shown strong correlation with invasive gold standard measurements of CO.[14] CBF was shown to be less prone to the measurement issues compared corrected CFT.[14] In this study, CBF saw an increase of 12% overall after the fluid bolus of 500 ml of crystalloid, and this change was statistically significant. An assessment of the intraclass changes in CBF among the responder group versus the nonresponders showed that CBF increased significantly in the responders while it decreased in the nonresponders after a fluid bolus.

Tests such as PLR have shown to increase the CO with volume expansion.[18] PLR mimics a fluid bolus by transferring blood from the lower limbs to the right heart. In this study, we assessed the effects of administering a fluid bolus of 500 ml, which is similar to the volume of fluid challenge by PLR.[19] Hence, we could hypothesize that PLR might also affect the carotid metrics similar to a fluid challenge in determining volume responsiveness.

Most of the studies on carotid metrics to determine volume responsiveness have been conducted on healthy individuals or a specific subgroup of patients.[9,20,21] To our knowledge, this is the first study comparing the change in CFT to CBF after a fluid bolus in such a large population of patients, 29.6% of whom presented in hypotension to the ED. This study showed that only 51% of the patients who were administered a fluid bolus were volume responders, which is consistent with several studies.[4,5,22] Hence, there is a need to differentiate patients who are fluid responders from the nonresponders.

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.

Conclusion

There was no correlation between CBF and CFT, and CFT did not predict volume responsiveness. CBF however showed a significant change after a fluid bolus and its role in determining fluid responsiveness must be studied further.

Financial support and sponsorship

Fluid Research Grant, Christian Medical College, Vellore, supported the study.

Conflicts of interest

There are no conflicts of interest.

Research Quality and Ethics Statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to require Institutional Review Board and Ethics Committee review, and the corresponding protocol/approval number is 11027. We also certify that we have not plagiarized the contents in this submission and have done a Plagiarism Check.

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