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Original Contribution

Corrected carotid flow time and passive leg raise as a measure of volume status

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ABSTRACT

Background: The aim of this study was to investigate the value of corrected carotid flow time (FTc) with passive leg raise (PLR) as a non-invasive marker of volume status in end stage renal disease (ESRD) patients.
Methods: Prospective observational study of ESRD patients presenting to the Emergency department requiring hemodialysis. The common carotid artery was evaluated in long axis. Flow time measurements pre- and post-dialysis as well as before and after PLR were recorded.
Results: 54 patients were enrolled, of which, 30 (55%) were male. The mean age was 47.4 years. The mean volume of fluid removed was 3.89 ± 0.91 L. In the pre-dialysis cohort, the mean FTc was 340.16 ms (95% CI, 330.36–349.95). Following PLR, the mean FTc was 341.34 ms (95% CI 331.74–350.94). In the post hemodialysis cohort, the mean FTc was 302.48 ms (95% CI, 293.63–311.32). Following the PLR maneuver, the mean FTc was 340.49 ms (95% CI 331.97–349.02). The mean decrease in corrected carotid flow time was 19.15 ms (95% CI, 22.86–41.17), 32.02 ms (95% CI 4.05–34.25) and 41.17 ms (95% CI, 36.47–54.76) for patients who had <3 L, 3-4 L and >4 L removed, respectively. In patients without CHF, the mean decrease in FTc after hemodialysis was 38.80 ms (95% CI, 30.12–47.49) whereas for CHF patients the mean decrease was 35.60 ms (95% CI, 25.05–46.15).
Conclusion: Corrected flow time in conjunction with passive leg raise seem to correlate with volume status in hemodialysis patients.

1. Introduction

1.1. Background

Fluid resuscitation and management in shock is a controversial topic. Protocols such as the early goal directed therapy (EGDT) advocated for aggressive fluid management based on static measures such as the Central Venous Pressure (CVP) [1]. More recent studies have shown that CVP measurement does not correlate with volume responsiveness and that aggressive resuscitation of septic shock patients is not as beneficial as once thought [2-6].

Several methods were introduced to look for non-invasive measures of volume responsiveness. Amongst these were the inferior vena cava (IVC) ultrasound evaluation, [7-10] as well as more advanced Doppler applications such as esophageal Doppler monitoring looking at changes in aortic flow to guide fluid therapy [11]. Flow time is the amount of time spent by systole throughout the cardiac cycle. While it was shown that descending aortic flow time correlated with patients' volume status, it remained an invasive study that required endotracheal intubation [11]. Blehar et al. studied a non-invasive way of looking at flow time through the carotids and they showed that it increased in dehydrated patients [12].

The aim of this study is to investigate the value of corrected carotid flow time as a non-invasive marker of volume status. We evaluated the effect of hemodialysis on corrected carotid flow time (FTc) and the effect of the passive leg raise (PLR) maneuver on the FTc before and after hemodialysis.

2. Materials and methods

2.1. Study design and setting

This was a prospective observational study conducted in a tertiary care Emergency Department looking at hemodialysis patients. A convenience sample of end stage renal disease (ESRD) patients presenting to the Emergency Department requiring hemodialysis were enrolled. Patients were recruited from July to October 2017. The ethics and institutional review board of Baylor College of Medicine approved this study

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(protocol #17-03-1601). Informed consent was taken from patients before enrolling them in the study. Inclusion criteria were an age of 18 years or older and completion of a full hemodialysis session with removal of at least 2 l of fluid. Exclusion criteria included patients who were placed on non-invasive positive pressure ventilation (NIPPV), patients who were in atrial fibrillation, and patients who were unable to tolerate the passive leg raise maneuver.

2.2. Outcomes

The primary outcome was the difference in corrected carotid artery flow time after passive leg raise, pre– and post–dialysis. The secondary outcome was the difference in corrected carotid artery flow time before and after dialysis. A subgroup analysis was done to look at congestive heart failure (CHF) patients and to compare the change in FTc after dialysis with non-CHF patients.

2.3. Interventions

Study investigators were 2 emergency physicians with fellowship training in emergency ultrasonography and an Emergency Ultrasound fellow. All investigators completed 10 ultrasound scans with the same measurements done on each scan. All three investigators reviewed all scans to standardize approach and technique before enrolling patients. All imaging measurements were performed with patients seated on a stretcher with their legs parallel to the ground and the head of the bed elevated at 45 degrees. Before and after hemodialysis session, the right common carotid artery was evaluated in long axis proximal to the carotid and a pulse wave Doppler tracing was obtained. Ultrasonographic images were obtained with a 10–5 MHz linear transducer on a SonoSite Xporte (SonoSite, Bothell, WA). The cardiac cycle time, and carotid flow time were recorded. (Fig. 1).

2.4. Measurement

Study participants' age, sex, blood pressure, pulse rate and oxygen saturation pre- and post-dialysis as well as before and after PLR were recorded. History of co-morbidities was obtained from their medical records. Patients' FTc was measured before hemodialysis. After this measurement, a passive leg raise maneuver was performed. The head of the bed was lowered to the flat position and the patients' legs were elevated 45 degrees above the level of the heart. After 1 min, another tracing of Doppler flow through the carotid artery was obtained, and the parameters were measured again. Another set of vital signs was taken after the passive leg raise maneuver. Patients were subsequently placed in the neutral position and taken to hemodialysis. Physicians were blinded to the amount of fluid removed during hemodialysis. This information was retrieved from the patient's medical record by the research assistant (RB). After hemodialysis, a new set of vital signs, Doppler tracings and measurements were obtained before and after passive leg raise. All images were saved as still pictures, with measurements. The cardiac cycle time was obtained with electronic calipers in the ultrasonographic machine's software by measuring the distance between heartbeats at the beginning of the Doppler flow upstroke. Carotid flow time was measured between the upstroke of the systolic flow tracing and the dicrotic notch. Corrected carotid artery flow time was calculated by dividing flow time by the square root of the cardiac cycle time. (Fig. 1).

2.5. Analysis

Based on the literature, we hypothesized that the FTc would increase by 10% following the PLR maneuver in the post-dialysis cohort whereas it will be unchanged in the pre-dialysis cohort [12-14]. Assuming a power of 0.8 and an α of 0.5, a sample size of 52 cases was calculated. All data were analyzed using SPSS for Windows, version 17.0 (SPSS, Inc., Chicago, IL). After meeting the normality assumption, differences

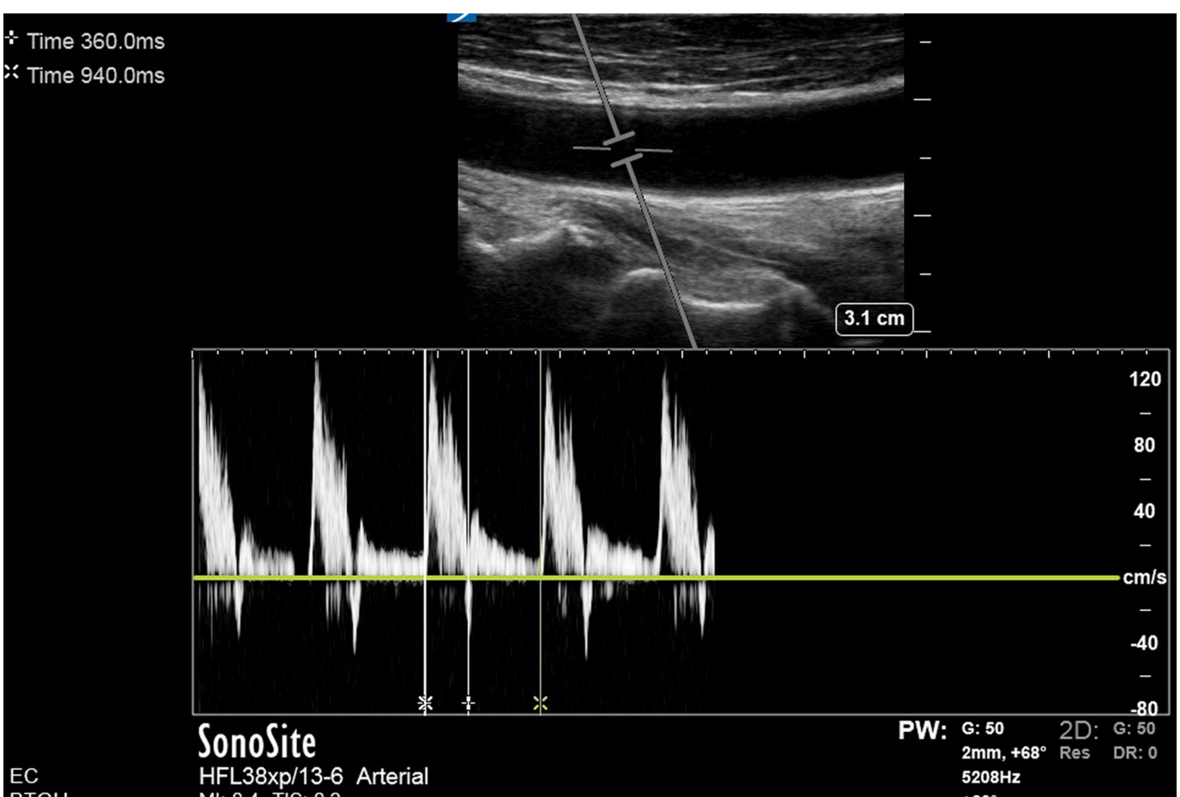

Fig. 1. Doppler ultrasound of the carotid artery showing carotid flow time and carotid cycle time.

between values before and after hemodialysis or between supine and passive leg raise positions were calculated.

Quantitative variables are presented as mean ± SD plus 95% confidence interval (95% CI) and categorical variables as frequency (percentage). Paired *t*-test was performed to assess the statistical significances observed in FTc, HR, and MAP before and after hemodialysis. Independent *t*-test was used to assess the statistical significance of differences observed between groups of patients with different amounts of fluid removal.

3. Results

3.1. Characteristics of study subjects

A total of 94 patients were approached for enrollment. 34 patients were excluded after 4 patients refused to participate, 8 were on BiPAP, 6 were in atrial fibrillation, 13 patients did not tolerate the PLR maneuver, and 9 were transferred for dialysis in an outside facility (Fig. 2). Of the 54 patients included in the study, 30 (55%) were male, and the remaining 24 (45%) were female. The mean age was 47.4 years. The mean volume of fluid removed via hemodialysis was 3.89 ± 0.91 L. All patients had a diagnosis of hypertension. In addition to end stage renal disease, 22 (41%) patients were diabetic, 14 (26%) patients had coronary artery disease diagnosed by cardiac catheterization. 19 (35%) patients had congestive heart failure with poor ejection fraction; which we had defined as an EF < 35%. Table 1 demonstrates patients' demographic data. The mean heart rate pre-dialysis was 73.43 bpm (95% CI, 70.27–76.58) and 73.91 bpm (95% CI, 71.36–76.45) post hemodialysis. The systolic blood pressure before dialysis was 157.78 mmHg (95% CI, 151.45–164.11) and 165.69 mmHg (95% CI, 159.91–171.46) after. The mean diastolic blood pressure before dialysis was 85.19 mmHg (95% CI, 80.60–89.77) and 83.74 mmHg (95% CI, 77.23–90.25) after. The complete list of vitals is provided in Table 2.

Table 1
Demographics of study participants.

Demographics	Mean (±SD)
Male	30 (56%)
Age (years)	47.4 years ± 10.11 years
Hypertension	54 (100%)
Diabetes	22 (41%)
Congestive heart failure with ejection fraction <35%	19 (35%)
CAD	14 (26%)
Asthma	1 (2%)
Days since last dialysis	7.8
Fluid removed (Liters)	3.89 ± 0.91

3.2. Main results

In the pre-dialysis cohort, the mean FTc was 340.16 ms (95% CI, 330.36–349.95). Following the PLR maneuver, the mean FTc was 341.34 ms (95% CI 331.74–350.94). In the post hemodialysis cohort the mean FTc was 302.48 ms (95% CI, 293.63–311.32), following the PLR maneuver, the mean FTc was 340.49 ms (95% CI 331.97–349.02).

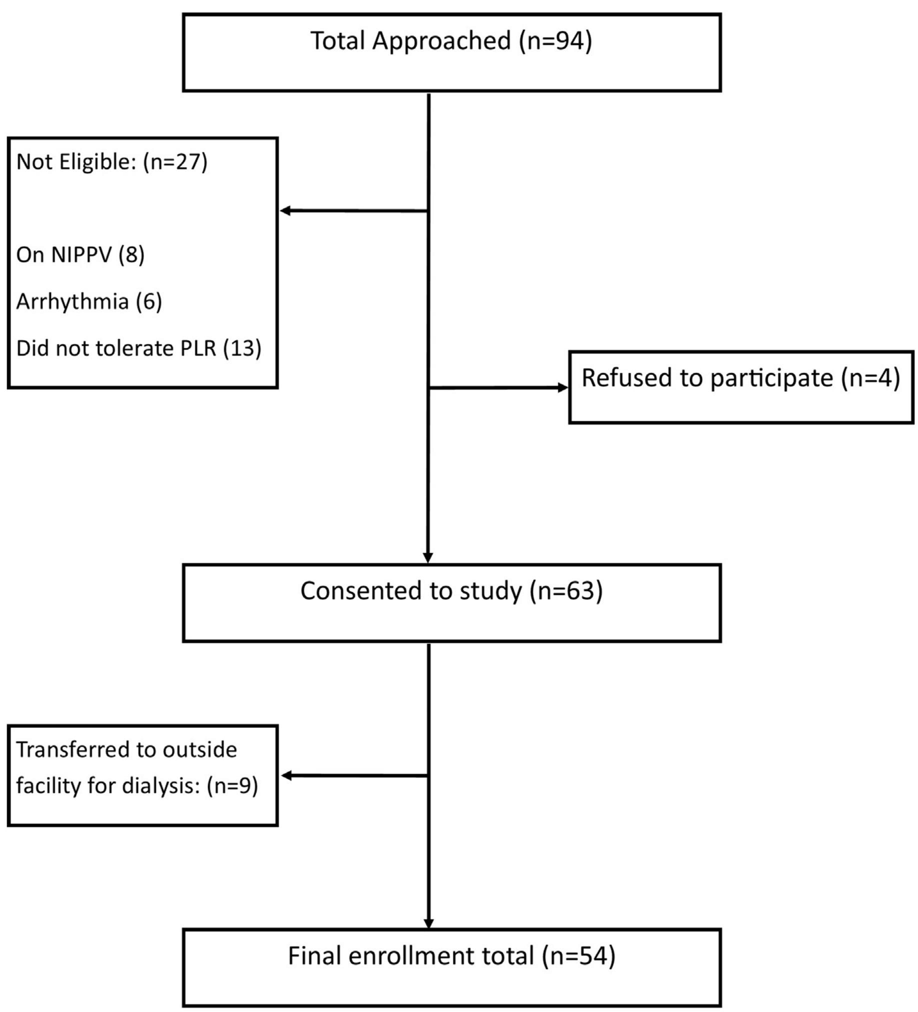

Fig. 2. Flow diagram of patient inclusion.

Table 2
Vital signs of study participants.

Vitals	Pre-dialysis (N = 54)		Post-dialysis (N = 54)	
	Mean	95% CI	Mean	95% CI
HR	73.43	70.27–76.58	73.91	71.36–76.45
SBP	157.78	151.45–164.11	165.69	159.91–171.46
DBP	85.19	80.60–89.77	83.74	77.23–90.25
O2 saturation	96.35	95.32–97.38	97.98	97.29–98.68
HR PLR	73.94	70.72–77.17	74.67	72.19–77.14
SBP PLR	159.43	153.03–165.82	168.43	162.79–174.06
DBP PLR	85.74	80.83–90.65	87.26	82.56–91.96
O2 saturation PLR	96.17	95.14–97.20	97.87	97.11–98.63

Patients were divided according to fluid removal. The mean decrease in FTc was 19.15 ms (95% CI, 4.05–34.25) For patients who had <3 L removed, 32.02 ms (95% CI 22.86–41.17) for patients who had 3–4 L removed and 41.17 ms (95% CI, 36.47–54.76) for the patients who had >4 L removed. (Fig. 3) There was a negative association between the volume of fluid removed by hemodialysis and the changes in FTc (Pearson correlation, −0.415; P = .071). Finally, patients were stratified according to CHF status and we looked at the mean change in FTc after hemodialysis. In patients without CHF, the mean decrease in FTc after hemodialysis was 38.80 ms (95% CI, 30.12–47.49) whereas for CHF patients the mean decrease in FTc was 35.60 ms (95% CI, 25.05–46.15). Table 3 shows a detailed list of carotid flow and cycle times in the pre and post-dialysis populations.

4. Discussion

In an effort to shift towards a non-invasive way of assessing volume status and volume responsiveness, researchers looked at aortic flow changes using an esophageal Doppler. They showed that a PLR-induced increase in aortic blood flow of >12% was predictive of volume responsiveness. [11,15]. They also showed that aortic flow fared better than flow time in predicting fluid responsiveness, however, the study was done on mechanically ventilated patients. Aortic flow calculation is associated with several drawbacks; it is highly invasive, and is also operator dependent. There are several advantages of looking at the carotid flow time; first, the artery is easily identifiable with bedside ultrasound and unlike flow, carotid flow time is not affected by the angle of insonation. The use of aortic flow time in the evaluation of patients' volume status was examined by Blehar et al. who were able to show that in dehydrated patients, the corrected carotid flow time decreases and that an administration of 1100 ml of fluid was associated with a 14% increase [12]. In contrast to the Blehar group, we opted to perform a passive leg raise maneuver instead of a fluid challenge to evaluate volume status. The PLR maneuver is a non-invasive, reversible; and easily performed on spontaneously breathing patients. Furthermore, it has been shown to be predictive of volume responsiveness in septic patients and a variety of critically ill patients [11,16-18].

Our results show that in hemodialysis patients, the corrected carotid flow time decreased by 10% after fluid removal. After performing a passive leg raise maneuver, we noticed that the corrected carotid flow time values returned to their pre-dialysis levels. These results suggest that a measurement of a carotid flow time coupled with a passive leg raise maneuver may be helpful in detecting dehydrated patients and can help physicians guide their fluid management. Our results also showed that the decrease in corrected flow time is volume dependent as patients who had >4 l removed had the greatest reduction in corrected carotid flow time. These findings are mirrored in the literature by a similar study done by Hossein-Nejad et al. who looked at the corrected carotid flow time in hemodialysis patients and also noticed a significant decrease in the FTc after dialysis (345.07 ± 37.19 vs 307.77 ± 31.76) that correlated with volume removal [13]. It is interesting to note that our values are similar to the studies by Hossein-Nejad. It is also important to note that in the Blehar study, the FTc before hydration was also 299 ms (95% CI, 282–317 ms) [12]. However, further studies are needed in order to set normal values of euvolemic and hypervolemic patients.

It is interesting to note that there were no differences in vital signs before and after hemodialysis except for systolic blood pressure, which we noted to be higher by 8 mmHg in the post dialysis cohort. This increase in systolic blood pressure after dialysis was described by Inrig et al. who explained that intradialytic hypertension is multifactorial and includes subclinical volume overload, sympathetic overactivity, activation of the renin angiotensin system, endothelial cell dysfunction, and specific dialysis techniques [19]. However, it is more important to note that there were no changes in vital signs after the PLR maneuver. Several studies on carotid flow time had similar findings, which strengthens the argument that FTc changes are more sensitive during volume changes than vital sign changes [13,14].

Another study done by Mckenzie et al. looked at the corrected carotid flow time in healthy volunteers before and after blood donation. They were able to show that the mean FTc decreased from 320 ms to 299 ms after the donation. Following a PLR maneuver, they were able to show that FTc values returned to pre-blood loss values [14]. It is important to note that this study was done on healthy volunteers with no

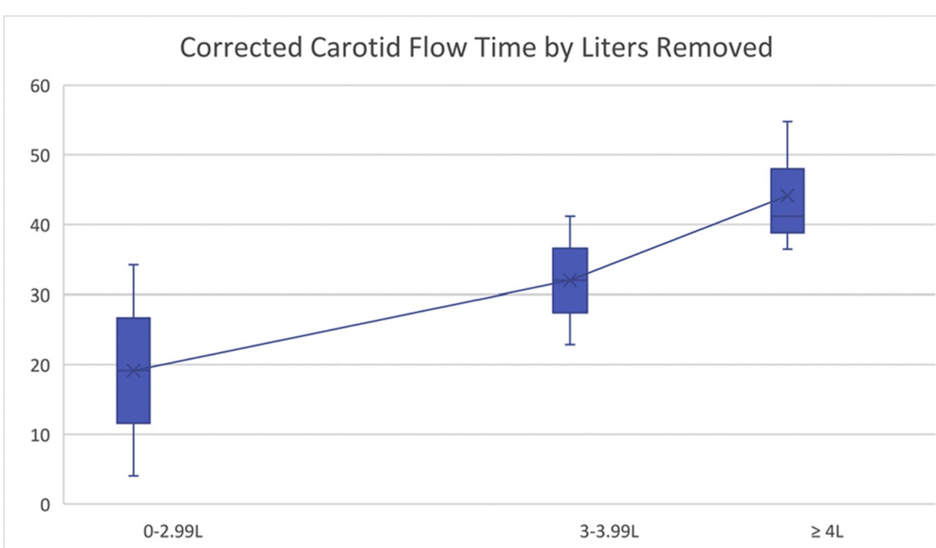

Fig. 3. Corrected carotid flow time change by fluid removal.

Table 3
Carotid flow and cycle time in the pre-dialysis and post-dialysis patient populations.

Pre-dialysis		Pre-dialysis PLR	
Carotid flow time	315.19 ms (95% CI, 303.95–326.42)	Carotid flow time	317.49 ms (95% CI, 306.27–328.91)
Carotid cycle	859.07 ms (95% CI, 832.05–886.10)	Carotid cycle	865.93 ms (95% CI, 838.58–893.27)
Corrected carotid flow time	340.16 ms (95% CI, 330.36–349.95)	Corrected carotid flow time	341.34 ms (95% CI, 331.74–350.94)
Post-dialysis		Post-dialysis PLR	
Carotid flow time	282.96 ms (95% CI, 273.53–292.40)	Carotid flow time	319.07 ms (95% CI, 310.02–328.12)
Carotid cycle	876.85 ms (95% CI, 852.46–901.24)	Carotid cycle	880.74 ms (95% CI, 856.36–905.12)
Corrected carotid flow time	302.48 ms (95% CI, 293.63–311.32)	Corrected carotid flow time	340.49 ms (95% CI, 331.97–349.02)

strict control of their hydration status prior to blood letting. Furthermore, it is not known what cutoff is needed to label someone as a volume responder using the FTc method. The Blehar study showed a 14% increase in FTc with hydration whereas the Hossein-Nejad study showed a 10% decrease after hemodialysis [12,13]. Our study showed an 11% decrease in FTc following hemodialysis. The more pronounced drop in FTc in our study compared to the Hossein-Nejad study can most likely be explained by the fact that more fluid was removed in our patient population (3.89 L vs 2.4 L). Finally, in comparison with the Blehar study, we did not reach a 14% reduction in our FTc. This could be due to the fact that the interval between dialysis sessions was longer than usual in our patients (7.8 days). Our patients do not receive scheduled hemodialysis and are dialyzed in the ED on an emergent basis based on criteria of fluid overload and hypoxia (oxygen saturation < 88%), severe acidosis (serum bicarbonate <10 mmol/L) or severe hyperkalemia (Potassium >6 mmol/L). As such, they usually go more than the standard 3 days without dialysis and might be more fluid overloaded than the scheduled hemodialysis patient. Another possible explanation is that hemodialysis is done over a period of 3–4 h which could allow the system time to adapt to the volume loss. One important difference to point out is that our patient population had a higher number of CHF patients as compared to other studies. When we looked at the change in FTc in CHF versus non-CHF patients, we showed that there was a similar drop in carotid flow time after hemodialysis. Our findings suggest that carotid flow time in conjunction with passive leg raise is an easy non-invasive method that may be helpful in judging volume status and guiding fluid resuscitation in clinically challenging patients, such as end stage renal disease patients and heart failure patients.

5. Limitations

The present study is an observational study performed on a specific group of ESRD patients with volume overload. Therefore, its findings should be interpreted cautiously as they are not applicable to the general ED population. Our results should be compared with the results of future studies on other populations with hypervolemia or hypovolemia. We only looked at the right common carotid during this study and we cannot state that the findings are applicable to both carotid arteries. The reference ranges and cut off points for FTc in the carotid artery have not been studied thoroughly, hence, we cannot state that our values should be used as reference ranges. Furthermore, considering ESRD patients after hemodialysis as euvolemic may not be accurate. Therefore, post hemodialysis FTc values should not be considered the exact predictors of normal volume status. Further studies are needed on carotid flow time in order to come up with reference values. Finally, the ultrasound examination was performed by physicians with extensive training in bedside ultrasound and therefore cannot be generalized to all emergency physicians.

6. Conclusion

Corrected carotid flow time in conjunction with a passive leg raise is a novel and simple, non-invasive method that could help in assessing volume status and in guide fluid management. Further large studies are needed to corroborate our findings.

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Consent to publish

All participating patients have granted consent for publication.

Author's contributions

RBC, JW and JC have made substantial contributions to conception and design of the study.

RBC, JW, JC, RB acquisition of data, analysis and interpretation of data.

RBC, GAD, SK and HZ have been involved in drafting the manuscript.

RBC, GAD, HZ, JC and JW for revising manuscript critically for important intellectual content.

All authors contributed substantially to its revision. GAD and RBC take responsibility for the paper as a whole.

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