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Carotid systolic flow time with passive leg raise correlates with fluid status changes in patients undergoing dialysis☆

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ABSTRACT

Corrected carotid systolic flow time (CFTc) has been proposed as a measure of volume status in acutely ill patients. This study endeavors to determine whether the change in CFTc with passive leg raise (PLR) maneuver correlates with volume status changes.

Dialysis patients at Kingston General Hospital (Kingston, Canada) underwent point-of-care carotid ultrasonography at the beginning and the end of dialysis. With each measurement, 2 values were recorded: the absolute CFTc, and the difference in CFTc before and after the PLR maneuver.

A total of 49 measurements were collected during the study period. CFTc changed with PLR by 5 ± 22 milliseconds (2.0%) pre-dialysis and by 40 ± 19 milliseconds (13.0%) post-dialysis ($P < .0001$). Incorporating PLR to the CFTc measurement improved the area under the ROC from 0.64 to 0.91. Particularly, in our sample of patients, a 30 milliseconds increase in CFTc with PLR predicted the post-dialysis volume state (LR+ = 11) whereas an increase of less than 20 milliseconds argued against it (LR− = 0.079).

The assessment of CFTc pre- and post-PLR correlates with intravascular volume changes in patients undergoing dialysis. Alternative to the currently available bedside modalities, this technique is non-invasive, objective, simple to perform at the bedside, and reversible with respect to volume challenge.

1. Introduction

Intravenous (IV) fluid administration remains the cornerstone of treating patients in circulatory shock. However, over-resuscitation can lead to volume overload, which can result in poor clinical outcomes [1-3]. Numerous approaches have been developed to monitor hemodynamic status and guide resuscitation therapy [4-8].

Passive leg raise (PLR) has gained popularity in the non-invasive assessment of volume responsiveness [4,9-11]. This technique causes a gravitational auto-bolus of 200-300 mL of whole blood from the lower limbs [4]. This volume is sufficient to increase left ventricular cardiac preload to challenge the Frank-Starling curve [12]. The ability of this technique to predict preload responsiveness has been well validated in numerous studies involving critically ill patients [11-13].

In order to utilize this technique, numerous hemodynamic indices have been developed to measure the hemodynamic response to PLR, such as transesophageal aortic Doppler, bioreactance, and cardiac velocity time integral (VTI) [4,9,14]. However, these methods are either invasive, require expensive equipment, or are technically challenging to measure. To circumvent these deficiencies, carotid Doppler has been studied as a non-invasive method of assessing hemodynamics [14].

Corrected carotid flow time (CFTc) has been proposed as a much more feasible and non-invasive measure of volume status [15]. It is simply the duration of the left ventricular systole, measured on a carotid Doppler tracing as the time in milliseconds from the onset of systole to the dicrotic notch. This value represents the duration of left ventricular systolic ejection phase, which is a function of preload, afterload, and inotropy [16-18]. However, afterload and inotropy are unlikely to change in a short time period; hence, CFTc have been considered a reflection of cardiac preload, revealing its potential utility in assessing volume status. Several small studies supported this hypothesis by demonstrating that the standalone CFTc value correlates with volume status in dehydrated patients receiving fluids, patients donating whole blood, and in patients undergoing dialysis [15,19,20].

Abbreviations: CFTc, corrected carotid flow time; PLR, passive leg raise; RBV, relative blood volume; ROC, receiver operator curve; AUROC, area under receiver operator curve; LR, likelihood ratio.

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Instead of measuring the absolute value of CFTc, we believe we can improve the diagnostic value of this test by marrying it to the PLR maneuver, thereby measuring the change in CFTc with PLR. To our knowledge, only one study by Mackenzie et al tested the effect of PLR on CFTc, revealing that PLR done after blood donation returned the CFTc value to pre-donation levels [19]. Here we report a prospective observational study to determine whether the change in CFTc with PLR correlates to the change in volume status in dialysis patients.

2. Methods

2.1. Setting and research ethics

This prospective observational study was performed between February 17th 2016 and March 16th 2016 at Kingston General Hospital Renal Unit (Queen's University, Kingston, Canada). This study has been reviewed for ethical compliance by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (DMED-1879-16). The protocol was explained by one of the investigators to all participants, and signatures were obtained to document consent.

2.2. Participant selection

Participants were recruited throughout the duration of the study, and selected from all-comers to the dialysis unit. To be included in the study, patients had to be older than 18, have more than 500ccs of targeted fluid removal, and must be able and willing to perform the PLR maneuver. Patients who were unable to perform the PLR, including amputees, were excluded from the study. We also excluded patients who did not have visible carotid flow or had an irregularly irregular pulse due to difficulty in measuring the carotid waveform.

2.3. Study protocol

At the start of their dialysis, eligible patients were placed in semi-recumbent position with the head of the bed at 45°, and the baseline carotid Doppler waveform was recorded. Next, we executed the PLR maneuver by lowering the head of the bed to 0°, and elevating the legs to 45°. After 30 seconds of PLR, another Doppler waveform was captured. From pre-dialysis waveforms, we specifically recorded 2 values: the semi-recumbent CFTc and the difference in CFTc values before and after PLR. Both of these values were re-measured just prior to the end of dialysis when the target fluid volume was removed. This allowed us to compare the absolute CFTc and the change in CFTc with PLR between 2 volume states. Other variables recorded include ultrafiltration volume, the rate of removal, and the relative blood volume (RBV), which is calculated by the dialysis system based on the measured hematocrit. Fresenius 5008 (Frankfurt, Germany) dialysis system was used in this study.

2.4. Ultrasound technique

Carotid flow Doppler measurements were taken using the Sonosite M-Turbo ultrasound device using the L25x 13–6 MHz 25 mm footprint linear probe (FujiFilm; California, USA). Each CFTc measurement involved visualizing the common carotid artery proximal to the bifurcation in longitudinal view, and gathering the pulsed wave Doppler tracing of the vessel. Each tracing was analyzed, and carotid flow time (CFT) was measured as the time from the upstroke of systole to the dicrotic notch as described previously [20]. The CFT time value was corrected for the heart rate by dividing the measured time by the square root of the cardiac cycle time in seconds as per Bazett's formula [21].

2.5. Statistical analysis

In this study we measured the absolute CFTc, as well as the change in CFTc with PLR. These measurements were done pre- and post-dialysis, which allows us to compare the operating characteristics of both variables. Statistical significance was assessed using a paired *t* test. Normality of data distribution was confirmed using the Shapiro–Wilk method and the Q-Q plot. ROC curves were constructed to assess the operating characteristics of CFTc alone, as well as CFTc with PLR. The area under the curve was calculated electronically. Correlation of measurements with ultrafiltration volume was done using the Pearson's Linear Correlation model. All statistical analysis was performed using SPSS (OSX, Version 23, IBM Inc., Armonk, NY).

3. Results

A total of 49 patients were enrolled in the study, and the summative results were tabulated in Table 1. The mean ultrafiltration volume was 1070 mL (414-2868 mL). The mean CFTc in the semi-recumbent position prior to dialysis was 333.34 ± 34.47 milliseconds (95% CI, 323.70-342.99 milliseconds), while post-dialysis CFTc decreased to 317.20 ± 34.68 milliseconds (95% CI, 307.49-326.91 milliseconds). This difference was statistically significant ($P = .02$). Performing the PLR maneuver produced a change in CFTc of 5 ± 22 milliseconds (2.0 ± 7.1%) pre-dialysis and 40 ± 19 milliseconds (13.0 ± 7.2%) post-dialysis, and the difference between pre- and post-dialysis was also statistically significant ($P < .0001$). The mean heart rate before ultrafiltration was 76 bpm (95% CI, 64-88 bpm), and 75 bpm (95% CI, 61-89 bpm) after ultrafiltration. The difference in heart rates was not statistically significant when comparing before and after ultrafiltration, as well as before and after PLR. However, cFTC measurement was still corrected for the heart rate using Bazett's formula because this was the convention in previous studies [15,19,20,22].

To assess the ability of the 2 measures to discriminate volume status, we constructed ROC curves for the standalone CFTc value and the change in CFTc with the PLR maneuver (Fig. 1). Area under the ROC curve (AUROC) using the CFTc alone was 0.64 (95% CI, 0.53-0.75), whilst measuring the CFTc with the PLR maneuver produced an AUROC of 0.91 (95% CI, 0.85-0.97). The PLR maneuver greatly improved the performance of the CFTc in discriminating pre- and post-ultrafiltration volume state. We used these operating characteristics to determine that a 30 milliseconds increase in CFTc with PLR can predict a post-ultrafiltration volume state with a sensitivity of 71% and a specificity of 94% (LR+ = 11), whereas an increase of less than 20 milliseconds made a post-ultrafiltration volume state very unlikely (LR− = 0.079) (Table 2).

The CFTc with PLR correlated poorly with ultrafiltration volume (Pearson's correlation coefficient of 0.112, R^2 = 0.013, $P = .224$) (Fig. 2, Supplemental Fig. 1A). However, when we assessed the change in CFTc without PLR, there was a stronger and statistically significant correlation with ultrafiltration volume (Pearson's correlation 0.35, R^2 = 0.121, $P = .007$). Similar correlation coefficients were seen

Table 1
Mean CTFc and change in CFTc (absolute value and percentage changed) with the PLR maneuver Pre- and Post-Hemodialysis

	Pre-hemodilaysis	Post-hemodilaysis	Difference
Mean CFTc	333.34± 34.47 ms	317.20± 34.68 ms	$P = .02$
Change in CFTc with PLR maneuver	5 ± 22 ms (2.0 ± 7.1%)	40± 19 ms (13.0 ± 7.2%)	$P < .0001$