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Reliability of oscillometric central hemodynamic responses to an orthostatic challenge

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ABSTRACT

Background: Monitoring central hemodynamic responses to an orthostatic challenge may provide important insight into autonomic nervous system function. Oscillometric pulse wave analysis devices have recently emerged, presenting clinically viable options for investigating central hemodynamic properties. The purpose of the current study was to determine whether oscillometric pulse wave analysis can be used to reliably (between-day) assess central blood pressure and central pressure augmentation (augmentation index) responses to a 5 min orthostatic challenge (modified tilt-table).

Methods: Twenty healthy adults (26.4 y (SD 5.2), 55% F, 24.7 kg/m^2 (SD 3.8)) were tested on 3 different mornings in the fasted state, separated by a maximum of 7 days. Central hemodynamic variables were assessed on the left arm using an oscillometric device.

Results: Repeated measures analysis of variance indicated a significant main effect of the modified tilt-table for all central hemodynamic variables ($P < 0.001$). In response to the tilt, central diastolic pressure increased by 4.5 mmHg (CI: 2.6, 6.4), central systolic blood pressure increased by 2.3 (CI: 4.4, 0.16) mmHg, and augmentation index decreased by an absolute − 5.3%, (CI: −2.7, −7.9%). The intra-class correlation coefficient values for central diastolic pressure (0.83–0.86), central systolic blood pressure (0.80–0.87) and AIx (0.79–0.82) were above the 0.75 criterion in both the supine and tilted positions, indicating excellent between-day reliability.

Conclusion: Central hemodynamic responses to an orthostatic challenge can be assessed with acceptable between-day reliability using oscillometric pulse wave analysis.

1. Introduction

Autonomic nervous system (ANS) dysfunction has been linked to a number of cardiovascular disturbances, including hypertension and stroke [1,2]. The ANS function can be assessed using an orthostatic challenge, which results in pooling of blood in the sub-diaphragmatic venous system and subsequent vasoconstriction of the resistance and capacitance vessels [3,4]. Thus, peripheral blood pressure is typically used to gauge the sympathetic response to an orthostatic challenge [3]. However, considering the marked differences in pulse pressure between the central aorta and peripheral limbs, peripheral blood pressure may not accurately reflect the effects of peak arterial blood pressure on centrally located organs [5]. For this reason, central hemodynamic assessments may provide a superior indication of ANS responses to an orthostatic challenge. However, in order to be of value in a clinical setting, these assessments must be accurate, precise, and relatively simple to conduct.

Central hemodynamic properties may be monitored with accuracy [6] and precision [7] using pulse wave analysis (PWA). Typically, the pressure waveform is non-invasively monitored at a peripheral site, and using a generalized transfer function, a corresponding aortic arterial waveform can be generated [8,9]. Besides central blood pressure, the generated waveform is used to estimate

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central pressure augmentation (arterial wave reflection). Peripheral waveform recordings are typically collected using radial artery applanation tonometry. However, this technique requires some expertise, can be time consuming, and may be impractical for use in the clinical setting. Recently, oscillometric devices have emerged, which are operator independent, user-friendly, and have been validated against tonometric [10,11] and direct aortic catheter assessments [12–14].

In addition to being accurate (valid), a clinical setting assessment tool must be precise (reliable). Knowledge of reliability is required to gauge the critical difference in a parameter that must be exceeded between two sequential results in order for a statistically significant change to occur in an individual [15]. While oscillometric PWA devices have been demonstrated to be highly reliable under standard resting conditions [10,11,16], to the best of our knowledge only one study has demonstrated that PWA can be used to reliably assess central hemodynamic responses to an orthostatic challenge (ANS function) [17]. The aforementioned study [17] utilized radial artery tonometry, which as previously stated may be unsuitable for clinical practice, and it is currently unknown whether user-friendly oscillometric devices provide acceptable reliability. Therefore, the purpose of the current study was to determine the between-day reliability of central blood pressure and central pressure augmentation responses to a modified tilt-table test, using oscillometric PWA.

2. Methods

2.1. Participants

To ascertain the upper limit of reliability, a relatively homogenous cohort of 20 young (19–35 y) and healthy participants were recruited. Participants were excluded if they smoked, reported any known cardio-metabolic disorders, or were taking medications known to affect cardiovascular function. Ethical approval was obtained from the Massey University Human Ethics Committee and all participants provided written informed consent prior to participating in the study.

2.2. Experimental design

Prior to beginning the study, participants were familiarized with all experimental procedures. Subsequently, participants were tested on 3 different days in a dimly-lit, climate controlled room between the hours of 7am and 10am. All participants were fasted, consuming only water, and refrained from caffeine and supplement intake that morning, and strenuous physical activity and alcohol for 24 h prior to experimentation. The maximum duration between the first and last study visit was 7 days (mean: 3.2 d SD (1.8)), and women were tested on consecutive days to avoid the possible confounding influence of menstrual cycle hormones. Following a 20 min rest period in the supine posture, baseline PWA assessments were collected. The participant was then rapidly (~1 s) tilted to a 60-degree upright position using a modified tilt-table for 5 min. During the tilt period, PWA assessments were collected at 2- and 5-min ($Tilt_2$, $Tilt_5$). The participant was returned to the supine position for a 5-min recovery period during which PWA assessments were collected at 2- and 5-min (Rec_2, Rec_5).

2.3. Pulse wave analysis

Oscillometric pressure waveforms were recorded on the left upper arm by a single observer using the SphygmoCor XCEL device (AtCor Medical, Sydney, Australia), following standard manufacturer guidelines [18]. Each measurement cycle lasted approximately 60 s, consisting of a brachial blood pressure recording and then a 10 s sub-systolic recording. A corresponding aortic pressure waveform was generated using a validated transfer function [14], from which central systolic, diastolic, pulse pressure (cSBP, cDBP, cPP), augmentation pressure (AP), and augmentation index (AIx) were derived. The AP is defined as cSBP minus the pressure at the inflection point, whereby the inflection point is the merging of the forward and reflected waves. The AIx is defined as the AP expressed as a percentage of cPP. AIx is influenced by heart rate, and thus an index corrected for a heart rate at 75 beats per minute (AIx75) was also calculated. At baseline, two measurements were taken, separated by a three-minute interval. If blood pressure differed by > 5 mmHG or if AIx >4% a third recording was taken and the closest recordings were averaged [19]. During the tilt and recovery conditions only 1 recording was taken at each time point.

2.4. Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences version 20.0 (SPSS, Inc., Chicago, Illinois). All data are reported as means and standard deviation (SD), unless specified. Statistical significance was defined as $P < 0.05$ (two tailed). The effects of the orthostatic challenge central hemodynamic parameters were assessed using analysis of variance (ANOVA) for repeated measurements with one within-subject factors (time: base, $Tilt_2$, $Tilt_5$, Rec_2, Rec_5). Effect sizes are reported using partial eta-squared (η_p^2), where 0.01, 0.06, and 0.14 represent a small, medium, and large effect, respectively [20].

Reproducibility of parameters was assessed by calculating the intra-class correlation coefficient (ICC), standard error of measurement (SEM), and reproducibility coefficient (RC). The ICC was calculated according to the formula: SD_b [2]/SD_b^2+SD_w [2], where SD_b [2] and SD_w [2] are the between and within-subject variance. In general, ICC values above 0.75 are considered to indicate excellent reproducibility [21]. The reproducibility coefficient (RC) is defined as the critical difference in a parameter that must be exceeded between two sequential results in order for a statistically significant change to occur in an individual [15]. Absolute RC was calculated using the formula: $1.96 \times SEM \times \sqrt{2}$, where 1.96 corresponds to 95% confidence interval, and SEM was calculated using the equation: $SD_b{}^* \sqrt{(1\text{-ICC})}$ [15].

3. Results

Data were successfully collected from all 20 healthy young men and women (26.4 y (SD 5.2), 55% F, 24.7 kg/m^2 (SD 3.8)).

3.1. Central blood pressure

In response to the modified-tilt table, there was a large main effect ($\eta_p^2 = 0.20–0.65$) for all peripheral and central blood pressure variables (Table 1). The main variables of interest, cSBP and cDBP, increased in response to the tilt-table when compared to baseline, with the peak change in cSBP occurring at $Tilt_2$ (2.3 mmHg, CI: 0.2, 4.4 mm Hg) and the peak change in cDBP occurring at $Tilt_5$ (4.5 mmHg, CI: 2.6, 6.4 mmHg). For all stages of the tilt-table test, the ICC values for cDBP and cSBP were above the criterion 0.75 (Table 2), indicating excellent between-day reliability. The RC values indicates that, for a given individual, in order for a significant change to have occurred between visits the cDBP at $Tilt_2$ (73 mmHg) must differ by 7.0 mmHg and the cSBP at $Tilt_2$ (103 mmHg) by 7.9 mmHg.