Comparison of Two Methods for Noninvasive Determination of Stroke Volume during Orthostatic Challenge

Donald F. Doerr, B.S.E.E.[1], Duane A. Ratliff, M.P.H.[2], Joseph Sithole[3], and Victor A. Convertino, Ph.D.[4]

[1]Technology Implementation Branch, NASA, Kennedy Space Center, FL 32899;
[2]Bionetics Corporation, NASA, Kennedy Space Center, FL 32899;
[3]Spaceflight and Life Sciences Training Program, NASA, Kennedy Space Center, FL 32899
[4]US Army Institute of Surgical Research, Fort Sam Houston, TX 78234

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Correspondence and
Reprint requests to: Victor A. Convertino, Ph.D.
US Army Institute of Surgical Research
3400 Rawley E. Chambers Avenue
Building 3611
Fort Sam Houston, TX 78234-6315
Telephone: 210/916-5633
Telefax: 210/916-5992
Email: victor.convertino@amedd.army.mil

Abstract

Background: The real time, beat-by-beat, non-invasive determination of stroke volume (SV) is an important parameter in many aerospace related physiologic protocols. In this study, we compared simultaneous estimates of SV calculated from peripheral pulse waveforms with a more conventional non-invasive technique. **Methods**: Using a prospective, randomized blinded protocol, ten males and nine females completed 12-min tilt table protocols. The relative change (%Δ) in beat-to-beat SV was estimated non-invasively from changes in pulse waveforms measured by application of infrared finger photoplethysmography (IFP) with a Portapres® blood pressure monitoring device and by thoracic impedance cardiography (TIC). The %Δ SV values were calculated from continuous SV measurements in the supine posture and over the first 10 s (T1), second 10 s (T2), and 3.5 minutes (T3) of 80° head-up tilt (HUT). **Results**: The average %Δ SV measured by IFP at T1 (-11.7 ± 3.7 %) was statistically less ($P < 0.02$) than the average %Δ SV measured by TIC at T1 (-21.7 ± 3.1 %), while the average %Δ SV measured by IPF at T2 (-16.2 ± 3.9 %) and T3 (-19.1 ± 3.8 %) were not statistically distinguishable ($P \geq 0.322$) than the average %Δ SV measured by TIC at T2 (-21.8 ± 2.5 %), and T3 (-22.6 ± 2.9 %). Correlation coefficients (r^2) between IFP and TIC were 0.117 (T1), 0.387 (T2), and 0.718 (T3). **Conclusion**: IFP provides beat-to-beat (real time) assessment of %Δ SV after 20 sec of transition to an orthostatic challenge that is comparable to the commonly accepted TIC. Our data support the notion that IFP technology which has flown during space missions can be used to accurately assess physiological status and countermeasure effectiveness for orthostatic problems that may arise in astronauts after space flight. While the peripherally measured IFP response is slightly delayed, the ease of implementing this monitor in the field is advantageous.

Key words: photoplethysmography; impedance cardiography; tilt table testing

Introduction

Orthostatic hypotension and frank syncope have proven to be debilitating for astronauts returning from space, leading to presyncope and intolerance in approximately 40% of crew members [1,9,16,23]. As a result, real-time assessments of cardiovascular function and hemodynamic responses during passive stand and tilt tests can be critical to the flight surgeon's ability to provide early detection of imminent orthostatic instability and apply appropriate therapeutic action. Traditional vital sign monitoring of blood pressure and pulse rate using standard sphygmomanometry has been used in post-space flight clinical cardiovascular assessments and orthostatic tests [1,2,11,14-18,20,23]. However, development of orthostatic hypotension and impending intolerance (presyncope) can occur too rapidly for traditional sphygmomanometric techniques to assist the flight surgeon in early diagnosis and application of effective intervention. On the other hand, low stroke volumes or peripheral vasoconstriction have some predictive value in orthostatic testing [1,3-6,15,16,23]. Therefore, the ability to obtain continuous noninvasive measures of change in stroke volume could prove valuable to flight surgeons in their clinical assessment and treatment of astronauts following space flight.

Stroke volume has been measured during orthostatic testing using echocardiography or thoracic impedance cardiography (TIC). The clinical usefulness of both techniques can be limited by body movement and inability to calculate and display stroke volume real-time data. The emergence of infrared finger photoplethysmographic (IFP) technology has been introduced as a method of providing continuous non-invasive estimation of stroke volume simultaneously with arterial blood pressure [12,24]. The ability to obtain continuous beat-to-beat stroke volume and blood pressure independent of changing body posture is an attractive feature because it provides the capability of obtaining real-time estimates of total peripheral vascular resistance. However, we are unaware of any investigation designed to provide a systematic comparison of the continuous measurement in stroke volume by IFP with some other acceptable non-invasive technique. The purpose of this investigation was therefore to compare stroke volume responses estimated by IFP during a standard tilt test protocol with measurements of stroke volume obtained from TIC.

Methods

Subjects. Twenty healthy, non-smoking subjects were recruited to participate in the present investigation, of which 10 men and 9 women volunteered as subjects. The subjects were normotensive with systolic blood pressure = 127 ± 3 mmHg and diastolic blood pressure = 68 ± 2 mmHg. Their average (±SE) age, height and weight were 34 ± 3 yr, 172 ± 2 cm, and 70.1 ± 3.9 kg. The subjects were not astronauts, neither trained specifically for this study, nor taking prescription medication to control hemodynamic function. A complete medical history and physical examination that included a resting 12-lead ECG and clinical orthostatic exam (supine/seated/standing consecutive blood pressure measurements) were obtained on each of the potential subjects. During an orientation period that preceded each experiment, all subjects were made familiar with the laboratory, the protocol, and procedures. Experimental procedures and protocols were reviewed and approved by the Institutional Review Board of the Kennedy Space Center for the use of human subjects. Each subject gave written informed voluntary consent to participate in the experiments.

Protocol. Each subject completed a head-up tilt table test (HUT) during spontaneous breathing through a face mask with an impedance threshold device (ITD; Advanced Circulatory Systems Inc., Eden Prairie, Minnesota) set at an inspiratory resistance of approximately -7 cm H_2O resistance. A detailed description of the ITD and its functional application during an orthostatic challenge has been reported elsewhere [7]. Subjects maintained a supine posture for 30 min prior to the start of data collection. At the start of data collection (indicated as time (T) = 0:00), recordings for SV determination were initiated as subjects breathed through a plastic medical facemask. At T = 3:45 min, the ITD valve was attached to the facemask and the subject was instructed to breath on the ITD with natural but deep breaths. At T = 4:00 min, subjects were tilted to 80° head-up tilt (HUT) and maintained this position for 4 min. At T = 8:00 min, subjects were returned to the supine position. Measurements of stroke volume were collected continuously throughout the baseline and HUT periods, and stored on a data acquisition system based in LabView. Relative (percent) changes in stroke volume that reflected the transition from supine baseline to upright posture were determined from beat-to-beat analysis during three time periods: 1) the initial 10-sec period starting immediately upon the assumption of HUT (T1); 2) the second 10-sec period (10 to 20 sec) after the assumption of HUT (T2); and 3) at 3 min after the assumption of HUT (T3). Each experimental session was conducted over a period of less than 90 min.

Stroke Volume Measurements: Beat-to-beat stroke volume (SV) was estimated non-invasively from changes in pulse waveforms measured by application of IFP with the

Portapres®. Stroke volume estimation by application of IFP is based on computed aortic flow pulsations from arterial pressure waveforms by simulating a nonlinear, time-varying three-element model (aortic characteristic impedance, arterial compliance, and systemic vascular resistance) of aortic input impedance [24]. Two of the model parameters, characteristic impedance and arterial compliance, are derived from an aortic pressure-area relationship applying the arctangent model of aortic mechanics. The third element, total peripheral resistance, is not known, but is an outcome of the model simulation. Using this approach, comparisons of 76 cardiac output measures using IFP during open-heart, bypass surgery in 8 patients produced a mean deviation of ±2% (with SD of 8%) when compared to 76 simultaneous thermodilution measurements [24]. These results indicated that the IFP method is capable of providing accurate estimates of continuous beat-to-beat stroke volume in supine anesthetized patients.

Thoracic impedance was measured using 4 circumferential electrodes, two placed around the base of the neck and two placed around the thorax at the level of and distal to the xiphoid process. A bioelectric impedance cardiograph unit (HIC-2000, Bio-impedance Technology, Inc., Chapel Hill, NC) was used to introduce a constant current of 4mA at 100 KHz frequency across the outer electrodes and detect changes in electrical impedance with each pulse beat across the inner pairs of electrodes [13]. The analog signal of the electrocardiogram waveform (ECG), baseline thoracic impedance (Z_0), and the change in impedance over time (dZ/dt) were converted to a digital signal for analysis using National Instruments LabView software (Fig. 1). The following algorithm was used to estimate SV from the ECG and impedance [13]:

$$SV = \frac{\rho L^2 T (dZ/dt)_{min}}{Z_0^2}$$

Where:

ρ = the average electrical resistivity of blood at 100 KHz (150 ohm-cm)
L = the mean distance between the two inner electrodes in cm
T = the ventricular ejection time in seconds as measured from the dZ/dt and ECG waveforms

[Figure 1 here]

Estimates of stroke volume using thoracic impedance have been reported with correlation coefficients of 0.70 to 0.93 in comparison with thermodilution techniques [19]. The relative change in SV (%ΔSV) from supine to HUT was calculated as follows:

$$\%\Delta SV = ((\text{pre-tilt SV} - \text{post-tilt SV})/\text{pre-tilt SV}) * 100^{-1}$$

Statistical Analysis. We performed a standard two-method (IFP, TIC) t-test statistical analysis to determine differences in relative (percent) SV change from supine to upright posture between the two techniques for SV measurement for each separate period of assessment (i.e., T1, T2, T3). Exact P values were calculated for each independent effect and reflect the probability of obtaining the observed or greater effect given only random departure from the assumption of no effects. Standard errors are raw measures of variation about the specific treatment group mean. Standard Pearson product correlation coefficients were performed to quantify the relationship between the two techniques for SV measurement at each of the 3 time periods of assessment.

Results

The average %Δ SV measured by IFP during HUT at all time intervals was less than that measured by TIC (Fig. 2). The average %Δ SV measured by IFP at T1 (-11.7 ± 3.7 %) was less ($P < 0.02$) than the average %Δ SV measured by TIC at T1 (-21.7 ± 3.1 %), while the average %Δ SV measured by IPF at T2 (-16.2 ± 3.9 %) and T3 (-19.1 ± 3.8 %) were not statistically distinguishable ($t \leq 1.019$; $P \geq 0.322$) from the average %Δ SV measured by TIC at T2 (-21.8 ± 2.5 %), and T3 (-22.6 ± 2.9 %). Correlation coefficients (r^2) between IFP and TIC were 0.117 (T1), 0.387 (T2), and 0.718 (T3) (Fig. 3).

[Figures 2 and 3 here]

Discussion

IFP in addition to standard sphygmomanometry has been used to monitor blood pressure in astronauts during their clinical orthostatic tests immediately after space flight [1,16,23]. Unfortunately, conventional blood pressure measurement techniques have not proven to be a reliable or early indicator of the onset of syncope since some astronauts who became orthostatically intolerant and could not finish a 10-min stand test after return from a space mission demonstrated no change in blood pressure while others showed gradual or abrupt reductions just prior to their presyncopal event [1]. However, low stroke volume and a limited ability to increase peripheral resistance has been associated with orthostatic intolerance after space flight [1,3,5,6,16,23]. It therefore seems that a noninvasive continuous assessment of central (stroke volume) and peripheral (vascular resistance) hemodynamics would prove a more sensitive clinical tool in predicting the orthostatic compromise to astronauts during and after re-entry than blood pressure alone. Although TIC has provided an effective noninvasive technique for the measurement of SV in human subjects [19], the requirement for electrodes and sensitivity to body and respiratory movements can make its use difficult in the operational environment. In contrast, IFP requires only the placement of a small pneumatic cuff around the middle finger. With this perspective, we compared the relative change in beat-to-beat stroke volume obtained from the same IFP methodology used to measure blood pressure with changes in SV measured continuously with noninvasive TIC. Our results demonstrated that IFP provided a non-invasive beat-to-beat measurement of percent reductions in stroke volume during a standard clinical tilt table protocol similar to that used to test astronauts.

Both IFP and TIC tracked reductions in stroke volume during the transient and steady-state phases of moving from the supine to head-up position. However, IFP significantly underestimated the %ΔSV measured by TIC and accounted for only about 18% of the total variance of the %ΔSV measured by TIC during the initial phase (T1 = 10 sec) of transition from supine to HUT. On the other hand, the measure of %ΔSV and intra-subject variability improved substantially with measurements conducted later in time from the transient phase (i.e., steady-state). This distinct difference between mean values and correlation coefficients generated from %ΔSV measurements with IFP and TIC during transient and steady-state phases of posture change provides unique insight into the limitation of using peripheral vascular responses to assess SV changes. The reduction in stroke volume during orthostatic challenges is closely related to a proportional (linear) elevation in sympathetic nerve activity [6,15]. Increased sympathetic nerve activity in turn causes reductions in arterial pulse wave magnitude through vasoconstriction. Since sympathetic activity controls peripheral vascular resistance, it is not surprising that changes in peripheral arterial waveforms measured by IFP would track changes in stroke volume measured by TIC. During the initial seconds of transition in posture from supine to HUT, a rapid mechanical redistribution of blood from the central circulation toward the lower extremities (blood pooling) causes an immediate reduction in cardiac filling and stroke volume [21]. The subsequent reflex-mediated increase in sympathetic nerve activity is manifested in reductions in the magnitude of peripheral arterial pulse waveforms only after a time delay of ~10 s [8,10,22]. This mismatch between the immediate change in central hemodynamics (i.e., reduction in cardiac filling and stroke volume) and a delay in sympathetically-mediated reflex vasoconstriction was manifested in the present investigation by the large difference and variability between IFP and TIC measurements obtained during the transition phase from supine to HUT postures. As sympathetically-mediated vasoconstriction approached complete compensation following the transient phase of the HUT maneuver, there was little difference between average %ΔSV measured by IFP and TIC with about 72% of the total variance in the %ΔSV accounted for. It is clear from our results that more realistic values of %ΔSV will be obtained with IFP when measurements are conducted after the transient phase of blood volume redistribution.

Operational Implications.

Like TIC, IFP provides a simple non-invasive, beat-to-beat measure of SV. However, IFP offers several advantages over TIC. Technically, the absence of requirement for electrodes makes

IFP application faster and easier for the attending health provider. In addition to central hemodynamic measurements (i.e., HR, SV and cardiac output), IFP provides concurrent measures of beat-to-beat arterial blood pressures. Thus, with cardiac output and blood pressure measurements, IFP offers the capability to calculate total peripheral vascular resistance which has proven to be a predictor of orthostatic tolerance.

There are three other considerations to be understood during field implementation of the IFP technique. The current version of the Portapres automatically compensates for the hydraulic difference between the vertical locations of the finger cuff and the heart. In this protocol, the finger was kept at heart level throughout the HUT by attaching the arm to an outstretched armboard to assure accuracy. Earlier use of this instrumentation utilized an open finger golf glove attached by Velcro to the clothing over the heart. A second consideration is the assurance of good circulation in the fingers. Our experience during rescue operations with hypothermic subjects included poor measurements associated with reduced blood flow in the hands (unpublished observations). Consequently, maintenance of body (hand) warmth may be required to obtain valid masurements. The third concern is accurate placement of a properly sized cuff on the finger. Experience is quickly gained in locating the cuff by comparison with conventional occlusive BP techniques.

With these simple factors in mind, measurements from peripheral arterial pulse waves are easily implemented and independent of body and respiratory motion which makes IFP more readily applicable for monitoring astronauts and other crew members in the austere aerospace environment.

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FIGURE LEGENDS

Figure 1. Example of an analog signal tracing of the electrical impedance cardiogram waveform used to determine baseline thoracic impedance (Z_0), the change in impedance over time (dZ/dt), and the ventricular ejection time (T).

Figure 2. Mean ± 1 standard error values for 19 subjects of percent change (%Δ) in stroke volume comparing infrared finger photoplethysmography (IFP; open bars) with thoracic impedance cardiography (TIC; lined bars) recorded during the first 10 s (T1), second 10 s (T2), and at 3.5 min of 80° head-up tilt. Asterisk indicates difference ($P < 0.02$) compared with TIC.

Figure 3. Individual values for 19 subjects of percent change (%Δ) in stroke volume comparing infrared finger photoplethysmography (IFP) with thoracic impedance cardiography (TIC) recorded during the first 10 s (T1), the second 10 s (T2), and at 3.5 min of 80° head-up tilt. For T1 (top panel), the linear equation is %ΔSV [IFP] = 0.53 %ΔSV [TIC] – 0.2 ($r^2 = 0.177$); for T2 (middle panel), the linear equation is %ΔSV [IFP] = 0.94 %ΔSV [TIC] – 2.5 ($r^2 = 0.387$); for T3 (bottom panel), the linear equation is %ΔSV [IFP] = 0.78 %ΔSV [TIC] – 7.0 ($r^2 = 0.718$).

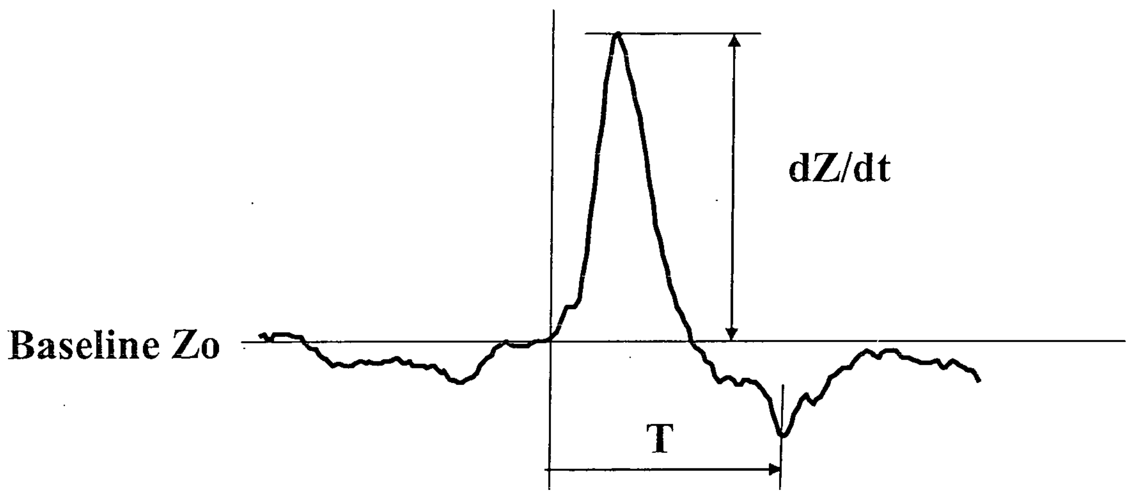

Figure 1

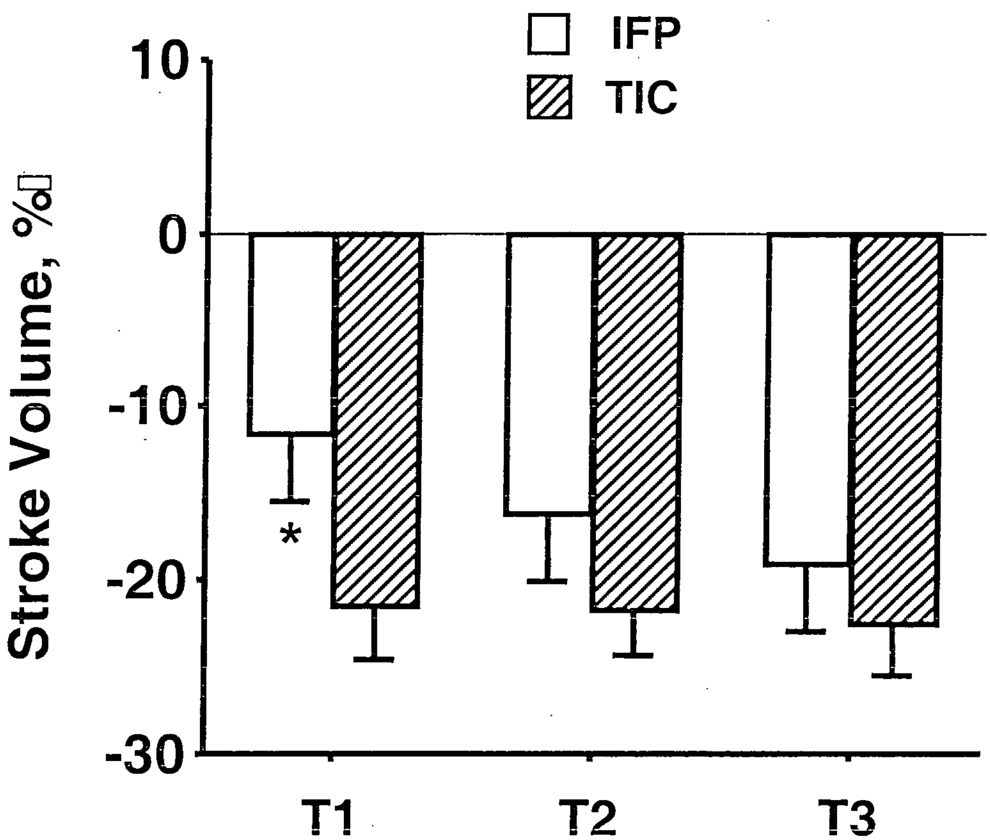

Figure 2

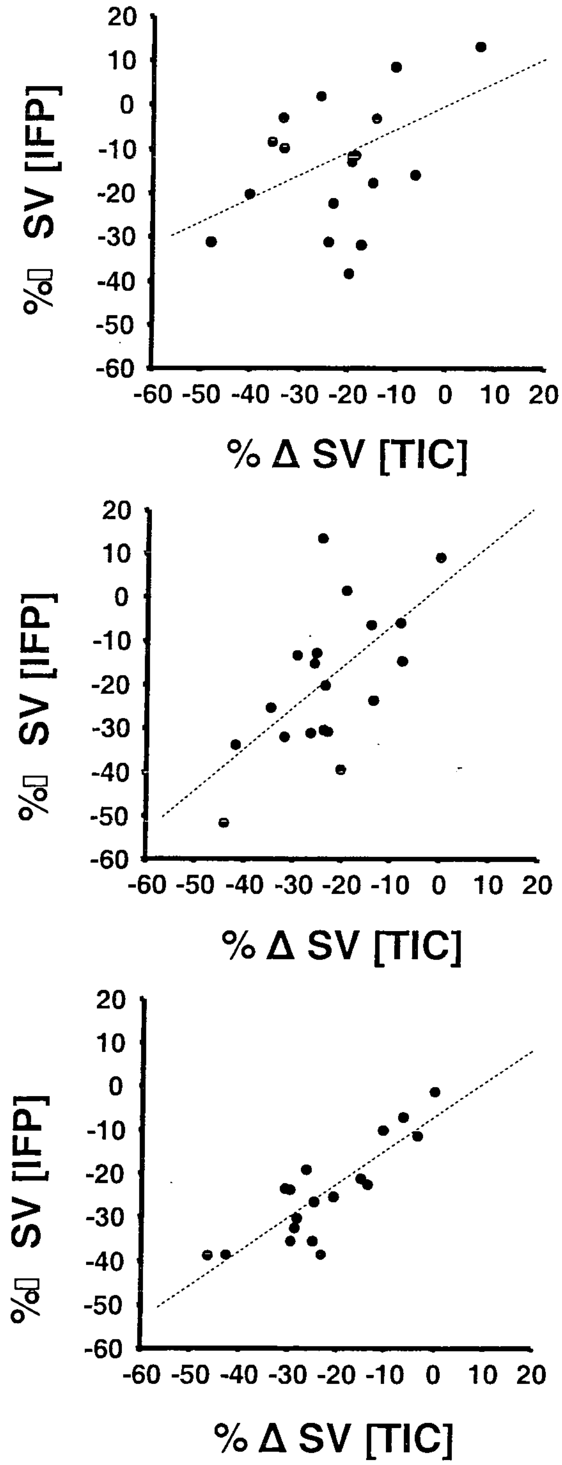

Figure 3