2018

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Gordon, N., Abbiss, C. R., Maiorana, A. J., Marston, K. J., & Peiffer, J. J. (2018). Intrarater reliability and agreement of the physioflow bioimpedance cardiography device during rest, moderate and high-intensity exercise. *Kinesiology, 50*, 140-149. Available here

INTRARATER RELIABILITY AND AGREEMENT OF THE PHYSIOFLOW BIOIMPEDANCE CARDIOGRAPHY DEVICE DURING REST, MODERATE AND HIGH-INTENSITY EXERCISE

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Original scientific paper
UDC: 796.012:519.2

Summary:

The PhysioFlow bioimpedance cardiography device provides key measures of central systolic and diastolic and peripheral vascular function. Many of these variables have not been assessed for intrarater reliability and agreement during rest, submaximal exercise and high-intensity interval exercise. Twenty healthy adults (age: 26±4 years) completed two identical trials beginning with five minutes of rest followed by two 5-minute submaximal cycling bouts at 50% and 70% of peak power output. Subjects then completed ten 30-second cycling intervals at 90% of peak power output interspersed with 60 s of passive recovery. Bioimpedance cardiography (PhysioFlow; Manatec Biomedical, France) monitored heart rate, stroke volume, cardiac output, stroke volume index, cardiac index, ventricular ejection time, contractility index, ejection fraction, left cardiac work index, end diastolic volume, early diastolic filling ratio, systemic vascular resistance and systemic vascular resistance index continuously throughout both trials. Intraclass correlation coefficients (ICC), standard errors of measurement and minimal detectable differences were calculated for all variables. Heart rate, stroke volume, cardiac output, left cardiac work index and end diastolic volume demonstrated a good level of reliability (ICC>.75) at rest, during submaximal exercise and high-intensity interval exercise. All other variables demonstrated inconsistent reliability across activity types and intensities. When using the PhysioFlow device, heart rate, stroke volume, cardiac output, left cardiac work index and end diastolic volume were deemed acceptable for use regardless of exercise type (continuous vs. interval) or intensity (low, moderate, or high). However, other variables measured by this device appear less reliable.

Key words: *bioimpedance cardiography, exercise, reliability, high-intensity interval exercise, cardiac output, minimal detectable differences, central haemodynamics, peripheral haemodynamics*

Introduction

The ability to continuously measure haemodynamic responses to exercise is important when assessing or monitoring individuals before, during and following acute and chronic exercise. For example, cardiac output has been used to determine exercise tolerance and cardiac function during exercise (Crisafulli, Orru, Melis, Tocco, & Concu, 2003; Fletcher, et al., 2001) as well as during clinical responses to physiological and pharmacological stimuli (Leitman, et al., 2006; Parry & McFetridge-Durdle, 2006; Richard, et al., 2001; Tahvanainen, Leskinen, Koskela, Ilveskoski, Nordhausen, et al., 2009). Several methods are available for measuring cardiac output (see reviews: Sangkum, et al., 2016; Thiele, Bartels, & Gan, 2015; Warburton, Haykowsky, Quinney, Humen, & Teo, 1999a, 1999b) during exercise, with the most common methods, based on the Fick principle, being thermodilution and dye-dilution techniques. These techniques are both accurate and reliable (Chris-

tie, et al., 1987; Thrush, Downs, & Smith, 1995); however, they are invasive and require experienced technicians. The use of Doppler echocardiography and rebreathing methods (Thiele, Bartels, & Gan, 2015) to measure cardiac output, while non-invasive, are themselves limited in use due to requiring an experienced technician and not providing beat-to-beat measurements, respectively (Jakovljevic, et al., 2008; Oberman, et al., 1989).

Bioimpedance cardiography provides non-invasive, beat-to-beat measures of cardiac output without the need for highly skilled technicians; however, the validity and reliability of these devices are equivocal (Saugel, Cecconi, Wagner, & Reuter, 2015; Thiele, Bartels, & Gan, 2015). It is likely the reliance on the evaluation of baseline thoracic impedance (Z_0) provides a degree of error in measurement for most devices as Z_0 depends on multiple factors (Bernstein, 1986; Jensen, Yakimets, & Teo, 1995; Kubicek, Karnegis, Patterson, Witsoe, & Mattson, 1966; Penney, 1986). The PhysioFlow (Manatec Biomedical, France) provides an alternative as it does not rely on the evaluation of Z_0 nor does it need to measure blood resistivity or the distance between electrodes, both which introduce additional measurement error (Jensen, Yakimets, & Teo, 1995; Warburton et al., 1999b). Previous studies have assessed the validity of PhysioFlow to measure cardiac output during rest and exercise against the direct Fick (Bougault, et al., 2005; Charloux, et al., 2000; Richard, et al., 2001), dye-dilution (Robach, et al., 2008) and rebreathing methods (Tordi, Mourot, Matusheski, & Hughson, 2004). Specifically, when assessed against the gold standard (i.e., direct Fick), the PhysioFlow has been shown to provide accurate measures of cardiac output during rest and exercise (correlation coefficient = 0.71-0.94, mean difference = 0.04-3.20 $L \cdot min^{-1}$) (Bougault, et al., 2005; Charloux, et al., 2000; Richard, et al., 2001). Additionally, studies have reported generally moderate to good reliability and agreement between repeated measures of cardiac output during rest and exercise (Charloux, et al., 2000; Hsu, et al., 2006; Richard, et al., 2001; Schultz, Climie, Nikolic, Ahuja, & Sharman, 2012; Tordi, Mourot, Matusheski, & Hughson, 2004; Welsman, Bywater, Farr, Welford, & Armstrong, 2005). Another often overlooked measurement relevant to a device's applicability is the minimal detectable difference (MDD). This measurement is defined as the smallest change detectable above the threshold of measurement error (Beaten, et al., 2001; Portney & Watkins, 2009) and provides an indication of the sensitivity of a device to detect meaningful changes. Knowing the MDD of all PhysioFlow measurements will provide important information regarding the ability of the PhysioFlow to detect differences between populations and changes over time. We are unaware of any study to date which has examined the reliability of the PhysioFlow during dynamic non-steady-state exercise (i.e., high-intensity interval exercise) and this is important given this mode of training is increasingly being prescribed to both healthy and chronic disease populations (Gibala, Little, Macdonald, & Hawley, 2012).

The majority of literature assessing the reliability of bioimpedance cardiography has focused on the measurement of heart rate, stroke volume and cardiac output. However, several other haemodynamic indices are provided, including variables relating to central systolic function (Leitman, et al., 2006; Miles, Gotshall, Quinones, Wulfeck, & Kreitzer, 1990; van der Meer, et al., 1996), central diastolic function (Pickett & Buell, 1993) and peripheral vascular function (Leitman, et al., 2006). Evidence related to the validity and reliability of many of these measures are lacking; however, the ability to assess and monitor central systolic and diastolic function as well as peripheral vascular function using one device in a variety of exercise conditions would be cost- and time-efficient for researchers and clinicians. As such, the purpose of this study was to assess the intrarater reliability and agreement as well as to calculate the MDD of all variables measured and calculated by the PhysioFlow at rest, during submaximal steady-state exercise and high-intensity interval exercise in a healthy population.

Methods

Subjects

Twenty healthy adults (15 males; age: 26±4 years; body mass index: 23.7±3.0 $kg \cdot m^2$) volunteered to participate in this study. Data from one subject were excluded from analyses due to poor signal quality during the interval section of the second trial, resulting in a total of 19 subjects included in the analyses. Subjects were excluded from the study if they presented with a history of cardiovascular or metabolic disorders. Subjects were required to attend the laboratory on three separate occasions during which they performed a graded exercise test and two experimental sessions. Each session was separated by seven days. Subjects were asked to avoid strenuous physical activity the day before and the day of testing, with all testing completed at a similar time of day. All risks and benefits of participating in the study were provided to the subjects and written informed consent was obtained prior to data collection. This study received ethical approval from the Murdoch University Human Research Ethics Committee (2015/146) prior to commencement of the study and conformed to the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Procedures

Subjects completed all trials on an electronically braked Velotron cycle ergometer (RacerMate; USA) that was individually set up for each subject and kept consistent throughout the study. During the first visit, subjects completed a graded exercise test starting at 70 W, and increased 35 $W \cdot min^{-1}$ for males and 20 $W \cdot min^{-1}$ for females, until volitional exhaustion. The volume of oxygen consumption and carbon dioxide production were measured at 1Hz and presented as 30-s mean values using a Parvo TrueOne metabolic analysis system (ParvoMedics; USA). The highest 30 s mean value was used to determine maximal oxygen consumption. The maximum power output achieved during this test was used to prescribe the intensity of exercise in the remaining sessions.

The second and third testing sessions were completed in an identical manner and in an environmental chamber controlled at 24°C and 50% relative humidity. Subjects arrived at the laboratory at least 3 h postprandial and in a euhydrated state. Hydration status was assessed using a hand-held refractometer (RHCN-200ATC Clinical Refractometer, G-tech, China) prior to beginning each trial. Urine specific gravity between 1.005-1.020 was classified as euhydrated, whereas values greater than 1.020 indicated dehydration (Kavouras, 2002). Subjects were informed that if they were not fasted or if presented as dehydrated, they were required to return on another day for testing, but this did not occur. Each session began with five minutes of passive rest on the cycle ergometer followed by two 5-minute submaximal cycling bouts at 50% (140±34 W) and 70% (196±48 W) of the maximum power output achieved during the graded exercise test (286±66 W). Following one minute of passive recovery, subjects then completed ten 30-second cycling intervals at 90% peak power output (252±62 W) interspersed with 60 s of passive recovery. Our interval configuration is in line with previous research (Freyssin, et al., 2012) and was chosen to elicit a physiological response high enough to be considered high-intensity, but still allowing adequate rest between intervals to minimise the effect of fatigue. Power output throughout the trials was maintained using Velotron cycling ergometer software.

The volume of oxygen consumed was measured at 1 Hz using the ParvoMedics metabolic analysis system. Haemodynamic responses were measured beat-by-beat using bioimpedance cardiography (PhysioFlow PF-07; Manatec Biomedical, France). Blood pressure, obtained by manual sphygmomanometry during the fourth minute of the rest period and each submaximal cycling bout, were entered into the software to update the systemic vascular resistance (SVR), systemic vascular resistance index (SVRi) and left cardiac work index (LCWi). Blood pressure measures were not updated during the interval cycling section due to the lag time evident between entering a new blood pressure and the adjustments observed in SVR, SVRi and LCWi; instead, the values obtained during the 70% peak power steady-state exercise were used for the determination of SVR, SVRi and LCWi during high-intensity interval exercise. While this may influence the validity of the data, it should have minimal influence on the reliability.

Impedance cardiograph measures

Continuous online haemodynamic monitoring was completed using the PhysioFlow PF-07, which uses changes in thoracic bioimpedance during cardiac ejection to calculate stroke volume. Detailed methodology of the PhysioFlow device has been described previously (Charloux, et al., 2000; Hsu, et al., 2006; Lepretre, Koralsztein, & Billat, 2004; Tonelli, Alnuaimat, Li, Carrie, & Mubarak, 2011). Two sets of two electrodes (Ag/AgCl, Skintact FS-50), one 'transmitting' and one 'sensing', were placed above the supraclavicular fossa on the left base of the neck and at the midpoint of the thoracic region of the spine. Another set of two electrodes were used to monitor a single electrocardiographic signal (ECG; V1/V6 position). A high frequency alternating current (66 kHz) of low amperage (4.5 mA peak to peak) was applied through the thorax producing an impedance waveform which was time-corrected to the simultaneous ECG recording. Since Z_0 evaluation is not required with the PhysioFlow device, electrode positioning is not crucial (Tan, Lai, & Hwang, 2006). Thorough skin preparation (i.e., shaving, abrasion and alcohol wiping) was completed to ensure effective conductivity between the electrode and the skin.

An initial stroke volume index (SVi_{cal}; $mL.m^2$) was calculated during the autocalibration phase based on 30 consecutive heart beats with the subject sitting in an upright position on the cycle ergometer. During autocalibration, the largest impedance variation observed during systole ($Z_{max} - Z_{min}$) and the largest rate of variation of the impedance signal (contractility index; dZ/dt_{peak}) were retained. The determination of SVi_{cal} also depends on the thoracic flow inversion time (TFIT), acquired from the first mathematical derivative of the impedance signal (dZ/dt), according to the following equation: $SVi_{cal} = k \cdot [(dZ/dt_{max}) / (Z_{max} - Z_{min})] \cdot W(TFIT_{cal})$, where k is an empirically adjusted constant and W is a propriety correction algorithm. During the data acquisition phase, stroke volume (SV; mL) was calculated according to the equation: $SV = SVi_{cal} \cdot ((dZ/dt_{max}) / (dZ/dt_{max})_{cal} \cdot TFIT_{cal} \cdot TFIT)^{1/3} \cdot BSA$, where body surface area (BSA; m^2) was calculated according to the Haycock equation ($BSA = 0.024265 \cdot height^{0.3964} \cdot weight^{0.5378}$) (Haycock, Schwartz, & Wisotsky, 1978). Cardiac output ($L \cdot min^{-1}$) was calculated using the following equation: $CO = HR \cdot$

SVi · BSA, where heart rate (HR; bpm) was determined from the R-R interval on the first derivative of the ECG signal (dECG/*t*) as this provides a more stable signal. Cardiac index (CI; $L \cdot min^{-1} \cdot m^2$) was calculated as the ratio of CO to BSA. Ventricular ejection time (VET; ms) was measured from the dZ/dt and was defined as the time between the opening (B point) and closing (X point) of the aortic valve. Left ventricular ejection fraction (EF; %) was calculated according the Capan equation (van der Meer, et al., 1996): EF = 0.84 – (0.64 · PEP) / VET, where PEP is the pre-ejection period, defined as the time between the onset of the Q wave of the ECG and the B point. LCWi ($kg \cdot m^{-1} \cdot m^2$) was calculated according to the following equation: LCWi = 0.0144 · CI · (MAP - PAOP), where MAP (mmHg) is the mean arterial pressure calculated from the systolic and diastolic blood pressure entered by the user, and PAOP is the pulmonary artery occlusion pressure which was by default set as 10 mmHg during the calibration procedure. End diastolic volume (EDV; mL) was calculated as the ratio of SV to EF. The early diastolic filling ratio (EDFR) was measured on the dZ/dt and was defined as the ratio of the O wave to the S wave. Systemic vascular resistance ($Dyn \cdot s^{-1} \cdot cm^5$) was calculated by the following equation: SVR = 80 · (MAP – CVP) / CO, where CVP is the central venous pressure, which was by default set as 7 mmHg during the calibration procedure. Systemic vascular resistance index ($Dyn \cdot s^{-1} \cdot cm^5 \cdot m^2$) was calculated by the following equation: SVRi = 80 · (MAP – CVP) / CI.

Statistical analysis

Guidelines for reporting reliability and agreement studies (Kottner, et al., 2011) suggest, for continuous variables, reliability should be assessed using intraclass correlation coefficients (ICC) and agreement using standard errors of measurement (SEM). Mean values for all variables (i.e., 19 paired measures) obtained during the final minute of the rest period and submaximal steady-state exercises (50% and 70% of peak power), were analysed for intrarater reliability and agreement. During the high-intensity interval exercise, mean values calculated only for data collected during the 10 intervals and not the recovery period (i.e., 19 paired measures) were used for analyses. Estimates of reliability (ICC with 95% confidence intervals) and agreement (SEM) were calculated for all the PhysioFlow-derived variables during all conditions. Variables with an ICC greater than 0.75 were considered indicative of good reliability, while those below 0.75 were considered poor to moderately reliable (Portney & Watkins, 2009). MDD using 95% confidence intervals were calculated according to the following equation: MDD = z · SEM · √2 (Beaten, et al., 2001; Portney & Watkins, 2009), where z = 1.96 for 95 % confidence intervals. Differences in urine specific gravity, oxygen consumption and all the PhysioFlow-derived variables between trials were determined using a dependent t-test. All data are presented as mean ± standard deviation, unless otherwise noted. All statistical analyses were conducted using SPSS (Version 22, IBM®, USA) software, with significance set at $p \leq .05$.

Results

No differences were observed between trial one and trial two for urine specific gravity (1.008±0.006 vs. 1.007±0.005; p=.37). Similarly, no differences were observed for oxygen consumption at rest (0.31±0.06 vs. 0.31±0.08 $L \cdot min^{-1}$; p=.92), during 50% steady-state cycling (2.02±0.45 vs. 2.05±0.50 $L \cdot min^{-1}$; p=.33), 70% steady-state cycling (2.86±0.67 vs. 2.88±0.70 $L \cdot min^{-1}$; p=.56), or during high-intensity interval cycling (1.87±0.46 vs. 1.82±0.46 $L \cdot min^{-1}$; p=.24).

The intrarater reliability and agreement of the PhysioFlow-derived variables for central systolic function (Table 1), central diastolic function (Table 2) and peripheral vascular function (Table 3) at rest, during steady-state cycling and interval cycling are presented. HR and LCWi were greater during the high-intensity interval exercise in trial one compared with trial two (p=.04 and p=.03, respectively). Additionally, EDV was greater during trial one compared with trial two during rest (p=.02), 50% steady-state (p=.03), 70% steady-state (p=.03) and during the high-intensity interval exercise (p=.02). No other significant differences were observed for any other variables between trial one compared to trial two.

Discussion and conclusions

The main objective of this study was to determine the intrarater reliability and agreement of all the PhysioFlow-derived variables at rest, during submaximal steady-state exercise and high-intensity interval exercise in a healthy population. Additionally, we have calculated MDD for all the variables during each condition to provide researchers and clinicians with valuable information regarding the sensitivity of PhysioFlow to detect changes between repeated measures. The variables demonstrating good reliability (ICC>0.75) across exercise conditions were HR, SV, CO, LCWi and EDV. All other central and peripheral haemodynamic variables demonstrated suboptimal reliability (ICC<0.75) during some or all of the rest and exercise conditions.

Central systolic function

The ability to measure HR, SV and CO is important to determine cardiovascular health (Esposito, Mathieu-Costello, Shabetai, Wagner, & Richardson, 2010) as well as monitor cardiovascular stress

Table 1. Intrarater reliability and agreement of central systolic function variables measured or calculated using PhysioFlow at rest, during steady-state cycling (50% and 70% peak power output) and interval cycling (90% peak power output)

		Trial 1 (mean±SD)	Trial 2 (mean±SD)	Difference	ICC (95% CI's)	SEM	MDD
Resting	HR	76±11	78±12	1.5±8.0	.86 (.63, .95)	3.01	8.35
	SV	88±24	82±18	-5.4±17.2	.81 (.49, .93)	7.60	21.05
	CO	6.57±1.64	6.25±1.13	-0.3±1.1	.81 (.52, .93)	0.47	1.31
	SVi	47.28±10.32	44.66±8.77	-2.6±9.1	.71 (.23, .89)	4.94	13.70
	CI	3.56±0.77	3.53±0.75	0.0±0.8	.60 (-.04, .85)	0.51	1.40
	VET	340±53	352±43	12.2±53.6	.56 (-.15, .83)	35.76	99.09
	CTI	218±84	245±67	27.7±77.6	.65 (.10, .87)	45.78	126.87
	EF	72.56±15.51	77.36±9.23	4.8±15.4	.43 (-.47, .78)	11.60	32.14
	LCWi	4.54±1.31	4.24±1.15	-0.3±0.9	.84 (.59, .94)	0.36	0.99
50% steady-state	HR	142±15	142±16	0.3±7.1	.94 (.85, .98)	1.70	4.70
	SV	113±27	109±23	-4.1±18.2	.85 (.60, .94)	7.14	19.79
	CO	15.78±3.31	15.29±2.87	-0.5±2.3	.85 (.60, .94)	0.91	2.51
	SVi	61.00±11.06	59.06±10.06	-1.9±10.0	.71 (.26, .89)	5.35	14.82
	CI	8.56±1.38	8.71±2.51	0.2±2.1	.62 (.00, .85)	1.30	3.61
	VET	242±26	240±29	-2.7±27.9	.64 (.07, .86)	16.72	46.33
	CTI	376±127	386±104	9.7±126.3	.58 (-.36, .84)	81.56	226.04
	EF	81.20±10.67	84.93±6.75	3.7±11.1	.38 (-.61, .76)	8.75	24.24
	LCWi	12.73±3.24	11.88±2.40	-0.9±2.2	.82 (.53, .93)	0.94	2.59
70% steady-state	HR	171±13	171±14	0.0±6.3	.94 (.84, .98)	1.54	4.28
	SV	115±26	110±22	-4.4±13.5	.91 (.78, .97)	3.96	10.97
	CO	19.42±3.93	18.71±3.41	-0.7±2.4	.88 (.70, .96)	0.82	2.28
	SVi	61.90±9.59	59.81±9.09	-2.1±7.1	.83 (.57, .94)	2.90	8.04
	CI	10.51±1.38	10.65±2.87	0.1±2.5	.56 (-.14, .83)	1.66	4.60
	VET	215±23	223±27	7.9±34.2	.17 (-1.15, .68)	31.16	86.35
	CTI	378±90	390±114	11.6±71.7	.86 (.64, .95)	26.64	73.82
	EF	81.97±8.09	84.54±6.75	2.6±8.7	.48 (-.35, .80)	6.27	17.37
	LCWi	16.17±3.79	15.32±3.03	-0.8±2.4	.86 (.64, .95)	0.89	2.48
Interval	HR	152±14*	148±14	-4.0±8.6	.89 (.86, .92)	2.83	7.83
	SV	117±26	112±21	-4.6±16.3	.87 (.83, .90)	5.90	16.35
	CO	17.66±3.75	16.47±2.99	-1.2±2.9	.79 (.72, .84)	1.34	3.72
	SVi	63.07±9.90	60.45±8.93	-2.6±8.2	.73 (.64, .80)	3.48	9.64
	CI	9.54±1.42	9.30±2.30	-0.2±2.2	.52 (.36, .64)	1.53	4.25
	VET	218±20	221±22	2.7±11.6	.61 (.48, .71)	7.23	20.03
	CTI	393±108	377±101	-15.6±65.6	.75 (.67, .811)	32.87	91.08
	EF	81.77±7.91	83.81±6.32	2.0±8.0	.51 (.35, .63)	5.59	15.50
	LCWi	14.70±3.73*	13.40±2.67	-1.3±2.5	.82 (.76, .86)	1.06	2.94

Note. SD: standard deviation; CV: coefficient of variation; ICC: intraclass correlation coefficient; CI: confidence interval; SEM: standard error of measurement; MDD: minimal detectable difference; HR: heart rate (bpm); SV: stroke volume (mL); CO: cardiac output ($L \cdot min^{-1}$); SVi: stroke volume index ($mL \cdot m^2$); CI: cardiac index ($L \cdot min^{-1} \cdot m^2$); VET: ventricular ejection time (ms); CTI: contractility index (AU); EF: ejection fraction (%); LCWi: left cardiac work index ($kg \cdot m^{-1} \cdot m^2$). *trial 1 greater than trial 2 ($p \leq .05$)

Table 2. Intrarater reliability and agreement of central diastolic function variables measured or calculated using PhysioFlow at rest, during steady-state cycling (50% and 70% peak power output) and interval cycling (90% peak power output)

		Trial 1 (mean±SD)	Trial 2 (mean±SD)	Difference	ICC (95% CI's)	SEM	MDD
Resting	EDV	123.98±32.40*	107.67±25.40	-16.3±26.3	.74 (.34, .90)	13.31	36.88
	EDFR	52.88±10.75	49.53±8.50	-3.3±12.0	.38 (-.62, .76)	9.49	26.29
50% steady-state	EDV	139.23±29.17*	129.29±30.25	-9.9±18.1	.90 (.73, .96)	5.78	16.02
	EDFR	58.39±10.26	58.48±7.43	0.1±9.3	.63 (.03, .86)	5.68	15.74
70% steady-state	EDV	140.17±29.75*	131.80±30.19	-8.4±15.0	.93 (.83, .97)	3.88	10.76
	EDFR	62.12±14.10	59.04±12.23	-3.1±18.4	.05 (-1.46, .64)	17.92	49.65
Interval	EDV	143±30.14*	134±29.23	-8.9±15.5	.91 (.88, .93)	4.62	12.82
	EDFR	65.05±9.28	65.48±9.18	0.4±7.4	.58 (.44, .68)	4.81	13.32

Note. SD: standard deviation; CV: coefficient of variation; ICC: intraclass correlation coefficient; CI: confidence interval; SEM: standard error of measurement; MDD: minimal detectable difference; EDV: end diastolic volume (mL); EDFR: early diastolic filling ratio (%). *trial 1 greater than trial 2 ($p \leq .05$)

Table 3. Intrarater reliability and agreement of peripheral vascular function variables calculated using PhysioFlow at rest, during steady-state cycling (50% and 70% peak power output) and interval cycling

		Trial 1 (mean±SD)	Trial 2 (mean±SD)	Difference	ICC (95% CI's)	SEM	MDD
Resting	SVR	1182±295	1137±142	-45.5±262.6	.53 (-.23, .82)	181	502
	SVRi	2083±530	2069±379	-13.7±655.1	-.02 (-1.65, .61)	648	1795
50% steady-state	SVR	552±87	552±97	-0.1±78.0	.78 (.43, .92)	37	101
	SVRi	969±177	997±215	27.4±218.6	.56 (-.16, .83)	146	404
70% steady-state	SVR	460±62	470±81	10.0±67.6	.72 (.26, .89)	36	100
	SVRi	810±139	852±180	42.0±198.2	.39 (-.59, .77)	155	429
Interval	SVR	539±128	555±99	16.3±140.6	.40 (.19, .54)	110	304
	SVRi	906±164	979±186	72.9±246.5	.46 (.28, .60)	181	502

Note. SD: standard deviation; CV: coefficient of variation; ICC: intraclass correlation coefficient; CI: confidence interval; SEM: standard error of measurement; MDD: minimal detectable difference; SVR: systemic vascular resistance ($Dyn \cdot s^{-1} \cdot cm^5$); SVRi: systemic vascular resistance index ($Dyn \cdot s^{-1} \cdot cm^5 \cdot m^2$).

during exercise (Fletcher, et al., 2001). Our findings indicate a good level of reliability (ICC>.75) for these variables, as assessed using the PhysioFlow, at rest and during submaximal steady-state exercise (Table 1). The level of reliability reported in this study is consistent with the previous PhysioFlow research (Schultz, et al., 2012; Welsman, et al., 2005), which has demonstrated good reliability for SV (ICC=.88) and CO (ICC=.86) measured at peak oxygen consumption during a graded exercise test (Welsman, et al., 2005), as well as good reliability for HR, SV and CO when measured at three submaximal steady-state exercise workloads (40 W, 60% HRmax and 70% HRmax) (Schultz, et al., 2012). The use of high-intensity interval exercise is a common technique to increase health and fitness in young (Rakobowchuk, et al., 2008), aging (Knowles, Herbert, Easton, Sculthorpe, & Grace, 2015) and chronic diseased populations (Wisloff, et al., 2007). Extending on previous works (Schultz, et al., 2012; Welsman, et al., 2005), we observed a good level of reliability for HR (ICC=.89), SV (ICC=.87) and CO (ICC=.79) during high-intensity interval exercise. The use of 30-second efforts in this study did not allow for a physiological steady-state, suggesting that the PhysioFlow is capable of obtaining reliable measures of HR, SV and CO in both steady-state and dynamic exercise conditions.

In addition to HR, SV and CO, the PhysioFlow provides additional central systolic variables, namely CI, SVi, VET, CTI, EF and LCWi (Table 1). Interestingly, only LCWi demonstrated good reliability across conditions. The use of LCWi as measured by bioimpedance cardiography has been shown to distinguish between levels of left ventricular dysfunction during a dobutamine stress test (Leitman, et al., 2006) and increases in LCWi are consistent with aerobic exercise training (Jakovljevic, et al., 2010). These data demonstrate the clinical utility of measuring LCWi and, in context of our reliability data, suggest this measure would be valuable in future research investigating the acute and chronic responses of LCWi during exercise. In contrast, the measurement of EF by bioimpedance cardiography is presented as a time- and cost-efficient alternative to echocardiography in a clinical setting (Parrott, Burnham, Quale, & Lewis, 2004); however, our results indicate this measure is unreliable. Our findings are not consistent with previous work (Schultz, et al., 2012) in which a good level of reliability (ICC=.92 to .97) was observed for the measure of EF using the PhysioFlow at three submaximal steady-state intensities. In the present study, measures of EF (Table 1) were greater than those reported by Schultz et al. (2012); thus, it is possible that the PhysioFlow can provide reliable measures of EF under a certain threshold (e.g., 61%) and become less reliable at higher values possibly due to changes in sensitivity of determining VET and PEP at higher heart rates. Irrespective, previous studies have observed equivocal results regarding the validity of EF estimated by bioimpedance cardiography devices (Miles, et al., 1990; van der Meer, et al., 1996). Taken together, these data warrant caution when considering using this measure.

It is important to note that while previous research has compared CI, SVi, VET and CTI between conditions or individuals, the results of the present study provide further insight into the confidence of these findings. For instance, Vella et al. (2011) observed 1.1 $L \cdot min^{-1} \cdot m^2$ higher CI (measured by PhysioFlow) in obese compared with non-obese adults during steady-state cycle exercise at 65% peak aerobic capacity suggesting excess body mass is associated with increased cardiac stress during moderate intensity exercise. However, the MDD of CI at 50-70% of peak power output within the present study (3.61-4.60 $L \cdot min^{-1} \cdot m^2$; Table 1) indicates this may not be a meaningful difference. Further, Boutcher et al. (2003) demonstrated greater CI and SVi at rest and in response to exercise in trained men compared with untrained and sedentary men. VET has been inversely correlated with aortic pulse wave velocity and thus arterial stiff-

ness (Salvi, et al., 2013) and positively correlated with pressure gradients in aortic stenosis (Kadem, et al., 2002). The 134.6 lower resting CTI in obese compared with non-obese adults observed by Vella et al. (2012), is greater than the MDD reported in the current study (126.9), supporting the conclusion that obese individuals do, indeed, have significantly lower cardiac contractility than non-obese individuals.

Central diastolic function

Resting and exercise EDV is greater in competitive compared with non-competitive runners (Crawford, Petru, & Rabinowitz, 1985) as well as following exercise training interventions (Esfandiari, Sasson, & Goodman, 2014). Our data demonstrate that the PhysioFlow can reliably estimate EDV at rest and during steady-state and interval exercise (Table 2) corroborating and expanding on data from Schultz et al. (2012). Nevertheless, caution should be exercised when using this device to estimate EDV within certain situations. For instance, our data indicate the PhysioFlow is capable of detecting differences in resting EDV (43 mL) between competitive and non-competitive runners (Crawford, Petru, & Rabinowitz, 1985) as they are beyond the calculated MDD at rest (Table 2; 36.88 mL); however, changes in submaximal EDV (12 mL) reported after a short-term high-intensity interval training program (Esfandiari, Sasson, & Goodman, 2014) are likely too small (MDD = 16.02 mL) to be considered a true effect when using this device. Bioimpedance-derived EDFR is analogous with the Doppler echocardiography-derived E/A ratio, a measure of diastolic function dependent on preload (Pickett & Buell, 1993). Indeed, E/A ratio is inversely correlated with age, blood pressure and aerobic capacity (Missault, et al., 1993). Given diastolic function is multifactorial (Little & Downes, 1990), it is unlikely this measure alone is of any clinical relevance; however, when combined with Doppler echocardiography, it may provide useful information regarding central diastolic function (Pickett & Buell, 1993).

Peripheral vascular function

Systemic vascular resistance and SVRi estimated by bioimpedance cardiography have been used to assess cardiovascular responses to various physiological stimuli (Bogaard, et al., 1997; Freimark, et al., 2007; Ouzounian, Masaki, Abboud, & Greenspoon, 1996; Tahvanainen, et al., 2011; Tahvanainen, Leskinen, Koskela, Ilveskoski, Alanko, et al., 2009; Tahvanainen, Leskinen, Koskela, Ilveskoski, Nordhausen, et al., 2009). Although demonstrating the clinical utility of measuring SVR and SVRi, these studies did not use the PhysioFlow device. Our results demonstrate that SVRi is temporally unreliable at rest and during exercise, while SVR demonstrated moderate to good reliability during steady-state exercise and suboptimal reliability at rest and during high-intensity interval exercise (Table 3). Our results are comparable with those reported by Schultz et al. (2012) who demonstrated moderate to good reliability of SVR during steady-state exercise. Consequently, researchers and clinicians should acknowledge this limitation when considering the use of these variables. It should be noted that the participants in the current study were healthy and had normal BMI. It is possible that the findings outlined in this study are not representative of other populations, such as overweight and obese. However, haemodynamic changes assessed by bioimpedance cardiography have previously been validated in obese individuals (Brown, et al., 2005; Richard, et al., 2001), patients with chronic obstructive pulmonary disease and hyperinflation (Bougault, et al., 2005), and pregnant populations (San-Frutos, et al., 2011), suggesting bioimpedance cardiography can be used across various body habitus.

Our results indicate that HR, SV, CO, LCWi and EDV demonstrated a level of reliability acceptable for use regardless of exercise type (continuous vs. interval) or intensity (low, moderate or high). Careful consideration should be given to the use of all other variables. Minimal detectable differences for all variables during rest and exercise were also provided to demonstrate the sensitivity of the PhysioFlow device.

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Acknowledgements

The authors thank all the participants for their time and effort dedicated to this study. No external funding was received for this study.

Conflicts of interest

The authors have no conflicts of interest.