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Non-invasive assessment of hemodynamics: a comparative analysis of fingertip pulse contour analysis and impedance cardiography

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Abstract

Objective—Systemic hemodynamic assessment is useful for characterizing the underlying physiology of hypertension, selecting individualized treatment approaches, and understanding the underlying mechanisms of action of interventions. Invasive methods are not suitable for routine clinic or research use, and non-invasive methods such as impedance cardiography have technical and practical limitations. Fingertip pulse contour analysis measured with the Nexfin device is a novel alternative for non-invasive assessment of blood pressure and hemodynamics. While both impedance cardiography and the Nexfin have been validated against invasive methods, the extent to which they correlate with each other is unknown. This study is a comparative analysis of data simultaneously obtained with impedance cardiography and the Nexfin device.

Methods—As part of a larger clinical trial, 13 adults with type 2 diabetes completed cardiovascular reactivity testing on three occasions: at study baseline and after two 4-week dietary treatment periods. Blood pressure, hemodynamics, and heart rate variability were assessed at rest and during acute mental stress.

Results—Blood pressure, heart rate, and heart rate variability data were significantly correlated between the two devices, but hemodynamic data (stroke volume, cardiac output, total peripheral resistance) were not significantly correlated. Both techniques detected treatment-related changes in blood pressure and total peripheral resistance, but significantly differed in magnitude and/or direction of the treatment effects.

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Conclusions—We conclude that Nexfin is not an appropriate alternative to impedance cardiography for measurement of underlying hemodynamics in psychophysiological research, but may be useful for beat-to-beat monitoring of blood pressure and heart rate variability.

Keywords

blood pressure; systemic hemodynamics; heart rate variability; impedance cardiography; pulse contour analysis

Introduction

Hypertension affects 40% of adults 25 years and older worldwide and is responsible for approximately 50% of heart and stroke deaths annually [1]. One of the challenges to achieving blood pressure control is identifying the unique physiologic phenomenon underlying hypertension in each individual and tailoring treatment recommendations accordingly. A recent meta-analysis concluded that such an approach can double rates of blood pressure control [2], but technical limitations have prevented widespread assessment of the hemodynamic profile. Invasive methods are not without risk and not suitable for routine use, whereas non-invasive methods can be difficult to perform. The primary non-invasive method for measuring hemodynamics in psychophysiological research is impedance cardiography, which uses a tetrapolar band configuration with spot electrocardiogram electrodes to estimate thoracic impedance and estimate cardiac output (heart rate $\times$ stroke volume, converted to l/min) and total peripheral resistance (mean arterial pressure / cardiac output $\times$ 80, converted to dynes/cm⁵) [3]. However, impedance cardiography requires an involved setup due to the specificity of the band electrode placement, is sensitive to movement, and requires post-acquisition processing to obtain total peripheral resistance estimates. A novel alternative to impedance cardiography is the Nexfin device (formerly Finapres; BMEYE, Amsterdam, The Netherlands), which estimates stroke volume by measuring arterial pulse pressure oscillations with a single inflatable finger cuff [4–6]. This technology has been validated against both invasive [7–12] and non-invasive [13–16] measures in a variety of populations. Compared to impedance cardiography, it is simple to apply, easier to use in both clinical and research settings, and does not require off-line processing. An important strength of the Nexfin device is that it calculates stroke volume and other hemodynamic measures on a beat-to-beat basis (rather than averaging hemodynamic data over a minute-by-minute basis like impedance cardiography). This is particularly useful in research settings where acute shifts in hemodynamics (such as cardiovascular reactivity studies) are of special interest. However, before Nexfin can be widely used as an alternative to impedance cardiography in psychophysiological research, it is important to understand how it performs in a side-by-side comparison with impedance cardiography.

Therefore, the purpose of this study was to conduct a comparative analysis of blood pressure and systemic hemodynamics simultaneously assessed with the impedance cardiography technique and the Nexfin device. Using data collected as part of a larger clinical trial, we compared the techniques on absolute hemodynamics and change during acute mental stress at the study baseline, as well as treatment-related changes observed throughout the study.

Both devices can collect inter-beat interval data for assessment of heart rate variability, which reflects autonomic control of the heart and is an independent predictor of cardiovascular disease [17–19]; therefore, we also compared heart rate variability for each technique. We hypothesized that data obtained from both techniques would be significantly correlated and treatment-related changes would be the same.

Methods

Data were collected from a study comparing a low-fat control diet to a moderate-fat diet containing pistachios on cardiovascular risk factors in adults with type 2 diabetes [20]. All data were collected at the Clinical Research Center at The Pennsylvania State University between July 2009 and March 2013. Written informed consent was obtained from all participants, and approval for the study was granted by the Institutional Review Board of The Pennsylvania State University. This study was registered at ClinicalTrials.gov (NCT00956735).

Participants

Eligibility and enrollment for the present study has been described in detail previously [20]. Briefly, we recruited adults with type 2 diabetes aged 30–75 years (women were post-menopausal) with a body mass index of 18.5–45.0 kg/m² and blood pressure < 160/100 mmHg. Exclusion criteria included self-reported history of chronic disease other than type 2 diabetes and anti-hypertensive medication use. Thirty participants (50% female) completed the full study, though data for the present analysis were available from only 13 participants (54% female, mean age 54.8 + 6.9 years), as the Nexfin technique was added to the protocol partway through the study. Baseline characteristics of these 13 participants are presented in Table 1.

Protocol

As part of the larger clinical trial, participants completed a randomized, crossover, controlled-feeding protocol with one 2-week baseline period and two 4-week treatment periods. The dietary intervention has been described in detail previously [20]; the nutrient composition of the study diets is summarized in Table 2. At the end of each diet period (including the baseline run-in period), blood pressure, systemic hemodynamics, and heart rate variability were assessed in a seated position during an acute mental stress testing session that included a 20-minute baseline rest period, a 5-minute math task (the Paced Auditory Serial Addition Task, [21]) and a 10-minute recovery period. Physiologic data was assessed simultaneously by impedance cardiography and the Nexfin device (Nexfin, BMEYE B.V., Amsterdam, The Netherlands). For impedance cardiography, a tetrapolar band configuration with spot electrocardiogram electrodes was used to estimate heart rate and stroke volume at 1–2 minute intervals (depending on task) during the stress protocol (Hutcheson Impedance Cardiograph and the Cardiac Output Program, Bio-Impedance Technology, Inc., Chapel Hill, NC). Systolic and diastolic blood pressures were obtained at the same time as the heart rate and stroke volume measurements with an automatic oscillometric blood pressure monitor attached to the left arm (Dinamap, Critikon Pro 100, GE Medical Systems). Cardiac output and total peripheral resistance were calculated

according to standard formulae [22]. The Nexfin finger cuff was placed between the two knuckles on the third finger of the participant's right hand and kept at heart level throughout the testing. Electrocardiogram data (interbeat or R-R intervals) were collected by both the spot electrodes and the Nexfin device. Data from both techniques were input to commercial software (Nevrokard, Medistar Inc.), and time-domain and frequency-domain measures of HRV (using autoregressive spectra) were calculated using standard methods [23]. Measures of HRV included the square root of the mean squared differences of successive R-R intervals (RMSSD, ms), high frequency power (ms^2), low frequency power (ms^2), the ratio of low to high frequency (low divided by high; L/H), and total power (ms^2). RMSSD and high frequency power are thought to reflect vagal modulation of heart rate, whereas low frequency power and the ratio of low to high frequency power are believed to reflect a complex interplay of sympathetic and parasympathetic influences (54).

Statistical Analyses

Data from the stress session were averaged for analysis in the following way: baseline data were an average of the final 3 minutes of the 20-minute baseline period, math task data are an average of the full 5 minutes of the 5-minute math task, and the recovery data are an average of the final 6 minutes of the 10-minute recovery period. Data were also combined across conditions to provide an overall average for the stress session.

All analyses were conducted using the Statistical Analysis Software (SAS v 9.3, Cary, NC, USA). Data were tested for normality and a natural log transformation was applied when necessary; raw (non-logged) values are presented in tabular format. Change scores were calculated to reflect stress reactivity (math minus baseline) and treatment effects (control minus run-in, pistachio minus run-in). The primary analysis used the Spearman correlation procedure to determine the association between the two methods in baseline, math, and reactivity data. The secondary analysis used the mixed models procedure to test for treatment effects for each method. Diet, diet period (first or second), task (baseline rest, math, recovery), and their interactions were entered as fixed effects; subject was a random effect. All mixed models analyses were also adjusted for age, sex, and BMI. For all analyses, an alpha of < 0.05 was considered statistically significant. Tables reflect adjusted means $\pm$ standard errors.

Results

Means and standard errors obtained with both techniques during the baseline rest, math task, and the stress reactivity (math – baseline) of the run-in diet period are presented in Table 3. Both techniques recorded increases in blood pressure, heart rate, stroke volume, and cardiac output during the stress task. Compared to baseline rest, total peripheral resistance increased during the math task when estimated by the Nexfin and decreased when estimated by impedance cardiography. Both techniques recorded decreases in heart rate variability during stress compared to baseline in all variables except L/H frequency. Absolute levels and reactivity scores of blood pressure (systolic, diastolic, mean arterial), heart rate, and all measures of heart rate variability were significantly correlated between the two methods (Spearman r range of 0.56 – 0.99, all $p < 0.05$; Table 3). Absolute levels and reactivity scores

for stroke volume, cardiac output, and total peripheral resistance were not significantly correlated (Spearman r range of 0.02 – 0.52, all $p>0.05$).

Effects of the study treatment diets on average blood pressure, hemodynamics, and heart rate variability during the stress testing session are presented in Table 4. Statistically significant treatment effects were observed with both methods for diastolic blood pressure (impedance cardiography $p<0.05$; Nexfin $p<0.05$) and mean arterial pressure (impedance cardiography: $p<0.05$; Nexfin: $p<0.05$). However, when measured with automated oscillometric device as part of the impedance cardiography technique, blood pressure was reduced to a significantly greater extent following the Pistachio diet than the Control diet (diastolic: -2.5 mmHg vs -0.7 mmHg, respectively, $p<0.05$; mean arterial: -3.2 mmHg vs -1.3 mmHg, respectively, $p<0.05$), and when measured with the Nexfin, blood pressure was reduced to a significantly greater extent following the Control diet than the Pistachio diet (diastolic: -2.0 mmHg vs 0.6 mmHg, respectively, $p<0.05$; mean arterial: -3.3 mmHg vs -0.1 mmHg, respectively, $p<0.05$). Similarly, treatment effects on total peripheral resistance differed in direction between the two devices. When measured via impedance cardiography, total peripheral resistance decreased following the Pistachio diet and increased following the Control diet ($p<0.001$). When measured via Nexfin, total peripheral resistance tended to increase following the Pistachio diet and decrease following the Control diet ($p=0.07$). No treatment effects were observed with either method for systolic blood pressure, heart rate, stroke volume, cardiac output, or any measures of heart rate variability.

Discussion

We have shown that impedance cardiography and fingertip pulse contour analysis (Nexfin) provide similar measurements of blood pressure, heart rate, and heart rate variability but not underlying hemodynamics (stroke volume, cardiac output, and total peripheral resistance). Additionally, the two techniques identified opposing effects of the nutrition treatments. Based on these results, we conclude that Nexfin and impedance cardiography are not interchangeable in the measurement of underlying systemic hemodynamics and that further research is needed to determine whether the Nexfin device can accurately detect shifts in the hemodynamics profile.

With regard to absolute levels, estimates of blood pressure obtained via Nexfin were generally higher (by approximately 4–13%) than those obtained with the external automated oscillometric monitor as part of the impedance cardiography technique. This could partially be due to the difference in measurement site, as the Nexfin obtained measurements from the fingertip while the automated blood pressure device obtained measurements from the brachial artery. We attempted to minimize this difference by keeping the fingertip at heart level (and therefore, the same level as the brachial artery measurement site); however, differences in absolute levels between the techniques will exist solely because of difference in measurement site [24]. Systolic, diastolic, and mean arterial pressure from both methods were significantly correlated under resting and mental stress conditions (with the exception of diastolic blood pressure at rest, which showed a trend for statistical significance at $p=0.08$). Importantly, reactivity data were strongly and significantly correlated, indicating that the Nexfin can accurately track changes in blood pressure even though the absolute

levels did not match those obtained via validated oscillometric monitors. On average, compared to impedance cardiography, the Nexfin provided higher estimates of stroke volume and cardiac output (by approximately 13%) and lower estimates of total peripheral resistance (by approximately 8%). Moreover, hemodynamic absolute levels and reactivity data were not significantly correlated with those obtained via impedance cardiography. The discrepancy between these two techniques is likely due to differences in how each calculates hemodynamic variables from measured data. Impedance cardiography *measures* actual electrical thoracic impedance across the cardiac cycle to estimate stroke volume, whereas the Nexfin measures fingertip pulse pressure oscillations and *estimates* stroke volume from derived intra-arterial pressure waveforms. While only direct three-way comparisons of the gold standard invasive method with impedance cardiography and Nexfin will clarify this point, we believe that direct measurement of thoracic impedance produces a more valid estimate of stroke volume than one derived from a more “downstream” assessment of arterial waveforms.

As part of the larger clinical trial, we assessed shifts in blood pressure, hemodynamics, and heart rate variability in response to dietary interventions. Both methods detected treatment-related changes in blood pressure and total peripheral resistance, but the magnitude and/or direction of the changes following the two study treatments differed by technique. Larger reductions in blood pressure were observed after the Pistachio diet with impedance cardiography and after the Control diet with the Nexfin. Total peripheral resistance decreased after the Pistachio diet and increased after the Control diet when measured via impedance cardiography, but increased after the Pistachio diet and decreased after the Control diet when measured via Nexfin. As stated above, we think it probable that impedance cardiography is the better estimate of the true treatment effect, but clearly further research is needed to determine the comparative ability of each technique to detect shifts in hemodynamics due to treatments, particularly in protocols that include the gold-standard invasive methods of measuring hemodynamics.

In contrast to the blood pressure and hemodynamic data, heart rate variability measurements were very similar between the two techniques, indicated by statistically significant Spearman correlation coefficients of 0.64 – 0.99. Compared to estimating stroke volume, it is relatively simple to measure heart rate, whether by electrocardiogram or pulse pressure oscillations. Both devices collect inter-beat interval data at a sampling frequency of 1000 Hz, which is then processed offline in specialized software using identical procedures. A notable strength of the Nexfin in collecting heart rate variability data is that it is not as sensitive to movement as impedance cardiography and therefore less data is lost due to technical difficulties. Studies in which heart rate variability is a primary outcome would benefit from using Nexfin over impedance cardiography for data collection.

Limitations of our study must be noted. First, the sample size was small and consisted only of adults with type 2 diabetes. Macro- and microvascular complications are common in diabetes and may have affected our results, particularly since impedance cardiography and the Nexfin collect data from different vascular beds. We believe this limitation is minimized because the participants were early in the progression of diabetes, free from any complications of diabetes (such as neuropathy), and served as their own controls in the

statistical analysis. Regardless, future research should compare the two techniques in a larger sample of healthy adults to increase validity and generalizability. We did not compare either technique to the invasive methods that are considered gold standards in assessing stroke volume, such as pulmonary artery catheterization with thermodilution, and therefore cannot comment on their relative validity. However, these non-invasive methods are more commonly used in psychophysiological research than invasive methods, and our comparative analysis demonstrates that researchers should use caution when comparing results from each technique across studies.

Conclusion

We have shown that the impedance cardiography and fingertip pulse contour analysis (Nexfin) techniques similarly estimate blood pressure, heart rate, and heart rate variability but not stroke volume, cardiac output, or total peripheral resistance. While both techniques have been validated against invasive methods of measuring stroke volume and cardiac output, there have been many more such studies with respect to impedance cardiography compared with fingertip pulse contour analysis. Furthermore, only impedance cardiography has shown clinical utility by significantly improving treatment success rates when used to tailor hypertension therapies [2]. Last, while impedance cardiography estimates stroke volume from directly measured thoracic impedance, the Nexfin uses a more distal method to assess pressure waveforms and estimate stroke volume. Thus we recommend that psychophysiological researchers and clinicians continue using impedance cardiography for non-invasive assessment of systemic hemodynamics, and that further validation studies be conducted with the Nexfin against invasive and non-invasive methods in both static and dynamic situations to determine the true clinical and research utility of this novel technique.

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Table 1

Baseline characteristics of the participants.

	Mean $\pm$ SE
Female (%)	53.8
Age (years)	54.8 $\pm$ 1.9
Body mass index (kg m ⁻²)	31.5 $\pm$ 1.8
Resting systolic blood pressure (mmHg)	115.6 $\pm$ 4.6
Resting diastolic blood pressure (mmHg)	72.1 $\pm$ 1.5
Fasting glucose (mmol/L)	106.5 $\pm$ 4.6
Glycated hemoglobin (%)	6.1 $\pm$ 0.1
Total cholesterol (mmol/L)	178.3 $\pm$ 10.0
LDL cholesterol (mmol/L)	111.1 $\pm$ 9.0
HDL cholesterol (mmol/L)	44.6 $\pm$ 3.2
Triglycerides (mmol/L)	128.5 $\pm$ 15.2
Taking diabetes medication(s) (%)	76.9
Taking statin therapy (%)	30.8

Table 2

Nutrient composition of the study diets.

	Run-In	Control	Pistachio
Energy (kcal)	2100	2100	2100
Total fat (g) (%)	85.6 (35.8)	64.0 (26.9)	78.5 (33.2)
Saturated fat (g) (%)	27.5 (11.5)	16.0 (6.7)	15.9 (6.8)
Monounsaturated fat (g) (%)	31.3 (13.1)	26.0 (10.9)	31.2 (13.1)
Polysaturated fat (g) (%)	20.2 (8.4)	16.8 (7.1)	24.6 (10.4)
Protein (g) (%)	85.0 (16.0)	95.6 (18.1)	88.5 (16.6)
Carbohydrate (g) (%)	261.5 (48.2)	302.8 (55.1)	270.6 (50.7)
Fiber (g)	23.4	31.2	35.6
Sodium (mg)	3791	3039	2553
Potassium (mg)	2338	3767	4045
Cholesterol (mg)	278	186	172

Table 3

Impedance cardiography and Nexfin data after the study run-in period.

	Condition	COP Mean $\pm$ SE	Nexfin Mean $\pm$ SE	Mean Difference (Nexfin – COP) Mean $\pm$ SE	Spearman <i>r</i>
Systolic blood pressure (mmHg)	Baseline	115.6 $\pm$ 4.6	127.9 $\pm$ 5.3	12.3 $\pm$ 4.1	0.61 [*]
	Math	132.2 $\pm$ 6.8	146.3 $\pm$ 6.7	14.1 $\pm$ 4.3	0.90 ^{***}
Diastolic blood pressure (mmHg)	Change	16.6 $\pm$ 4.3	18.4 $\pm$ 3.7	14.4 $\pm$ 2.2	0.86 ^{***}
	Baseline	72.1 $\pm$ 1.5	74.8 $\pm$ 2.0	2.7 $\pm$ 1.7	0.50
Mean arterial pressure (mmHg)	Math	78.0 $\pm$ 2.1	84.3 $\pm$ 2.6	6.3 $\pm$ 2.0	0.79 ^{**}
	Change	5.9 $\pm$ 1.4	9.5 $\pm$ 1.4	5.4 $\pm$ 1.1	0.61 [*]
Heart rate (bpm)	Baseline	86.7 $\pm$ 2.4	94.7 $\pm$ 3.2	8.0 $\pm$ 2.5	0.56 [*]
	Math	96.1 $\pm$ 3.5	108.1 $\pm$ 4.1	12.1 $\pm$ 2.7	0.79 ^{**}
Stroke volume (ml/beat)	Change	9.4 $\pm$ 2.1	13.5 $\pm$ 2.3	11.0 $\pm$ 1.5	0.74 ^{**}
	Baseline	65.9 $\pm$ 1.7	66.6 $\pm$ 1.7	0.7 $\pm$ 0.2	0.98 ^{***}
Cardiac output (l/min)	Math	73.4 $\pm$ 2.3	73.4 $\pm$ 2.2	0.0 $\pm$ 0.3	0.95 ^{***}
	Change	7.5 $\pm$ 1.4	6.9 $\pm$ 1.3	0.4 $\pm$ 0.2	0.86 ^{***}
Total peripheral resistance (dyne-s/cm ⁵)	Baseline	72.1 $\pm$ 5.2	81.3 $\pm$ 3.5	9.1 $\pm$ 6.8	-0.17
	Math	73.7 $\pm$ 6.8	82.2 $\pm$ 3.9	10.1 $\pm$ 7.3	0.05
RMSSD (ms)	Change	1.5 $\pm$ 3.0	0.9 $\pm$ 1.9	9.8 $\pm$ 4.0	-0.03
	Baseline	4.7 $\pm$ 0.3	5.4 $\pm$ 0.3	0.7 $\pm$ 0.4	0.02
High frequency HRV (ms ²)	Math	5.4 $\pm$ 0.5	6.0 $\pm$ 0.3	0.7 $\pm$ 0.5	0.52
	Change	0.7 $\pm$ 0.3	0.6 $\pm$ 0.2	0.7 $\pm$ 0.3	0.38
RMSSD (ms)	Baseline	1586.3 $\pm$ 171.6	1447.3 $\pm$ 73.2	-139.0 $\pm$ 180.1	0.31
	Math	1573.4 $\pm$ 198.1	1501.9 $\pm$ 76.5	-103.4 $\pm$ 202.2	0.24
High frequency HRV (ms ²)	Change	-18.0 $\pm$ 53.3	54.5 $\pm$ 37.4	-104.0 $\pm$ 104.7	0.05
	Baseline	25.5 $\pm$ 3.5	32.5 $\pm$ 5.4	2.5 $\pm$ 0.5	0.99 ^{***}
High frequency HRV (ms ²)	Math	21.3 $\pm$ 2.5	25.5 $\pm$ 2.5	2.9 $\pm$ 0.9	0.84 ^{***}
	Change	-4.2 $\pm$ 1.6	-6.9 $\pm$ 3.4	3.3 $\pm$ 0.4	0.84 ^{***}
High frequency HRV (ms ²)	Baseline	265.7 $\pm$ 82.4	468.1 $\pm$ 165.0	58.0 $\pm$ 9.2	0.96 ^{***}

	Condition	COP Mean $\pm$ SE	Nexfin Mean $\pm$ SE	Mean Difference (Nexfin – COP) Mean $\pm$ SE	Spearman <i>r</i>
Low frequency HRV (ms ²)	Math	160.3 $\pm$ 41.4	240.2 $\pm$ 46.1	62.7 $\pm$ 10.5	0.94***
	Change	-105.4 $\pm$ 44.7	-227.9 $\pm$ 134.8	70.5 $\pm$ 8.2	0.92***
	Baseline	653.6 $\pm$ 247.5	601.3 $\pm$ 173.1	-79.6 $\pm$ 72.9	0.96***
	Math	410.6 $\pm$ 148.3	431.4 $\pm$ 135.2	27.4 $\pm$ 25.8	0.98***
	Change	-242.9 $\pm$ 169.3	-169.9 $\pm$ 120.2	-14.4 $\pm$ 27.9	0.89***
	Baseline	2.5 $\pm$ 0.5	1.6 $\pm$ 0.3	-0.8 $\pm$ 0.3	0.64*
L/H frequency HRV (ms ²)	Math	2.6 $\pm$ 0.3	1.7 $\pm$ 0.2	-0.8 $\pm$ 0.2	0.66*
	Change	0.1 $\pm$ 0.5	0.2 $\pm$ 0.3	-0.8 $\pm$ 0.1	0.66*
	Baseline	1417.4 $\pm$ 461.4	1548.6 $\pm$ 415.6	-120.2 $\pm$ 122.4	0.94***
	Math	944.7 $\pm$ 259.0	1075.3 $\pm$ 248.0	129.6 $\pm$ 51.5	0.89***
Total power (ms ²)	Change	-472.7 $\pm$ 311.8	-473.2 $\pm$ 326.6	32.0 $\pm$ 50.7	0.90***

RMSSD = square root of the mean squared differences of successive R-R intervals; HRV = heart rate variability.

* p<0.05;

** p<0.01;

*** p<0.001

Table 4

Impedance cardiography and Nexfin data after each treatment period, averaged across the baseline rest, math task, and recovery period of the stress testing session.

	COP				Nexfin			
	Baseline Mean $\pm$ SE	Control Mean $\pm$ SE	Pistachio Mean $\pm$ SE	P-value	Baseline Mean $\pm$ SE	Control Mean $\pm$ SE	Pistachio Mean $\pm$ SE	P-value
Systolic blood pressure (mmHg)	121.4 $\pm$ 3.3	-2.4 $\pm$ 1.8	-4.6 $\pm$ 1.8	0.08	135.9 $\pm$ 3.4	-4.5 $\pm$ 4.6	-1.5 $\pm$ 4.6	0.19
Diastolic blood pressure (mmHg)	73.7 $\pm$ 1.1	-0.7 $\pm$ 1.0	-2.5 $\pm$ 1.0	0.018	79.1 $\pm$ 1.4	-2.0 $\pm$ 1.7	0.6 $\pm$ 1.7	0.014
Mean arterial pressure (mmHg)	89.6 $\pm$ 1.7	-1.3 $\pm$ 1.2	-3.2 $\pm$ 1.2	0.011	100.7 $\pm$ 2.1	-3.3 $\pm$ 2.6	-0.1 $\pm$ 2.6	0.030
Heart rate (bpm)	68.5 $\pm$ 1.3	0.2 $\pm$ 1.3	1.3 $\pm$ 1.3	0.20	68.8 $\pm$ 1.2	0.7 $\pm$ 1.3	1.5 $\pm$ 1.3	0.05
Stroke volume (ml/beat)	72.3 $\pm$ 3.3	-3.0 $\pm$ 2.2	-1.5 $\pm$ 2.2	0.26	81.5 $\pm$ 2.1	-1.4 $\pm$ 1.2	-2.8 $\pm$ 1.2	0.24
Cardiac output (l/min)	4.9 $\pm$ 0.2	-0.2 $\pm$ 0.1	0.0 $\pm$ 0.1	0.11	5.6 $\pm$ 0.2	-0.1 $\pm$ 0.1	-0.1 $\pm$ 0.1	0.96
Total peripheral resistance (dynes/cm ⁵)	1586.6 $\pm$ 99.3	86.6 $\pm$ 40.1	-39.2 $\pm$ 40.2	0.001	1492.9 $\pm$ 43.7	-15.6 $\pm$ 46.9	41.7 $\pm$ 46.9	0.07
RMSSD (ms)	23.5 $\pm$ 1.7	-0.4 $\pm$ 1.7	0.6 $\pm$ 1.7	0.49	30.1 $\pm$ 2.6	-1.9 $\pm$ 1.6	-0.1 $\pm$ 1.6	0.27
High frequency HRV (ms ²)	222.6 $\pm$ 37.2	-0.8 $\pm$ 34.3	-4.4 $\pm$ 34.5	0.92	386.2 $\pm$ 73.6	-100.8 $\pm$ 55.8	-40.9 $\pm$ 55.8	0.27
Low frequency HRV (ms ²)	493.9 $\pm$ 106.2	-56.8 $\pm$ 95.4	-11.6 $\pm$ 95.9	0.69	497.5 $\pm$ 84.1	1.1 $\pm$ 70.7	28.8 $\pm$ 70.6	0.78
Low:high frequency HRV (ms ²)	2.4 $\pm$ 0.2	0.3 $\pm$ 0.5	0.4 $\pm$ 0.5	0.53	1.5 $\pm$ 0.1	0.3 $\pm$ 0.2	0.4 $\pm$ 0.2	0.87
Total power (ms ²)	1168.1 $\pm$ 207.3	-14.8 $\pm$ 267.3	62.6 $\pm$ 269.2	0.63	1359.8 $\pm$ 203.0	-120.1 $\pm$ 133.5	-43.0 $\pm$ 133.5	0.68

RMSSD = square root of the mean squared differences of successive R-R intervals; HRV = heart rate variability.

P-value derived from the mixed models procedure comparing Control and Pistachio values for cardiovascular parameters.