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Title: Within day and between day reproducibility of baroreflex sensitivity in healthy adult males

Key words: Reliability; repeatability; sequence; spectral; supine; tilt

Abstract

Within day and between day reproducibility of supine and tilt baroreflex sensitivity was investigated utilising sequence and spectral indices in 46 healthy adult males employing three repeat measures; baseline, + 60 min and + 24 h. Reproducibility was assessed via the 95% limits of agreement and by the technical error of the measurement. For spectral parameters, the limits of agreement indicated same day was marginally better than between day reproducibility. For sequence parameters, between day had marginally better agreement than same day reproducibility. Tilt markedly improved reproducibility across all outcome measures. Precision expressed by the technical error of the measurement for all spectral outcomes was good in both supine and tilt baroreflex sensitivity (< 6 %). Precision was lower, but acceptable, for sequence baroreflex sensitivity outcomes in both positions (< 11%). Baroreflex sensitivity transfer gain provided the best agreement and reproducibility during supine and tilt conditions. These findings suggest time and spectral techniques may be employed to assess within day and between day baroreflex sensitivity changes in healthy individuals. The inclusion of a tilt manoeuvre may improve the reproducibility of the outcome measure which may aid in the detection of modest baroreflex sensitivity changes in studies employing limited sample sizes.

Introduction

Changes in baroreflex sensitivity (BRS) have been found to be of clinical value for diagnostic [15] and prognostic [20] purposes and ongoing clinical research supports a link between BRS and disease and health outcomes [27]. Diminished BRS appears to be linked to unfavourable health outcomes [8,17,35,37,38] while conversely, enhancements in BRS may be beneficial to cardiovascular health. One factor that appears to enhance BRS in some circumstances is exercise [6,23,44]. However, if findings are to be of practical use an understanding regarding the magnitude of error or level of variance present in the outcome measure is required as such error or level of variance is a component of the effect size [28,47]. A reproducibility study allows the exploration of the magnitude of error or level of variance providing a basis for future research testing [28].

Reproducibility may be determined on the same day and/ or following a specified period of time i.e., $\geq$ 24 h and should have reference to the repeated measures protocol to be incorporated in future research. The BRS assessment technique has been implicated in the variability of the BRS outcome measure [11,19,31] with improved reproducibility reported with low frequency (LF) BRS spectral techniques compared to high frequency (HF) BRS spectral techniques [31] during spontaneous breathing and, in some spectral techniques compared to sequence measures [11,19]. The posture position of the participant may also influence the reproducibility and variability of the measure with improved reproducibility reported during standing compared to measures achieved under supine resting conditions [14,19,25]. The improved reproducibility of spontaneous BRS in standing over the mid (1 wk) to long term (1 y) suggested small significant changes (3 or/to 5 ms/mmHg) could be detected

via small sample size (24 - 4 participants), in both the time and spectral domains in follow-up studies [19]. This may be an important finding because in some experimental studies it is only practically possible to recruit small participant numbers, and the previously reported significant changes in BRS following various interventions and events have been small [10,16,24,32,33,41].

Although the spontaneous non-invasive BRS techniques have been routinely employed for baroreflex testing, there are only a few studies that have assessed the absolute reproducibility of these techniques [11,12,19,25,29,31]. Absolute reproducibility provides information regarding the intraindividual variability of a measurement [31]. Limitations in BRS reproducibility studies have been reported [31] and include low sample size [11,19,25,29], limited choice of BRS technique [25] and lack of protocols for between day reproducibility [11,12,19,29]. In the one study which has included a large sample size, a wide selection of BRS parameters and a protocol for between day reproducibility, it did not include same day reproducibility or an orthostatic manoeuvre [31]. Different statistical techniques have also been employed to assess absolute reproducibility and include the coefficient of variation (CV) and the limits of agreement (LOA) [7]. The use of the correlation coefficient has been criticised [2,26] because it provides information regarding the degree of association between the measures and is unable to distinguish between different linear relationships [7,30]. Thus it is possible to have good correlation but a lack of agreement between the measures. The CV requires heteroscedasicity to be explored and quantified before assuming its presence and is considered to be a liberal measure as only 68% of the variability is described [2]. Sample heterogeneity and systematic bias are possible problems with regression analysis in reproducibility investigations

[2] and all of these techniques are reported in dimensionless ratios. The LOA plot overcomes these limitations, providing a schematic measurement of error utilising the bias (mean difference across subjects) and 95% limits of agreement (test-retest differences across 95% of population) and aids in identifying heteroscedasticity and skewness in the data [7]. Overall, reproducibility assessed via CV (%) ranged from 14 to 52% (11,12,25,29) and the measurement error in LOA (ms/mmHg) ranged from 8 to 26 ms/mmHg in supine BRS measures and 3 to 4 ms/mmHg in standing BRS measures (11,19). Spectral indices were markedly improved in BRS measures incorporating the LF component compared to those measures incorporating HF (11,29,31) with spectral BRS measures providing better reproducibility than time (sequence) BRS measures. A further statistical technique is the technical error of the measurement (TEM) which estimates the level of precision (or imprecision) associated with the measure i.e., the level of error of the method due to biological and technical factors (34]. The identification and quantification of TEM enhances the opportunity to find genuine change and contributes to a valid interpretation of the results following testing in future studies.

The present study included a large sample size, a range of BRS parameter selection and an orthostatic manoeuvre to comprehensively assess the same day and between day reproducibility of BRS in a healthy adult male population. Reproducibility was assessed via the LOA (actual unit of measure) to assess the level of agreement between the measures and by the TEM.

Methods

Participants

The forty six non-smoking healthy male participants (18 – 35 y) (table 1) who volunteered to participate had no history of diabetes, hypertension or cardiac disease, showed no signs of disease, were not taking medication and were undertaking regular exercise (moderate exercise 5 ± 2 $h \cdot wk^{-1}$). All participants completed health screening and subsequently provided informed consent. All procedures conformed to those approved and cleared by the University Research Ethics Committee and were in accordance with recognised ethical standards and national/ international laws [18].

******Table 1 near here**

Study Design

A test-retest reproducibility study of the procedure for assessment of BRS was conducted. Testing was undertaken in controlled laboratory conditions and across all tests (mean ± SD): air temperature 22.8 (± 1)°C; humidity 36 (± 9) %; barometric pressure 1009 (± 13) hPa. Each participant was required to visit the laboratory on three separate occasions. Visit 1 allowed determination of resting HR and brachial BP and familiarisation with equipment and testing procedures. During visits 2 and 3, data collection in supine and tilt positions was undertaken at baseline, + 60 min and + 24 h respectively. Participants were requested not to: drink alcohol 24 h before each test; not to drink caffeine on day of each test; not to eat 3 h before each test; not to drink 1 h before each test and, not to exercise 48 h before each test beyond normal daily activities. All participants confirmed that they had complied with the pretesting guidelines. Testing at baseline and + 24 h was scheduled at the same time of day to

avoid a circadian influence. During supine conditions, participants lay on a tilt bed (Model 501, Plinth 2000, Stowmarket, Suffolk, UK) in a horizontal position. The tilt manoeuvre employed a 60º upright tilt in accordance with consensus protocols [4,43]. All tilt manoeuvres followed supine data collection to ensure cardiovascular outcomes were not influenced prior to tilt conditions. Participant breathing was not controlled during testing procedures as consistently improved reproducibility has not been found following paced breathing, albeit $BRS_{\alpha HF}$ determination [12,31], and LF spectral analysis avoids most respiratory influence.

Data collection

Participants rested supine for 20 min before data collection. Continuous 10 min collections of R-R interval data and beat by beat BP data were undertaken while participants were in supine and tilt positions. A three lead ECG (Absolute Aliens Oy, Turku, Finland) was attached to the participants' chest and R-R interval measures were determined from the recorded ECG. The collection of beat-by-beat BP signal data was determined via finger servo-plethysmomanometry (Portapres Model-2, FMS, Finapres Medical Systems BV, Amsterdam, The Netherlands) with the hand kept at heart level throughout the measurement process. Full signal acquisition was achieved via the physiocal immediately prior to each supine and each tilt measurement.

Data analysis

The signal data were fed into an acquisition system (WinAcq, Absolute Aliens Oy, Turku, Finland) where the signals were interpolated and relayed to a laptop computer (Tecra S1, Toshiba, Finland) using a sampling rate of 800 Hz and stored for later analysis. The data were processed with dedicated software (WinCPRS, Absolute

Aliens Oy, Turku, Finland) and both time (BRS_{UpUp} and $BRS_{DownDown}$) and spectral ($BRS_{\alpha LF}$ and BRS_{TFTG}) analyses of BRS were undertaken. The WinCPRS software was utilised to calculate the moving average of the signal over the data range (0.05 s) for the BP data. The ECG data was filtered using a Butterworth low pass filter at 45 Hz to reduce noise and minimise any measurement error. R-R intervals were calculated from ECG signals and the data was visually inspected to identify and correct any irregular or missing R-R intervals. Three analysis techniques for BRS determination were employed; one technique in the time domain (sequence) and two techniques in the spectral domain (α coefficient and transfer gain) [5,13,22,25,36,37,39,40,45,48].

Statistical analysis

The reproducibility analyses were undertaken in Microsoft Excel using a scatter plot to display agreement and LOA employing the technique of Bland and Altman [7]. This technique is known to be affected by heteroscedastic data, so initially the relationship between the mean of the two repeat measures and the mean absolute difference of the two repeat measures was plotted and quantified (equation of line of best fit). Given the weak relationship and low slope, the bias and LOA were determined with the standard approach. The LOA plots provided a visual examination of the agreement between the measures; narrow confidence intervals (CI) suggested good agreement (lesser variability in the measure) while wide CI's suggested poor agreement (greater variability in the measure). An alternative approach of estimating the TEM to assess reproducibility was also undertaken in accordance with an accepted assessment protocol [34]. Criterion levels [3,34,46] for reproducibility (TEM) may be interpreted as good (≤ 6%), 'fair' (7 - 20%) or 'poor'

(> 20%) as measurement error for experimental testing purposes i.e., anthropometric assessment processes suggest a satisfactory level of precision for skinfold measurement is ≤ 5% while biomechanical investigations have reported precision levels of ≤ 20%. Sample size calculation for follow-up studies to detect a given change in tilt BRS was defined with the formula $n = 8s^2/d^2$, where n is the sample size, s is the typical error (95% CI) and d is the required meaningful change (Δ BRS) [21].

Results

Data for BRS outcome measures, bias, standard deviation, 95% LOA and CI's are provided in table 2, data for TEM are provided in table 3 and LOA plots are provided in figures 1 - 4. In general, same day reproducibility and between day reproducibility was similar i.e., supine (mean) BRS_{UpUp}: 30 ms/mmHg vs. 28 ms/mmHg and 10% vs 9% respectively (tables 2 and 3; figures 1 - 2). The bias (mean difference across subjects) was small (i.e., close to zero) for all BRS outcomes at all time points. Thus because there were no consistent differences between the first and second measurements, the data could be used to assess reproducibility. Overall, poorer agreement (i.e., lower reproducibility) and between subject heterogeneity was observed for parameters in supine position (7 – 30 ms/mmHg) (i.e., figures 1 and 3) compared to tilt position (3 – 5 ms/mmHg) (i.e., figures 4 - 5) with all BRS outcomes. In the supine position the sequence outcomes provided poorer agreement and heterogeneity (14 – 30 ms/mmHg) (i.e., figures 1) than the spectral outcomes (7 – 11 ms/mmHg) (i.e., figures 3). The adopted criteria suggested there was markedly better (good) agreement and reduced heterogeneity with all BRS outcomes in the tilt position (3 – 5 ms/mmHg) (table 2). In practice, to be confident of genuine change post-intervention, change must be greater than the measurement error. For example,

in this study population post-intervention change should be greater than 9 ms/mmHg in supine $BRS_{\alpha LF}$ and/ or greater than 4 ms/mmHg in tilt $BRS_{\alpha LF}$ (mean ± 95% LOA ms/mmHg). The findings of lesser variability in all BRS measures under tilt conditions suggest reproducibility was better following an orthostatic manoeuvre compared to resting supine BRS measures. The findings for TEM under the adopted criteria suggested precision for all spectral outcomes was good in both supine and tilt (< 6%) although precision was lower for the time (sequence) outcomes in both positions (4 – 10%) (table 3). Sample sizes for follow-up studies intended to detect given changes in BRS are provided in table 4.

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Discussion

The present study investigated the same day and between day reproducibility of the measurement of BRS in a healthy adult male population and the influence of a tilt manoeuvre on the reproducibility of BRS outcome measures. Key findings included minimal differences between same day reproducibility and between day

reproducibility and a marked improvement in reproducibility in all BRS outcome measures in the tilt position.

Same day reproducibility was assessed previously in two studies [11,29] and reproducibility over various time periods have included 24 h (between day) [25,31] and up to one year [12,19,29]. Although previous studies assessing reproducibility > 24 h were not directly applicable to the present study, they did provide additional evidence for the reproducibility of BRS and for the usefulness of an orthostatic manoeuvre during testing [19]. Differences between study procedures (i.e., sample size, BRS parameter selection, re-testing time lag and testing manoeuvres) did not allow direct comparison between studies however overall, the measurement error assessed via 95% LOA (ms/mmHg) ranged from 8 to 26 ms/mmHg in supine BRS measures [11,19] and 3 to 4 ms/mmHg in standing BRS measures [19]. The present study observed similar findings with 95% LOA ranging from 7 to 30 ms/mmHg in supine BRS measures and 3 to 5 ms/mmHg in tilt BRS measures. None of the previous studies had included an assessment of TEM which indicates the level of precision of the measure. The present study observed good precision for the spectral measures in supine (≤ 6%) and for all measures in tilt (≤ 5%) (table 3). Although same day reproducibility and between day reproducibility was similar, same day reproducibility was minimally better than between day reproducibility for the spectral parameters while between day reproducibility was minimally better than same day reproducibility for the sequence parameters (tables 2 and 3). This was an unexpectant finding and no explanation could be found for this result.

Sequence outcome measures had poorer reproducibility compared to spectral measures under supine conditions (i.e., figures 1 - 2; table 2) with 95% LOA ranging from 14 to 30 ms/mmHg compared to 7 to 11 ms/mmHg respectively. The greater magnitude and variability of the supine sequence measure may be attributed in part to two practical features; the influence of respiration on the measure and the lack of suitable sequences to achieve an accurate measure. Sequence BRS is determined over a wide frequency range including the HF domain (0.15 – 0.4 Hz), the frequency band which is synchronized with respiratory rate [9]. Thus sequence measures may be influenced by respiration because respiration affects the naturally occurring oscillations which modulate BP and HR [1]. However, when spectral BRS measures are undertaken in the LF domain only, respiratory influence is attenuated. Reproducibility of different spectral techniques was markedly reduced in BRS HF measures (under spontaneous breathing) compared to those measures incorporating LF only [11,29,31]. Therefore the findings in the present study are consistent with previous research i.e., as respiration was not controlled and LF only was employed for spectral measures, poorer reproducibility was found in sequence outcome measures compared to spectral measures. In conditions of low BP variability, only a few acceptable sequences may be obtained resulting in sequence BRS measures having limited accuracy [5,22,37,42]. The number of recognised sequences may be increased by a longer recording length but such action may have practical implications i.e., satisfaction of stationarity requirements for spectral analysis and the servo-adjustment (Physiocal) requirements of the Portapres over time [30] and an incompatibility with study design requirements where multiple short time measures are required. The achievement of greater BP variability and increased identifiable sequences may be induced by an imposed modification i.e., tilt. The present study found greater

identification of acceptable sequences under tilt conditions compared to supine conditions. These findings suggest the selection of the BRS technique may be an important consideration in research testing because the magnitude of the outcome measure for BRS may be highly variable under the same condition, in the same population and under the same testing environment [31]. Such variability may obscure the detection of genuine change and provide comparability issues between studies.

In the present study a marked improvement in reproducibility in all tilt BRS outcome measures was found (LOA 3 - 5 ms/mmHg; TEM < 2) (i.e., figures 4 - 5; tables 2 and 3) and may be due to a reduction of neural influences of internal and external stimuli on the sympthvagal balance, mitigating the variability in the measure [19,25]. These findings could have implications for future study design considerations [19] and the ability to find a significant effect, if such an effect is indeed present. This is because small participant numbers are often recruited for experimental research studies and modest significant changes in BRS (3 – 6 ms/mmHg) have been observed from natural [33,41] and imposed [32] events and interventions [10,16,24]. Sample size estimation (table 4) implies BRS changes (3 or/to 5 ms/mmHg) may be found utilising tilt BRS via small sample sizes (26 – 2 participants) in time and spectral domains. This suggests tilt BRS may offer the opportunity to detect meaningful changes in follow-up studies incorporating small participant numbers.

Limitations

Intra-participant control was achieved via testing guidelines although it was impossible to be sure participants followed the routine exactly. Participants were

healthy adult males (18 – 35 y) undertaking regular exercise thus the findings should be limited to this study population. Spontaneous respiration may have influenced sequence BRS determination by a greater extent than spectral BRS_{LF} and it was not possible to assess the extent of any respiratory influence.

Conclusion

The employment of a tilt manoeuvre markedly improved the reproducibility of both time and spectral BRS measures for both same day and between day reproducibility and overall the BRS_{TFTG} technique had the highest reproducibility under both supine and tilt conditions. The improvement in BRS reproducibility during tilt suggests the inclusion of the manoeuvre may be of benefit for future studies, especially where participant sample sizes are limited.

[1]Airaksinen KEJ, Tahvanainen KUO, Kuusela TA, Huikuri HV, Niemelä MJ, Karjalainen P, Eckberg DL. Cross spectral analysis in assessment of baroreflex gain in patients with coronary artery disease. Ann Noninvasive Electrocardiol 1997; 2: 229-235

[2]Atkinson G, Nevill AM. Statistical methods for assessing measurement error (reliability) in variables relevant to sports medicine. Sports Med 1998; 26: 217-238

[3]Ayala F, De Ste Croix M, Sainz de Baranda P, Santonja F. Absolute reliability of hamstring to quadriceps strength imbalance ratios calculated using peak torque, joint angle-specific torque and joint ROM-specific torque values. Int J Sports Med 2012; 33: 909-916

[4]Benditt DG, Ferguson DW, Grubb BP, Kapoor WN, Kugler J, Lerman BB, Maloney JD, Raviele A, Ross B, Sutton R, Wolk MJ, Wood DL. ACC Expert Consensus Document: Tilt table testing for assessing syncope. J Am Coll Cardiol 1996; 28: 263-275

[5]Bertinieri G, Di Rienzo M, Cavallazzi A, Ferrari AU, Pedotti A, Mancia G. Evaluation of baroreceptor reflex by blood pressure monitoring in unanesthetized cats. Am J Physiol Heart Circ Physiol 1988; 23: H377-H383

[6]Billman GE, Schwartz PJ, Stone HL. The effects of daily exercise on susceptibility to sudden cardiac death. Circulation 1984; 69: 1182-1189

[7]Bland JM, & Altman DG. Statistical methods for assessing agreement between two methods of clinical agreement. Lancet 1986; 1: 307-310

[8]Bristow D, Honour AJ, Pickering GW, Sleight P, Smyth HS (1969). Diminished baroreflex sensitivity in high blood pressure. Circulation 1969; 39: 48-54

[9]Cerutti S, Bianchi AM, Mainardi LT. Spectral analysis of the heart rate variability signal. In: Malik M, Camm AJ (eds). Heart rate variability. Armonk: Futura, 1995: 63-74

[10]Costes F, Roche F, Pichot V, Vergnon JM, Garet M, Barthelemy J-C. Influence of exercise training on cardiac baroreflex sensitivity in patients with COPD. Eur Respir J 2004; 23: 396-401

[11]Davies LC, Francis DP, Jurák P, Kára T, Piepoli M, Coats AJS. Reproducibility of methods for assessing baroreflex sensitivity in normal controls and in patients with chronic heart failure. Clin Sci 1999; 97: 515-522

[12]Dawson SL, Robinson TG, Youde JH, James MA, Martin A, Weston P, Panerai R, Potter JF. The reproducibility of cardiac baroreceptor activity assessed non-invasively by spectral and sequence techniques. Clin Auton Res 1997; 7: 279-284

[13]De Boer RW, Karemaker JM, Strackee J. Hemodynamic fluctuations and baroreflex sensitivity in humans: a beat-to-beat model. Am J Physiol Heart Circ Physiol 1987; 253: H680-H689

[14]Dietrich A, Rosmalen JGM, Althaus M, van Roon AM, Mulder LJM, Minderaa RB, Oldehinkel AJ, Riese H. Reproducibility of heart rate variability and baroreflex sensitivity measurements in children. Biol Psychol 2010; 85: 71-78.

[15]Frattola A, Parati G, Gamba P, Paleari F, Mauri G, Di Rienzo M, Castiglioni P, Mancia G. Time and frequency domain estimates of spontaneous baroreflex sensitivity provide early detection of autonomic dysfunction in diabetes mellitus. Diabetologia 1997; 40: 1470-1475

[16]Galbreath MM, Shibata S, Vangundy TB, Okazaki K, Fu Q, Levine BD. Effects of exercise training on arterial-cardiac baroreflex function in POTS. Clin Auton Res 2011; 21: 73-80

[17]Grassi G, Seravalle G, Cattaneo BM, Lanfranchi A, Vailati S, Giannattasio C, Del Bo A, Sala C, Bolla GB, Pozzi M, Mancia G. Sympathetic activation and loss of reflex sympathetic control in mild congestive heart failure. Circulation 1995; 92: 3206-3211

[18]Harriss DJ, Atkinson G. Ethical standards in sport and exercise science research: 2014 update. Int J Sports Med 2013; 34: 1025-1028

[19]Herpin D, Ragot S. Mid and long-term reproducibility of noninvasive measurements of spontaneous arterial baroreflex sensitivity in healthy volunteers. Am J Hypertens 1997; 10: 790-797

[20]Hohnloser SH, Klingenheben T, van de Loo A, Hablawetz E, Just H, Schwartz PJ. Reflex versus tonic vagal activity as a prognostic parameter in patients with sustained ventricular tachycardia or ventricular fibrillation. Circulation 1994; 89: 1068-1073

[21]Hopkins WG. Measures of reliability in sports medicine and science. Sports Med 2000; 30: 1-15

[22]Hughson RL, Quintin L, Annat G, Yamamoto Y, Gharib C. Spontaneous baroreflex by sequence and power spectral methods in humans. Clin Physiol 1993; 13: 663-676

[23]Hull SS Jr, Vanoli E, Adamson PB, Verrier RL, Foreman RD, Schwartz PJ. Exercise training confers anticipatory protection from sudden death during acute myocardial ischemia. Circulation 1994; 89: 548-552

[24]Iellamo F, Legramante JM, Massaro M, Raimondi G, Galante A. Effects of a residential exercise training on baroreflex sensitivity and heart rate variability in patients with coronary artery disease. Circulation 2000; 102: 2588-2592

[25]Iellamo F, Legramante JM, Raimondi G, Castrucci F, Massaro M, Peruzzi G. Evaluation of reproducibility of spontaneous baroreflex sensitivity at rest and during laboratory tests. J Hypertens 1996; 14: 1099-1104

[26]Iga J, George K, Lees A, Reilly T. Reliability of assessing indices of isokinetic leg strength in pubertal soccer players. Pediatr Exerc Sci 2006; 18: 436-445

[27]La Rovere MT, Schwartz PJ. Baroreflex sensitivity as a cardiac and arrhythmia mortality risk stratifier. PACE 1997; 20: 2602-2613

[28]Lipsey MW. Treatment effectiveness research and design sensitivity. In: Design sensitivity: statistical power for experimental research. London: Sage, 1990: 11-27

[29]Lord SW, Clayton RH, Hall MC, Gray JC, Murray A, McComb JM, Kenny RA. Reproducibility of three different methods of measuring baroreflex sensitivity in normal subjects. Clin Sci 1998; 95: 575-581

[30]Maestri R, Pinna GD, Mortara A, La Rovere MT, Tavazzi L. Assessing baroreflex sensitivity in post-myocardial infarction patients: comparison of spectral and phenylephrine techniques. J Am Coll Cardiol 1998; 31: 344-351

[31]Maestri R, Raczak G, Torunski A, Sukiennik A, Kozlowski D, La Rovere MT, Pinna GD. Day-by-day variability of spontaneous baroreflex sensitivity measurements: implications for their reliability in clinical and research applications. J Hypertens 2009; 27: 806-812

[32]Mancia G, Groppelli A, Di Rienzo M, Castiglioni P, Parati G. Smoking impairs baroreflex sensitivity in humans. Am J Physiol Heart Circ Physiol 1997; 273: H1555-H1560

[33]Monahan KD, Dinenno FA, Tanaka H, Clevenger C, DeSouza CA, Seals DR. Regular aerobic exercise modulates age-associated declines in cardiovagal baroreflex sensitivity in healthy men. J Physiol 2000; 529: 263-271

[34]Norton K, Marfell-Jones M, Whittingham N, Kerr D, Carter L, Saddington K, Gore C. Anthropometric assessment protocols. In: Gore CJ (ed). Physiological tests for elite athletes. Leeds: Human Kinetics, 2000: 83-85

[35]Osculati G, Grassi G, Giannattasio C, Seravalle G, Valagussa F, Zanchetti A, Mancia G. Early alterations of the baroreceptor control of heart rate in patients with acute myocardial infarction. Circulation 1990; 81: 939-948

[36]Pagani M, Somers V, Furlan R, Dell'Orto S, Conway J, Baselli G, Cerutti S, Sleight P, Malliani A. Changes in autonomic regulation induced by physical training in mild hypertension. Hypertension 1988; 12: 600-610

[37]Parati G, Di Rienzo M, Bertinieri G, Pomidossi G, Casadei R, Groppelli A, Pedotti A, Zanchetti A, Mancia G. Evaluation of the baroreceptor-heart rate reflex by 24-hour intra-arterial blood pressure monitoring in humans. Hypertension 1988, 12: 214-222

[38]Parati G, Di Rienzo M, Castiglioni P, Villani A, Tortorici E, Mancia G. Spontaneous baroreflex sensitivity: from the cardiovascular laboratory to patient's bedside. In: Di Rienzo M, Mancia G, Parati G, Pedotti A, Zanchetti A (eds). Frontiers of blood pressure and heart rate analysis. Amsterdam: IOS Press, 1997: 219-240

[39]Parati G, Di Rienzo M, Mancia G. How to measure baroreflex sensitivity: from the cardiovascular laboratory to daily life. J Hypertens 2000; 18: 7-19

[40]Parati G, Di Rienzo M, Mancia G. Dynamic modulation of baroreflex sensitivity in health and disease. Ann N Y Acad Sci 2001; 940: 469-487

[41]Parati G, Frattola A, Di Rienzo M, Castiglioni P, Pedotti A, Mancia G. Effects of aging on 24-h dynamic baroreceptor control of heart rate in ambulant subjects. Am J Physiol Heart Circ Physiol 1995; 268: H1606-H1612

[42]Parlow K, Viale J-P, Annat G, Hughson R, Quinton L. Spontaneous cardiac baroreflex in humans: Comparison with drug-induced responses. Hypertension 1995; 25: 1058-1068

[43]Parry SW, Reeve P, Lawson J, Shaw FE, Davison J, Norton M, Frearson R, Kerr S, Newton JL. The Newcastle protocols 2008: an update on head-up tilt table testing and the management of vasovagal syncope and related disorders. Heart 2009; 95: 416-420

[44]Raczak G, Pinna GD, La Rovere MT, Maestri R, Danilowicz-Szymanowicz L, Ratkowski W, Figura-Chmielewska M, Szwoch M, Ambroch-Dorniak K. Cardiovagal response to acute mild exercise in young healthy subjects. Circ J 2005; 69: 976-980

[45]Robbe HWJ, Mulder LJM, Ruddel H, Langewitz WA, Veldman JBP, Mulder G. Assessment of baroreceptor reflex sensitivity by means of spectral analysis. Hypertension 1987; 10: 538-543

[46]Sauret J, De Ste Croix M, Deighan M, Iga J, James D. Reproducibility of an isokinetic eccentric muscle endurance task. Eur J Sport Sci 2009; 9: 311-319

[47]Schultz BB, Sands WA. Understanding measurement concepts and statistical procedures. In: Maud PJ, Foster C (eds). Physiological assessment of human fitness. Leeds: Human Kinetics, 1995

[48]Zöllei E, Zoltán G, Kardos A, László R. Comparison between different non-invasive indices of baroreflex gain. Cardiologia Hungarica 1999; 6: 269-272

Table 1. Participant physical characteristics

Characteristic (n = 46)	Mean ± (SD)
Age (y)	22 (± 5)
Mass (kg)	79.3 (± 11)
Stature (m)	1.80 (± 0.1)
Resting HR (b·min-1)	67 (± 11)
Resting BP(br) (mmHg)	
Systolic	124 (± 9)
Diastolic	69 (± 6)

HR, heart rate; BP(br), resting brachial blood pressure

Table 2. Limits of Agreement for supine and tilt BRS measures

BRS (ms/mmHg)	Bias Mean Difference	SD Differences	95% Limits of Agreement (+) (ms/mmHg)	95% Limits of Agreement (-) (ms/mmHg)	Confidence Intervals (+) (ms/mmHg)	Confidence Intervals (-) (ms/mmHg)
Base / +60 min						
Seq UpUp (S)	0.57	15.45	30.84	-29.70	34.79	-33.65
Seq UpUp(T)	0.36	2.24	4.75	-4.04	5.33	-4.61
Seq DownDown (S)	-0.17	11.21	21.80	-22.13	24.67	-19.27
Seq DownDown (T)	-0.38	1.95	3.44	-4.20	3.94	-4.70
α LF (S)	0.85	4.42	9.50	-7.81	10.63	-8.93
α LF (T)	-0.31	1.77	3.17	-3.78	3.62	-4.23
TFTG (S)	1.69	3.34	8.24	-4.85	9.09	-5.07
TFTG (T)	0.09	1.28	2.60	-2.43	2.93	-2.76
Base / +24 h						
Seq UpUp (S)	0.99	14.17	28.76	-26.78	32.38	-30.40
Seq UpUp(T)	-0.52	2.78	4.93	-5.97	5.64	-6.68
Seq DownDown (S)	-0.23	7.45	14.36	-14.83	16.26	-16.73
Seq DownDown (T)	-0.80	1.83	2.78	-4.38	3.25	-4.84
α LF (S)	-0.62	5.45	10.06	-11.30	11.45	-12.69
α LF (T)	-0.54	2.36	4.08	-5.16	4.68	-5.76
TFTG (S)	0.34	4.75	9.65	-8.97	10.86	-10.18
TFTG (T)	-0.15	1.97	3.71	-4.00	4.21	-4.50

Note: BRS, baroreflex sensitivity; Seq, sequence; LF, low frequency; TFTG, transfer function transfer gain; (S), supine; (T), tilt

Table 3. BRS parameters and Technical Error of Measurement

BRS (ms/mmHg)	TEM	% TEM
Base / +60 min		
Seq UpUp (S)	10.81	10.41
Seq UpUp(T)	1.59	4.06
Seq DownDown (S)	7.84	9.11
Seq DownDown (T)	1.39	4.83
α LF (S)	3.15	4.70
α LF (T)	1.26	3.56
TFTG (S)	2.62	4.11
TFTG (T)	0.90	2.77
Base / +24 h		
Seq UpUp (S)	9.93	9.49
Seq UpUp(T)	1.98	5.29
Seq DownDown (S)	5.21	6.06
Seq DownDown (T)	1.40	5.00
α LF (S)	3.84	6.00
α LF (T)	1.69	4.86
TFTG (S)	3.33	5.44
TFTG (T)	1.38	4.31

Note: BRS, baroreflex sensitivity; Seq, sequence; LF, low frequency; TFTG, transfer function transfer gain; (S), supine; (T), tilt

Table 4. Number of participants required for follow-up studies with tilt BRS

	Same day reproducibility (+ 60 min)				Between day reproducibility (+ 24 h)			
Δ BRS	Seq UpUp	Seq DownDown	α LF	TFTG	Seq UpUp	Seq DownDown	α LF	TFTG
1	155	117	96	51	238	103	171	119
2	39	29	24	13	59	26	43	30
3	17	13	11	6	26	11	19	13
4	10	7	6	3	15	6	11	7
5	6	5	4	2	10	4	7	5

Note: Δ BRS, change in baroreflex sensitivity (ms/mmHg); Seq, sequence; LF, low frequency; TFTG, transfer function transfer gain

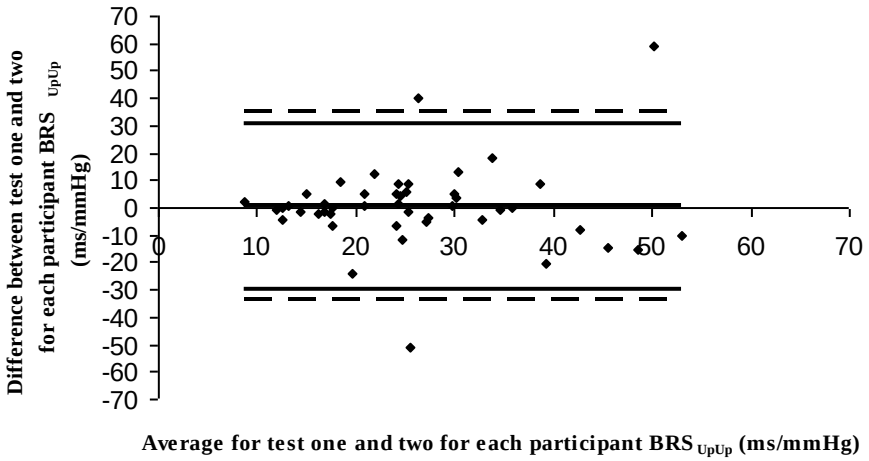

Figure 1. Bland and Altman plot in supine BRS_{UpUp} between baseline and + 60 min

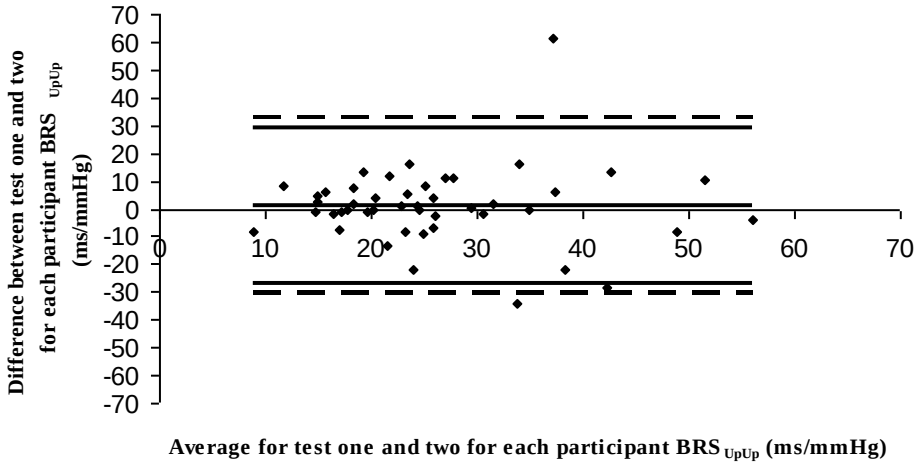

Figure 2. Bland and Altman plot in supine BRS_{UpUp} between baseline and + 24 h

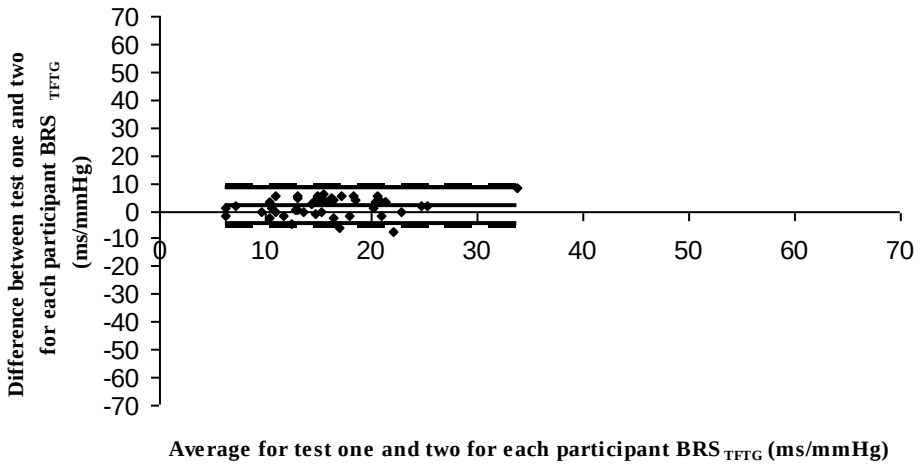

Figure 3. Bland and Altman plot in supine BRS_{TFTG} between baseline and + 60 min

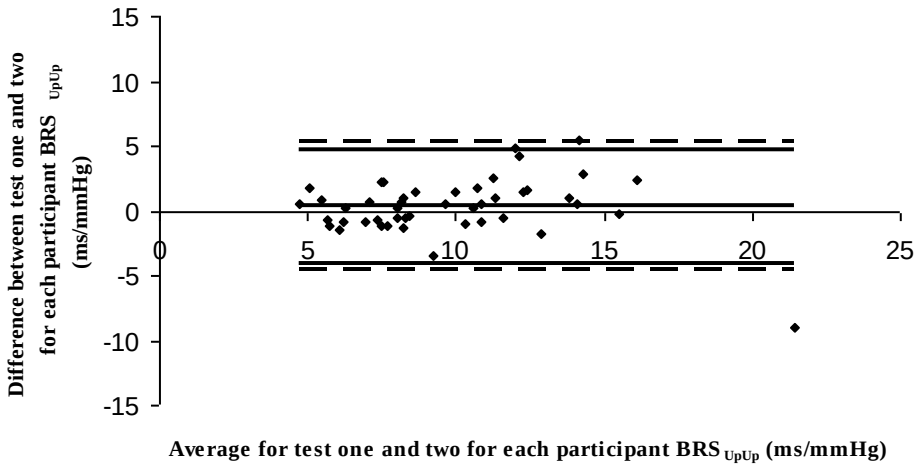

Figure 4. Bland and Altman plot in tilt BRS_{UpUp} between baseline and + 60 min

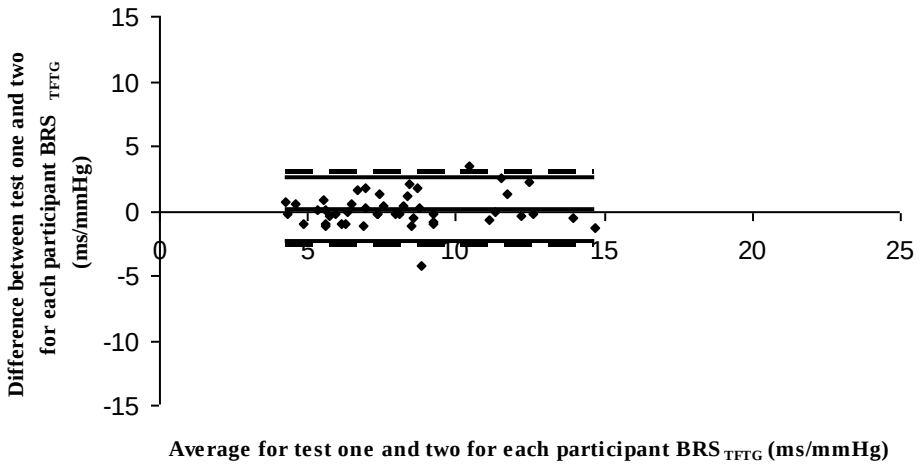

Figure 5. Bland and Altman plot in tilt BRS_{TFTG} between baseline and + 60 min