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Determination of Vagal Baroreflex sensitivity in Normal Subjects

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Abstract

Introduction—The Valsalva maneuver (VM) is used widely to quantify the sensitivity of the vagal baroreflex loop (vagal baroreflex sensitivity, BRS_v), but most studies have focused on the heart rate (HR) response to blood pressure (BP) decrement (BRS_{v↓}), even though the subsequent response to an increment in BP following the VM (BRS_{v↑}) is important and different.

Methods—We evaluated recordings of HR and BP in 187 normal subjects during the VM and determined both BRS_{v↑} determined by relating HR to the BP increase following phase III and BRS_{v↓}.

Results—BRS_{v↑} was related inversely to age. In addition, BRS_{v↓}, age, and magnitude of phase IV were independent predictors of BRS_{v↑} in a multivariate model, accounting for 47% of the variance of BRS_{v↑}.

Discussion—The results indicate that both BRS_{v↑} and BRS_{v↓} become blunted with increasing age and that these indices relate to each other.

Keywords

baroreflex sensitivity; Valsalva maneuver; normal subject; age; blood pressure

Introduction

The baroreflex plays a key role in maintenance of postural normotension. Testing of baroreflex sensitivity (BRS) has been used increasingly to quantitate the vagal component of the reflex. The Mayo Clinic Autonomic Laboratory has evaluated adrenergic and vagal components of the baroreflex by studying dynamic alterations in blood pressure (BP) and heart rate (HR) during the Valsalva maneuver (VM). There are 4 main phases in the VM. Phase I is a transient rise in BP due to increased intrathoracic pressure induced by blowing. Early phase II (phase II_E) is a fall in BP due to reduced preload (venous return) and stroke volume. The baroreflex then results in an efferent sympathetic discharge to muscle and to an increase in plasma norepinephrine concentration, resulting in a rise in BP. This rise in BP is described as late phase II (phase II_L). At the end of the VM, the sudden fall in intrathoracic

pressure results in a transient fall in BP (phase III) lasting 1 to 2 seconds. In phase IV, venous return and cardiac output gradually return to normal while the arterial vascular bed remains constricted, resulting in a transient BP overshoot.

Our program has made significant headway into developing non-invasive methodology to quantify the 2 components of the baroreflex.^{1,2} The vagal component of the baroreflex (BRS_v) is indexed by the heart period (HP) response to changes in BP. Traditionally, BRS_v is measured by the modified Oxford method, where the HP response to an induced fall in BP (by intravenous boluses of nitroprusside) followed by an induced rise in BP (by intravenous boluses of phenylephrine) and studied sequentially.³ BRS_v is determined as the slope of the BP-HP response and expressed as ms/mmHg. In the Autonomic Laboratory, we can calculate BRS_v by relating the HP response to a fall in SBP (phase II-E). We have validated the method in patients with graded autonomic failure¹ and have generated a normative database.²

More limited studies have been devoted to the HP response to a rise in BP. Studies have been performed relating HP to the BP increase in phase IV of the maneuver^{4-7,4-7} However, in the clinical Autonomic Laboratory, the described methodology has only limited application, since phase IV is typically absent in patients with autonomic failure. What is needed is an approach that relates HP to BP increase that is reliably present. For this reason, we determined BRS_v by relating HP to a rise in BP following phase III.

The aims of this study were to: (1) provide normative data on BRS_v in response to SBP increase (BRS_v↑) determined using phase III-IV of the Valsalva maneuver; (2) evaluate the effect of age and gender on BRS_v; and (3) study whether there is a differential effect of age on the BRS_v to a fall in SBP (BRS_v↓) and BRS_v↑.

Materials and Methods

The study was approved by the Mayo Clinic Institutional Review Board. We evaluated 187 normal subjects, primarily of northern European descent of either gender who were free of disorders or medications known to affect autonomic function. All subjects underwent routine autonomic testing to evaluate cardiovagal and adrenergic function, and no caffeinated beverages, food, or nicotine were permitted for 4 hours prior to testing. Heart rate was recorded using a standard 3-lead electrocardiogram (Ivy Biomedical Systems, Inc, Branford, Conn). Arterial BP was continuously measured at the finger using beat-to-beat photoplethysmographic recordings (Finapres BP monitor model 2300 and Finometer; Ohmeda, Englewood, Colo).

The VM was performed with the subject lying supine. The subject was instructed to perform the VM by maintaining a pressure of 40 mm Hg for 15 seconds via a tube with an air leak (to ensure an open glottis). After a practice run, the subject performed a series of maneuvers until 2 reproducible responses were obtained. We utilized strict criteria for an acceptable maneuver. We excluded: (1) expiratory pressure less than 30 mmHg or 10 seconds; (2) no producible qualitative configuration of phases; and (3) a “flat-top” response of the response with systolic pressure of early phase II (II-E) or phase III above baseline.

The baseline values of systolic, diastolic, and mean arterial BP average were determined with the subject rested and lying supine for at least 20 minutes preceding the VM. SBP magnitude was also determined for 3 phases: phase II_E, phase II_L, and phase IV. Percent of phase II pulse pressure compression (%pIIppc) was defined as the percentage of the difference between the range of BP (SBP – DBP) at the valley of Phase II-E and the baseline divided by the range of BP at the baseline. Adrenergic barosensitivity (BRS_a) was defined as the systolic BP decrement associated with phase III divided by PRT. PRT was defined as time in seconds from the valley of phase III until SBP returned to baseline. HP response to BP rise (BRS_v↑) was defined as the regression slope of HP over SBP from phase III to IV. HP response to BP fall (BRS_v↓) is expressed as the regression slope of HP over SBP during early phase II.

Statistical Analysis

Subject data are expressed as mean ± standard deviation. Because the distribution of BRS_v was skewed positively, data were analyzed after logarithmic transformations. For subsequent analysis, participants were divided into 6 subgroups according to age. We used multiple comparison one-way analysis of variance and Tukey HSD methods to examine group differences. The student *t*-test was used to analyze the significance between genders. The relationship between SBP and HP was assessed using regression analysis. Univariate correlation analysis, using the Pearson test, was also performed. In addition, stepwise multiple-regression analysis was used to evaluate the independent correlates of BRS. All statistical tests were two-tailed, and $P < 0.05$ was considered significant for all comparisons.

Results

Of our recordings from 187 subjects, 166 were accepted for analysis. The excluded data were mainly comprised of VM with “flat-top” responses, where BP changes failed to fall below baseline.

Gender effect on baseline hemodynamic indices, BRS indices, and parameters of VM

When separating the subjects according to gender, 2 groups matched with respect to age. Baseline hemodynamic indices, BRS indices, and the parameters of VM are summarized in Table 1. SBP was significantly higher in men. HR and magnitude of phase IV were higher in women. When subjects were divided by decade, there were significant gender effects in some adrenergic parameters (phase IV, BRS_a, and PRT) in older subjects (Table 2). However, we did not find a gender effect in BRS indices.

Age effect on baseline hemodynamic indices, BRS indices and parameters of VM

The age coefficient for SBP and %pIIppc was positive, indicating that these parameters increased with age [SBP = $120.4 + 0.25 \times \text{age}$; $R^2 = 0.05$, $P = 0.0035$, %pIIppc = $11.7 + 0.71 \times \text{age}$; $R^2 = 0.28$, $P < 0.0001$] (Fig. 1, A and B). A significant inverse correlation with aging was found in both $\ln \text{BRS}_{v\uparrow}$ and $\ln \text{BRS}_{v\downarrow}$ [$\ln \text{BRS}_{v\uparrow} = 2.72 - 0.02 \times \text{age}$; $R^2 = 0.28$, $P < 0.0001$, $\ln \text{BRS}_{v\downarrow} = 2.04 - 0.01 \times \text{age}$; $R^2 = 0.11$, $P < 0.0001$] (Fig. 1, C and D). When subjects were divided by decade, the tendency was seen in groups older than age 40 years (Table 2).

Correlations between baseline hemodynamic indices, BRS indices, and parameters of VM

We correlated the parameters of BRS to indices of baseline hemodynamics and indices of VM. The correlations between BRS_v↑ and the parameters of BRS_v↓, age, SBP, HR, magnitude of phase II_E, phase IV, %pIIppc, and BRS_a were significant. The correlation coefficients are listed in Table 3.

Multivariate correlates of BRS

When the significant univariate correlates of BRS_v↑ were analyzed in a multivariate model, only age, magnitude of phase IV, and BRS_v↓ were independent predictors of BRS_v↑ (Table 4). All these factors together accounted for 43% ($r^2 = 0.43$) of the interindividual variation of BRS_v↑.

Relationship of BRS_v↑ to BRS_v↓

The relationship between $\ln$ BRS_v↑ and $\ln$ BRS_v↓ is seen in Fig. 2. The r square value was 0.283. BRS_v↑ and BRS_v↓ for each subject were also analyzed by using paired t -test. BRS_v↑ was significantly higher than BRS_v↓ in younger groups (Fig. 3).

Discussion

Our primary goal in this study was to provide normative data on BRS_v determined by HP response to SBP increase (BRS_v↑) using phase III–IV of the Valsalva maneuver. We evaluated BRS_v↑ in 187 subjects whose ages extended across 8 decades. The data suggest that measurement of BRS_v↑ is feasible in about 90% of healthy subjects ranging from ages 18 to 81 years. The mean value of BRS_v↑ was 7.3 ± 3.6 ms/mmHg (range 0.4–18.5, 95% CI 6.7–7.8). This value is similar to that value obtained in a previous study by relating HP to BP increase in phase IV (5.8 ± 3.4 , 6.9 ± 3.5 , 7.8 ± 4.0 , 9.7 ± 7.2).^{4–7}

Our secondary goal was to evaluate the effect of age and gender on BRS_v. BRS_v↑ and BRS_v↓ were both inversely related to age. BRS_v with aging in healthy subjects has been demonstrated in several previous studies.^{2,4,5,7–16} Some studies used spontaneous analysis techniques,^{10–14} and some used Valsalva maneuver,^{2,4,5,7–9} premature ventricular contraction,¹⁷ or phenylephrine injection.^{15,16} Spontaneous baroreflex sensitivity methods have been compared systematically.¹⁸ In all of these studies, BRS_v was found to decrease with age, regardless of the analysis method. The mechanism responsible for this decrease is not known. Virtanen et al.¹¹ demonstrated that arterial stiffening with aging may decrease BRS_v by increasing pulse pressure, pulse wave velocity, and baroreceptor load, and thereby downregulating BRS_v. Labrova et al.¹⁰ reported a significant negative correlation between BRS_v and carotid wall thickness (IMT). In the study of Lucini et al.,¹⁹ there was a significant correlation between BRS_v and wave speed of the carotid artery. Normal human aging is associated with a reduction in baroreflex sensitivity. In our study, SBP also increased with age. We have also shown an inverse relationship between BRS_v↑ and SBP. The decrease in arterial distensibility that accompanies aging and hypertension results in diminished baroreceptor stretch, less tonic inhibition of the brainstem vasomotor center, and increased sympathetic outflow. Increased sympathetic outflow results in increased

circulating noradrenaline, which in turn may result in further vasoconstriction, blood pressure elevation, and baroreflex impairment.

There was no effect of gender for BRS_v in our study. Gender has been found to be an independent predictor of BRS_v in some studies,^{14,16,20} but not in others.⁴ We found gender effects in some adrenergic parameters (phase IV, BRS_a, and PRT) in older subjects (Table 2). These adrenergic parameters were decreased in men older than 70 years.

BRS_v is used widely and provides a quantitative index of the vagal response to alterations in BP. It is also possible to separately evaluate the adrenergic component of the baroreflex (BRS_a) or by the index BP recovery time (PRT), which was found to vary directly with severity of adrenergic impairment.²¹ In their study Huang et al.² found that BRS_v decreased with age, but there was no correlation with adrenergic parameters. We found a weak, but significant negative relationship between BRS_v and BRS_a. We also found a negative correlation between BRS_v and the magnitude of phase IV. The index of phase IV has been well accepted as an index to track adrenergic activation. The mechanism of phase IV is complex, as it is more dependent on cardiac than peripheral adrenergic tone. Sandroni et al.²² concluded from their study that, while phase IV overshoot of the Valsalva maneuver is mostly dependent on cardiac sympathetic innervation, the late phase II of the maneuver is affected mostly by peripheral sympathetic innervation. Our findings indicate that BRS_v is affected by cardiac adrenergic function.

BRS_v↑ correlated well with BRS_v↓ in our study. The smaller phase II_E reduces cardiac and peripheral sympathetic activity, resulting in a smaller change in phase IV. In this study, BRS_v↓ was significantly lower than BRS_v↑. A previous study reported that patients had a normal heart rate increase in phase II, but 75% did not develop the reflex bradycardiac response that is characteristic of phase IV.²³

The main limitations of our study are that it is retrospective and depends on the accuracy of Finapres-recorded beat-to-beat BP changes. BRS calculated using this method is also substantially different from that using the modified Oxford method, where boluses of drugs raise and lower BP, so that BRS values should not be directly compared.

Conclusion

We conclude that vagal baroreflex sensitivity is reduced with healthy aging, thus confirming other studies. The novel finding from our research is that both BRS_v↑ and BRS_v↓ relate closely to each other and are influenced by age and cardiac adrenergic function.

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Abbreviations

BRS	Baroreflex sensitivity
BRS_a	adrenergic barosensitivity
DBP	diastolic blood pressure
HP	heart period
HR	heart rate
MBP	mean blood pressure
Phase II-E	early phase II
Phase II-L	late phase II
%PIIppc	percent of phase II pulse pressure compression
PRT	pressure recovery time
SBP	systolic blood pressure
VM	Valsalva maneuver

References

- Schrezenmaier C, Singer W, Muentert Swift N, Sletten D, Tanabe J, Low PA. Adrenergic and vagal baroreflex sensitivity in autonomic failure. *Arch Neurol*. 2007; 64:381–386. [PubMed: 17353381]
- Huang CC, Sandroni P, Sletten D, Weigand S, Low PA. Effect of age on adrenergic and vagal baroreflex sensitivity in normal subjects. *Muscle Nerve*. 2007; 36(5):637–642. [PubMed: 17654557]
- Rudas L, Crossman AA, Morillo CA, Halliwill JR, Tahvanainen KU, Kuusela TA, Eckberg DL. Human sympathetic and vagal baroreflex responses to sequential nitroprusside and phenylephrine. *Am J Physiol*. 1999; 276:H1691–1698. [PubMed: 10330255]
- Dawson SL, Robinson TG, Youde JH, Martin A, James MA, Weston PJ, Panerai RB, Potter JF. Older subjects show no age-related decrease in cardiac baroreceptor sensitivity. *Age Ageing*. 1999; 28(4):347–353. [PubMed: 10459786]
- Airaksinen K, Hartikainen K, Niemela M, Huikuri H, Mussalo H, Tahvanainen K. Valsalva manoeuvre in the assessment of baroreflex sensitivity in patients with coronary artery disease. *Eur Heart J*. 1993; 14(11):1519–1523. [PubMed: 8299635]
- Smith SA, Stallard TJ, Salih MM, Littler WA. Can sinoaortic baroreceptor heart rate reflex sensitivity be determined from phase IV of the Valsalva manoeuvre? *Cardiovasc Res*. 1987; 21(6):422–427. [PubMed: 3652109]
- Zollei E, Paprika D, Rudas L. Measures of cardiovascular autonomic regulation derived from spontaneous methods and the Valsalva maneuver. *Auton Neurosci*. 2003; 103(1–2):100–105. [PubMed: 12531403]
- Monahan KD, Dinunno FA, Seals DR, Clevenger CM, Desouza CA, Tanaka H. Age-associated changes in cardiovagal baroreflex sensitivity are related to central arterial compliance. *Am J Physiol Heart Circ Physiol*. 2001; 281(1):H284–H289. [PubMed: 11406495]
- Shimada K, Kitazumi T, Sadakane N, Ogura H, Ozawa T. Age-related changes of baroreflex function, plasma norepinephrine, and blood pressure. *Hypertension*. 1985; 7:113–117. [PubMed: 3980053]
- Labrova R, Honzikova N, Maderova E, Vysocanova P, Novakova Z, Zavadna E, Fiser B, Semrad B. Age-dependent relationship between the carotid intima-media thickness, baroreflex sensitivity,

- and the inter-beat interval in normotensive and hypertensive subjects. *Physiol Res*. 2005; 54(6): 593–600. [PubMed: 16351497]
11. Virtanen R, Jula A, Huikuri H, Kuusela T, Helenius H, Ylitalo A, Voipio-Pulkki LM, Kauma H, Kesaniemi YA, Airaksinen J. Increased pulse pressure is associated with reduced baroreflex sensitivity. *J Hum Hypertens*. 2004; 18(4):247–252. [PubMed: 15037873]
 12. Boettger MK, Schulz S, Berger S, Tancer M, Yeragani VK, Voss A, Bar KJ. Influence of age on linear and nonlinear measures of autonomic cardiovascular modulation. *Ann Noninvasive Electrocardiol*. 2010; 15(2):165–174. [PubMed: 20522058]
 13. Brown CM, Hecht MJ, Weih A, Neundorfer B, Hilz MJ. Effects of age on the cardiac and vascular limbs of the arterial baroreflex. *Eur J Clin Invest*. 2003; 33(1):10–16. [PubMed: 12492447]
 14. Kardos A, Watterich G, de Menezes R, Csanady M, Casadei B, Rudas L. Determinants of spontaneous baroreflex sensitivity in a healthy working population. *Hypertension*. 2001; 37(3): 911–916. [PubMed: 11244017]
 15. Ebert TJ, Morgan BJ, Barney JA, Denahan T, Smith JJ. Effects of aging on baroreflex regulation of sympathetic activity in humans. *Am J Physiol*. 1992; 263:H798–803. [PubMed: 1415605]
 16. Laitinen T, Hartikainen J, Vanninen E, Niskanen L, Geelen G, Lansimies E. Age and gender dependency of baroreflex sensitivity in healthy subjects. *J Appl Physiol*. 1998; 84(2):576–583. [PubMed: 9475868]
 17. Haensch CA, Jorg J. Beat-to-beat blood pressure analysis after premature ventricular contraction indicates sensitive baroreceptor dysfunction in Parkinson's disease. *Mov Disord*. 2006; 21(4):486–491. [PubMed: 16258941]
 18. Laude D, Elghozi JL, Girard A, Bellard E, Bouhaddi M, Castiglioni P, Cerutti C, Cividjian A, Di Rienzo M, Fortrat JO, Janssen B, Karemaker JM, Leftheriotis G, Parati G, Persson PB, Porta A, Quintin L, Regnard J, Rudiger H, Stauss HM. Comparison of various techniques used to estimate spontaneous baroreflex sensitivity (the EuroBaVar study). *Am J Physiol Regul Integr Comp Physiol*. 2004; 286(1):R226–231. [PubMed: 14500269]
 19. Lucini D, Palombo C, Malacarne M, Pagani M. Relationship between carotid artery mechanics and the spontaneous baroreflex: a noninvasive investigation in normal humans. *J Hypertens*. 2012; 30(9):1809–1816. [PubMed: 22871887]
 20. Huikuri HV, Pikkujamsa SM, Airaksinen KE, Ikaheimo MJ, Rantala AO, Kauma H, Lilja M, Kesaniemi YA. Sex-related differences in autonomic modulation of heart rate in middle-aged subjects. *Circulation*. 1996; 94(2):122–125. [PubMed: 8674168]
 21. Vogel ER, Sandroni P, Low PA. Blood pressure recovery from Valsalva maneuver in patients with autonomic failure. *Neurology*. 2005; 65:1533–1537. [PubMed: 16301478]
 22. Sandroni P, Benarroch EE, Low PA. Pharmacological dissection of components of the Valsalva maneuver in adrenergic failure. *J Appl Physiol*. 1991; 71(4):1563–1567. [PubMed: 1757382]
 23. Opfer-Gehrking TL, Low PA. Impaired respiratory sinus arrhythmia with paradoxically normal Valsalva ratio indicates combined cardiovagal and peripheral adrenergic failure. *Clin Auton Res*. 1993; 3:169–173. [PubMed: 8400816]

Figure 1. Correlation between age and SBP, %pIppc and $\ln$ BRS. Regression slope and 95% confidence intervals are shown.

Figure 2.
Correlation between $\ln \text{BRS}_{v\downarrow}$ and $\ln \text{BRS}_{v\uparrow}$

Figure 3.

Difference between BRS_v↓ and BRS_v↑ in the different age groups. Error bar represents a 95% confidence interval.* $P < 0.05$

Table 1

Clinical characteristics of men and women study subjects

	Total (n=166)	Men (n=73)	Women (n=93)	P
Age (y)	44.6 ± 17.1 (18–81)	44.8 ± 19.0 (18–81)	44.1 ± 15.5 (18–79)	0.6887
SBP (mmHg)	131.5 ± 18.8 (93–215)	134.7 ± 19.0 (97–215)	128.8 ± 19.0 (93–189)	0.0378*
MBP (mmHg)	90.5 ± 12.2 (64–139)	91.9 ± 13.0 (69–139)	89.2 ± 11.5 (64–139)	0.1255
DBP (mmHg)	70.3 ± 10.6 (50–101)	70.9 ± 11.1 (50–101)	69.7 ± 10.1 (50–96)	0.3746
HR (beat/min)	65.3 ± 8.9 (42–92)	63.8 ± 8.8 (42–92)	66.6 ± 8.8 (50–89)	0.0383*
Phase II-E (mmHg)	4.5 ± 12.1 (–27–45)	5.1 ± 11.6 (–24–45)	5.1 ± 11.6 (–27–38)	0.6166
Phase II-L (mmHg)	17.5 ± 11.3 (0–53)	16.3 ± 10.6 (0–53)	18.4 ± 11.7 (1–52)	0.2269
Phase IV (mmHg)	21.8 ± 11.2 (–1–58)	19.6 ± 9.7 (–1–45)	23.5 ± 12.0 (–1–58)	0.0229*
%PIIppc (%)	39.6 ± 22.9 (–15–85)	39.6 ± 24.4 (–15–80)	46.4 ± 21.3 (1–85)	0.0576
BRS_a (mmHg/s)	32.2 ± 22.1 (1–133)	30.0 ± 19.9 (1–113)	34.0 ± 23.7 (2–133)	0.2529
PRT (s)	1.7 ± 1.1 (0.4–8.1)	1.8 ± 0.9 (0.5–4.6)	1.6 ± 1.2 (0.4–8.1)	0.1404
BRS_v↑ (ms/mmHg)	7.3 ± 3.6 (0.4–18.5)	7.5 ± 3.9 (1.1–18.5)	7.1 ± 3.5 (0.4–15.0)	0.5150
BRS_v↓ (ms/mmHg)	5.3 ± 3.2 (0.5–18.5)	5.2 ± 2.5 (1.5–12.0)	5.4 ± 3.6 (0.5–18.5)	0.5961

SBP, systolic blood pressure; MBP, mean blood pressure; DBP, diastolic blood pressure; HR, heart rate; Phase II-E, magnitude of early phase II; Phase II-L, magnitude of late phase II; Phase IV, magnitude of phase IV; %PIIppc, percent of phase II pulse pressure compression; BRS_a, adrenergic barosensitivity; PRT, pressure recovery time; BRS. Baroreflex sensitivity

Table 2

Autonomic Parameters in the different age groups

	A (18–29 y) (n=40)	B (30–39 y) (n=34)	C (40–49 y) (n=29)	D (50–59 y) (n=22)	E (60–69 y) (n=24)	F (70–81 y) (n=17)
Age (y)						
Total	23.4 ± 3.6	35.2 ± 2.8*	44.1 ± 2.8*	54.7 ± 2.4*	64.0 ± 2.7*	73.5 ± 3.9*
Men	22.6 ± 3.7	35.1 ± 2.5*	44.3 ± 2.4*	55.8 ± 2.3*	64.7 ± 3.1*	73.3 ± 3.9*
Women	24.1 ± 3.4	35.3 ± 3.1*	44.1 ± 2.9*	54.1 ± 2.3*	63.4 ± 2.2*	74.0 ± 4.3*
SBP (mmHg)						
Total	128.0 ± 16.7	127.9 ± 13.6	130.4 ± 15.4	129.8 ± 21.7	136.4 ± 24.9	143.6 ± 19.8*
Men	130.0 ± 17.6	131.3 ± 12.6	135.1 ± 10.3	127.3 ± 20.0	146.7 ± 27.8	142.4 ± 18.5
Women	126.2 ± 16.1	124.6 ± 14.0	129.0 ± 16.7	131.3 ± 23.3	127.7 ± 19.1*	145.8 ± 23.6
HR (beat/min)						
Total	65.2 ± 7.2	64.2 ± 7.1	66.9 ± 9.9	65.0 ± 8.1	66.2 ± 12.6	64.5 ± 9.5
Men	64.9 ± 6.6	63.5 ± 8.1	71.1 ± 9.8	66.5 ± 9.2	57.6 ± 7.3	61.6 ± 10.7
Women	65.4 ± 7.9	65.0 ± 6.2	65.5 ± 9.7	64.1 ± 7.6	73.6 ± 11.5*	69.7 ± 3.1*
Phase II-E (mmHg)						
Total	4.2 ± 13.8	3.8 ± 10.9	1.7 ± 9.1	3.3 ± 11.3	9.3 ± 12.6	6.4 ± 13.9
Men	4.6 ± 12.5	4.4 ± 9.6	-1.3 ± 11.7	6.2 ± 7.3	9.2 ± 13.5	5.9 ± 13.4
Women	3.8 ± 15.2	3.3 ± 12.3	2.6 ± 8.3	1.7 ± 13.1	9.4 ± 12.3	7.3 ± 15.9
Phase II-L (mmHg)						
Total	16.6 ± 9.9	18.0 ± 10.0	18.7 ± 10.9	20.2 ± 14.5	15.4 ± 10.6	15.6 ± 14.0
Men	17.3 ± 9.0	19.9 ± 16.1	24.0 ± 15.4	17.5 ± 14.8	10.1 ± 5.1	9.3 ± 8.3*
Women	16.0 ± 10.8	16.1 ± 11.3	17.0 ± 8.9	21.7 ± 14.6	19.9 ± 12.0*	27.3 ± 15.4*
Phase IV (mmHg)						
Total	19.2 ± 10.4	21.4 ± 11.6	25.3 ± 12.2	25.2 ± 10.2	22.6 ± 11.0	17.0 ± 9.5
Men	18.1 ± 9.6	19.5 ± 8.8	25.4 ± 10.6	24.7 ± 10.6	20.5 ± 9.7	13.8 ± 7.4
Women	20.2 ± 11.3	23.3 ± 14.0	25.3 ± 12.9	25.5 ± 10.3	24.4 ± 12.2	23.0 ± 10.6*
%PIIppc (%)						
Total	29.0 ± 22.2	36.7 ± 22.1	38.2 ± 19.4	54.0 ± 16.5*	61.0 ± 16.3*	60.8 ± 13.1*
Men	23.3 ± 21.5	29.7 ± 23.0	29.0 ± 22.1	54.0 ± 10.7*	55.4 ± 16.2*	63.6 ± 11.4*
Women	34.3 ± 22.0	43.6 ± 19.4*	41.1 ± 18.1	54.1 ± 19.4*	65.8 ± 15.3*	55.8 ± 15.7
BRS_a (mmHg/s)						
Total	28.1 ± 19.0	29.8 ± 20.1	37.4 ± 25.4	33.6 ± 19.2	33.1 ± 24.0	34.8 ± 27.9
Men	27.5 ± 15.6	32.9 ± 23.3	42.3 ± 32.6	36.7 ± 26.0	27.4 ± 9.6	19.8 ± 6.3
Women	18.7 ± 22.0	26.6 ± 16.6	35.8 ± 23.4	31.9 ± 15.0	38.0 ± 31.1	62.3 ± 31.6*
PRT (s)						
Total	1.7 ± 1.2	1.6 ± 1.3	1.3 ± 0.6	1.5 ± 0.6	1.9 ± 0.8	2.4 ± 1.2*
Men	1.6 ± 0.6	1.4 ± 0.7	1.2 ± 0.6	1.7 ± 0.7	2.0 ± 0.7	3.1 ± 0.9*

	A (18–29 y) (n=40)	B (30–39 y) (n=34)	C (40–49 y) (n=29)	D (50–59 y) (n=22)	E (60–69 y) (n=24)	F (70–81 y) (n=17)
Women	1.7 ± 1.6	1.8 ± 1.7	1.3 ± 0.6	1.4 ± 0.6	1.8 ± 0.9	1.2 ± 0.7 [‡]
BRS_v↑ (ms/mmHg)						
Total	9.7 ± 3.5	8.6 ± 3.4	6.6 ± 2.9 [*]	6.8 ± 3.0 [*]	5.3 ± 2.6 ^{*,†}	3.6 ± 2.8 ^{*,†,§}
Men	9.9 ± 4.3	8.8 ± 3.5	6.0 ± 2.9	6.5 ± 3.0	6.3 ± 2.4	4.1 ± 2.8 ^{*,†}
Women	9.5 ± 2.7	8.4 ± 3.4	6.8 ± 2.9	7.0 ± 3.0	4.4 ± 2.5 ^{*,†}	2.7 ± 2.6 ^{*,†,§}
BRS_v↓ (ms/mmHg)						
Total	5.7 ± 3.2	6.4 ± 2.7	5.8 ± 3.9	5.6 ± 3.5	3.9 ± 1.9 [†]	3.0 ± 1.8 ^{*,†,‡}
Men	5.2 ± 2.5	6.7 ± 2.4	4.5 ± 2.6	5.5 ± 2.9	4.4 ± 2.2	3.8 ± 1.8 [†]
Women	6.2 ± 3.8	6.1 ± 2.9	6.3 ± 4.2	5.7 ± 3.9	3.4 ± 1.7	1.7 ± 0.8 ^{‡,‡}

* Different from group A;

[†] different from group B;

[‡] different from group C;

[§] different from group D;

^{||} different from group E;

[#] different from men

Table 3

Correlations between BRS with components of Valsalva maneuver

	BRS_v↑	BRS_v↓	Age	SBP	HR	PI-E	PI-L	PIV	%PIppc	PRT	BRS_a
BRS_v↑	—	0.472*	-0.521*	-0.211*	-0.262*	-0.191*	-0.099	-0.319*	-0.343*	-0.058	-0.323*
BRS_v↓		—	-0.290*	-0.136	-0.279*	-0.418*	-0.263*	-0.268*	-0.320*	-0.108	-0.312*
Age			—	0.225*	0.027	0.110	-0.007	-0.035	0.531*	0.155*	0.102
SBP				—	-0.023	0.106	0.120	0.051	0.086	-0.090	0.283*
HR					—	0.164*	0.314*	0.284*	0.033	-0.229*	0.294*
PI-E						—	0.121	-0.001	0.588*	0.259*	0.325*
PI-L							—	0.304*	-0.001	-0.452*	0.595*
PIV								—	0.131	-0.470*	0.474*
%PIppc									—	0.280*	0.230*
PRT										—	-0.462*
BRS_a											—

* $P < 0.05$

PI-E, magnitude of early phase II; PI-L, magnitude of late phase II; PIV, magnitude of phase IV

Table 4

Multivariate correlates of BRS-v↑

Dependent Variables	Regression coefficient (95% CI)	<i>P</i>
Age	−0.092 (−0.118 – −0.065)	< 0.0001
Phase IV	−0.074 (−0.113 – −0.034)	0.0003
BRS-v↓	0.328 (0.183–0.474)	< 0.0001