Heart Vessels (2013) 28:467–472
DOI 10.1007/s00380-012-0267-0

ORIGINAL ARTICLE

Aortic artery distensibility shows inverse correlation with heart rate variability in elderly non-hypertensive, cardiovascular disease-free individuals: the Ikaria Study

Christina Chrysohoou · John Skoumas · Evangelos Oikonomou · Dimitris Tsiachris · Vasiliki Metaxa · Stavroula Lagoudakou · John Felekos · Constadina Masoura · Stavroula Athanassopoulou · Hara Kosyfa · Christos Pitsavos · Christodoulos Stefanadis

Received: 9 April 2012 / Accepted: 1 June 2012 / Published online: 19 July 2012
© Springer 2012

Abstract The aim of this study was to evaluate the relation between aortic artery distensibility, expressed by pulse pressure (PP) and autonomic nervous system function expressed by heart rate variability (HRV), among elders. During 2009, 469 individuals (50 % males, mean age 75 ± 6 years old), permanent inhabitants of Ikaria Island, were enrolled. Among several sociodemographic, bioclinical, lifestyle, and dietary characteristics, and biochemical parameters related to cardiovascular risk, a digital, standard, 12-lead electrocardiogram (ECG) and 5-min ECG monitoring were recorded. Smart ECG measurement and interpretation programs were used for the automated measurement and interpretation of ECG intervals. Autonomic nervous system tone was estimated with the HRV—standard deviation of normal to normal intervals (SDNN)—in surface ECG. Pulse pressure was calculated as the difference between systolic and diastolic blood pressures. Pulse pressure showed a positive association with age, systolic blood pressure levels, and presence of diabetes mellitus (all $P < 0.001$) and an inverse correlation with logSDNN. Multiadjusted logistic regression analysis revealed that 10-unit increase in SDNN values decreases by 26 % the likelihood of having PP above 70 mmHg; when the analysis was stratified according to hypertension status, the relationship remained significant only among non-hypertensive individuals. These data support the hypothesis that cardiac sympathovagal disturbance correlates with impaired elasticity properties of aorta, indicating parallel impairment in cardiac autonomic modulation and mechanical vessel wall properties in elderly non-hypertensive individuals.

Keywords Aortic artery compliance · Aortic distensibility · Autonomic nervous system · Autonomic modulation · Heart rate variability · Mechanical vessel wall properties

C. Chrysohoou (✉) · J. Skoumas · E. Oikonomou · D. Tsiachris · V. Metaxa · S. Lagoudakou · J. Felekos · C. Masoura · S. Athanassopoulou · H. Kosyfa · C. Pitsavos · C. Stefanadis
First Cardiology Clinic, Hippokration Hospital, University of Athens Medical School, 46 Paleon Polemiston Street, Glyfada, Attica, 166-74 Athens, Greece
e-mail: chrysohoou@usa.net

Introduction

The mechanical properties of the aorta have been recognized as important determinants of blood pressure regulation and left ventricular performance [1]. Aging causes progressive stiffness, dilatation, and lengthening of the arteries, while low arterial distensibility has long been recognized as an indicator of atherosclerosis and future cardiovascular events [2, 3]. Systolic and diastolic blood pressures have also been related with increased cardiovascular mortality [4]. By increasing the load on the heart, hypertension leads to vascular changes and neurohormonal activation, which causes increases in vascular stiffness and reduced elasticity. Thus, diastolic blood pressure (BP) rises with increased peripheral arterial resistance and falls with increased central artery stiffness; the relative contributions of these two opposing forces determine diastolic BP and, ultimately, pulse pressure (PP) [5]. In the Framingham Heart Study, hypertension-related mortality was best correlated with PP, while Benetos et al. reported that a high PP was an independent predictor of coronary mortality among 19,000 French men [6, 7].

The mechanical behavior of the aortic wall is complex and is determined by several factors [8]. Sympathetic stimulation might also play an important role [9]. Heart rate variability (HRV) provides an accurate view of the influence of autonomic nervous system on heart activity, while low HRV has been related with increased cardiovascular morbidity and mortality [10–12]. Because of the lack of literature regarding parallel alterations in autonomic function and aortic elastic properties in elderly individuals, the aim of this study was to evaluate in a population of elderly individuals, without known cardiovascular disease, the relation between aortic artery distensibility, expressed by PP and autonomic function expressed by HRV, according to hypertension status. In this study we decided to exclude individuals with known atherosclerotic disease, as it is known that coronary heart disease and its therapeutic approaches influence HRV, BP levels, and aortic distensibility in a variable way, while controlling for such factors in the statistical models cannot eliminate residual confounding. This work is part of a large project, the Ikaria Study [13], involving 1420 individuals permanently residing on Ikaria Island, now recognized worldwide as having among the highest longevity and lowest mortality rates from cardiovascular disease [14].

Materials and methods

Study sample

The Ikaria Epidemiological Study has been carried out on the island of Ikaria, from June to October 2009; during this period 1420 middle-aged and elderly inhabitants (65 ± 12 years) were voluntarily enrolled in the study [15, 16]. All participants were interviewed by trained personnel (i.e., cardiologists, general practitioners, dietitians, and nurses) who used a standard questionnaire.

Bioethics

All subjects were informed about the aims of the study and gave their written informed consent. The study was approved by the local Ethics Committee of our institution and was carried out in accordance with the Declaration of Helsinki (1989).

Designation of electrocardiographic measurements

All participants underwent digital electrocardiography, and a standard 12-lead electrocardiogram (ECG) was recorded (10 s duration) using an SE-1010 PC ECG (EDAN Instruments, Singapore). The Smart ECG Measurement and Interpretation Program (SEMIP version 1.5) was used for the automated measurement and interpretation of ECG intervals [17]. In addition, after a 10-min resting period, a 5-min ECG recording of lead II, at a speed of 100 samples/s, was acquired in subjects lying in the supine position. Analysis of HRV was performed in accordance with current international guidelines [18], and standard deviation of normal to normal intervals (SDNN) was measured. At present, spectral analysis methods of HRV are widely used. The use of spectral analysis allows the quantitative assessment of the different frequencies that constitute heart rate oscillation, and the graphic visualization of the relationships between the different components of heart rate, which reflect the activity of certain regulatory components [19]. The base of the low-frequency (LF) components is the activity of the vasomotor center and the sympathetic system.

Sociodemographic and lifestyle variables

The survey included basic demographic items, such as age, gender, and anthropometric measurements, such as weight and height, which were measured following standard procedures. Body mass index (BMI) was then calculated, and obesity was defined as a BMI >29.9 kg/m^2. Current smokers were defined as those who smoked at least one cigarette per day; never-smokers those who has never tried a cigarette in their life; and former smokers were defined as those who had stopped smoking for at least 1 year. Occasional smokers (<7 cigarettes per week) were recorded and combined with current smokers because of the small sample size. Physical activity was evaluated using the shortened version of the self-reported International Physical Activity Questionnaire (IPAQ) [20]. Frequency (times per week), duration (minutes per time), and intensity of physical activity during sports, occupation, and/or free-time activities were assessed. In accordance with the standard IPAQ scoring procedures, participants were classified into one of the following groups: upper tertile: "vigorous" physical activity (>2500 MET/min/week or expended calories >7 kcal/min, i.e., walking briskly uphill, cycling fast or racing, swimming fast crawl, etc.); middle tertile: "moderate" physical activity (500–2500 MET/min/week or expended calories 4–7 kcal/min, i.e., walking briskly, cycling outdoors, swimming with moderate effort, etc.); lower tertile: "low" physical activity (<500 MET/min/week or expended calories <4 kcal/min, i.e., walking slowly, cycling slowly, light stretching exercise, etc.).

Clinical and biochemical characteristics

Resting arterial BP was measured three times in the right arm, at the end of the physical examination with the subject in the sitting position. Patients whose average BP levels were greater or equal to 140/90 mmHg or were under antihypertensive medication were classified as having hypertension. Fasting blood samples were collected from 08:00 to 10:00 h. All the biochemical evaluation was carried out in the same laboratory that followed the criteria of the World Health Organization Reference Laboratories. Blood lipid examinations (serum total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides) were measured using a chromatographic enzymatic method in an RA-1000 automatic analyzer.

Hypercholesterolemia was defined as total serum cholesterol levels >200 mg/dl or the use of lipid-lowering agents. Finally, diabetes mellitus type 2 was determined by fasting plasma glucose tests and was analyzed in accordance with the American Diabetes Association diagnostic criteria (fasting blood glucose levels >125 mg/dl or use of special medication indicating the presence of diabetes) [21]. Cardiovascular disease was defined as known prior history of hospitalization for heart disease (acute coronary syndrome, chronic angina, peripheral arteries disease) or stroke, or alterations on ECG suggestive of prior myocardial infarction.

Statistical analysis

Continuous variables with normal distribution are presented as mean ± standard deviation. Categorical variables are presented as frequencies. The independent-samples *t* test was used for comparisons between means of normally distributed continuous variables. Associations between categorical variables were tested by forming contingency tables and performing Chi-square tests. Investigation of differences between clinical variables and PP groups was performed with analysis of variance (ANOVA), after controlling for equality of variances (homoscedacity) or with generalized linear regression models for fixed effects, after adjustment for several potential confounders. Pearson or Spearman correlation coefficients were used, as appropriate, to test for correlations between continuous variables. The results derived from linear regression model are presented as *b*-coefficients, standardized coefficients (beta), and 95 % confidence interval or standard errors of the coefficients. Normality of residuals, homoscedacity, and colinearity were evaluated by plotting standardized residuals against the predicted values. Differences in values between particular subgroups according to PP were tested using post hoc analysis after Bonferroni correction. In addition, logistic regression analysis estimated the odds of a PP >70 mmHg after controlling for potential confounders. All reported *P* values were based on two-sided hypotheses, and a value of 5 % was considered as statistically significant. All statistical calculations were performed using SPSS software (version 18.0; SPSS, Chicago, IL, USA).

Table 1 Characteristics of the cardiovascular disease-free elderly participants from the Ikaria Study (n = 382)

Age (years)	74 ± 6
Current smokers (%)	18
Physical activity (%)	83
Body mass index (kg/m^2)	28 ± 4
Hypertension (%)	71
Hypercholesterolemia (%)	67
Diabetes mellitus (%)	25
Obesity (%)	29
Heart rate variability (SDNN) (ms)	73 ± 54
Systolic blood pressure (mmHg)	145 ± 19.4
Diastolic blood pressure (mmHg)	80.2 ± 11.2
Pulse pressure (mmHg)	64.8 ± 17
Heart rate (beats/min)	65 ± 10

SDNN standard deviation of normal to normal intervals

Results

Demographic and clinical characteristics

After deletion of cases with missing values, the studied sample consisted of 429 individuals (208 men, mean age 75 ± 6 years old, and 221 women, mean age 75 ± 6 years old). From these, 47 individuals with known cardiovascular disease were excluded, so the study sample finally consisted of 382 individuals (47 % males). Demographic, clinical, and behavioral characteristics of the participants are presented in (Table 1).

Regarding the PP tertile, those in the highest tertile showed higher prevalence of hypertension and higher prevalence of diabetes mellitus, while showing no significant difference regarding type of medication, as well as other clinical and lifestyle characteristics, compared with those in the lowest tertile of PP (i.e., good aortic distensibility) (Table 2).

Pulse pressure and electrocardiographic indices of heart rate variability

In the univariate analysis, PP showed a positive association with age, diabetes mellitus, systolic BP levels, and BMI (all *P* values <0.001).

Linear regression analysis with PP as the dependent variable revealed that PP was positively associated with age (b ± SE: 0.471 ± 0.142, beta = 0.175, P = 0.001), diabetes mellitus (b ± SE: 6.122 ± 2.015, beta = 0.157, P = 0.003), and hypertension (8.169 ± 1.917, beta = 0.22, P = 0.001); and was inversely associated with logSDNN (b ± SE: −2.296 ± 1.216, beta = −0.099, P = 0.05) and LF

Table 2 Descriptive characteristics of the participants according to the tertile of pulse pressure ($n = 382$)

Pulse pressure	1st tertile (<57 mmHg)	2nd tertile (57–70 mmHg)	3rd tertile (>70 mmHg)	*P* value
Age (years)	73.0 ± 5.6	74.5 ± 6.3	76.3 ± 6.6	0.002
Male gender (%)	41	50	48	0.32
Body mass index (kg/m^2)	27.6 ± 4	28.4 ± 4	28 ± 4	0.37
Smoke (%)	16	22	16	0.38
Hypertension (%)	56	73	80	0.001
Hypercholesterolemia (%)	69	67	59	0.26
HF (ms^2)	102 ± 24	103 ± 22	80 ± 18	0.73
LF (ms^2)	50 ± 9	48 ± 8	48 ± 12	0.98
SDNN (ms)	72 ± 53	71 ± 52	68 ± 54	0.88
Diabetes mellitus (%)	16	26	35	0.001
Physical activity (%)	82	88	83	0.29
Heart rate (beats/min)	65 ± 9	64 ± 10	65 ± 12	0.61
SBP (mmHg)	128 ± 13	144 ± 11	164 ± 16	0.001
Obese (%)	25	36	25	0.13
β-Blockers (%)	8	12	15	0.3
ACE-I (%)	79	93	85	0.11
Calcium antagonists (%)	31	40	44	0.51
Diuretics (%)	56	60	45	0.38

ANOVA was used for continuous variables and Chi-square test for categorical variables

ACE-I angiotensin-converting enzyme inhibitors, *HF* high-frequency component of spectral analysis of R–R intervals, *LF* low-frequency component of spectral analysis of R–R intervals, *SBP* systolic blood pressure, *SDNN* standard deviation of normal to normal intervals

(b ± SE: −0.791 ± 0.456, beta = −0.09, $P = 0.08$). Furthermore, logistic regression analysis among non-hypertensive individuals revealed that a 10-unit increase in SDNN values decreases by 26 % the likelihood of having PP in the upper tertile of the sample distribution, after controlling for age, sex, physical activity status, diabetes mellitus, hypercholesterolemia, BMI, and smoking habits (Table 3); this relationship was not evident in hypertensive individuals. The significant relationship from the logistic regression between PP and HRV in non-hypertensive subjects remained significant, even after adjustment was made for β-blocker uptake (odds ratio (OR) 0.97, 95% confidence interval (CI) 0.946–0.994, $P = 0.01$).

Discussion

The present study revealed that in elderly non-hypertensive individuals who are permanent inhabitants of Ikaria Island, decreased HRV correlated with impaired aortic elastic properties, indicating parallel impairment in cardiac autonomic modulation and mechanical vessel wall properties. This work is part of the study conducted on Ikaria Island,

Table 3 Results from logistic regression analysis with pulse pressure above 70 mmHg (upper tertile of pulse pressure distribution) as the dependent variable in non-hypertensive individuals

	Odds ratio	95 % Confidence interval	*P* value
SDNN (per 10 unit)	0.74	0.54–0.90	0.01
Age (per 1 year)	0.99	0.89–1.10	0.89
Gender (men vs. women)	0.86	0.25–2.91	0.81
Diabetes mellitus (yes vs. no)	4.09	0.99–17.19	0.054
Hypercholesterolemia (yes vs. no)	0.171	0.04–0.71	0.02
Physical activity (yes vs. no)	0.51	0.07–3.38	0.48
Body mass index (per 1 kg/m^2)	0.91	0.75–1.09	0.32
Smoking (yes vs. no)	1.189	0.02–1.30	0.09

SDNN standard deviation of normal to normal intervals

which aims to evaluate clinical characteristics and lifestyle factors related with longevity [22], as Ikaria has been recognized as one of the main areas worldwide with a high percentage of longer-living persons.

During the human lifetime several alterations occur in morphology and function of the cardiovascular system. With aging, arteries become stiffer and aortic mechanical properties are altered. The loss of arterial compliance has been proposed as a possible mechanism in the initiation, progression, and etiology of arterial hypertension, and as a prognostic marker of cardiovascular disease. This has also direct consequences on BP transmission through the aorta and cardiac function. Pulse pressure reflects a simple noninvasive approach for the evaluation of aortic dilatation. At middle age and thereafter, systolic BP rises while diastolic BP remains unaltered or even falls with increased central artery stiffness. In this way the difference between these two components, which represent PP increase, acts as an index of limited elasticity. This also has consequences for cardiac function, as left ventricular load is influenced by the increase in cardiac afterload owing to the increased peripheral resistance [23–25]. It would be favorable for the cardiac function to diminish arterial impedance, either by decreasing systolic BP in the case of arterial hypertension, or by decreasing PP through improvement in aortic distensibility [26]. The mechanical behavior of the aorta is complex, and changes in vascular tone by sympathetic stimulation have been shown to play an important role. It has been shown that sympathetic activation regulates smooth muscle tone in resistance medium and larger arteries, such as the carotid artery [25]. This influence may play an important role in the modification of elastic properties of even larger arteries, such as the aorta. In previous studies, lower arterial compliance was seen in the presence of an augmentation in sympathovagal balance, which further reduces distensibility of small, medium, and large arteries, resulting in a tonic restraint of elastic and resistance-type vessels [27]. From this perspective, alterations in HRV, which reflect autonomic system balance, may influence aortic elastic properties beyond aging, in cardiovascular disease-free elderly individuals. In the present study, SDNN was used as an indicator of HRV, reflecting autonomic system balance. Heart rate variability seems to affect aortic elastic properties, showing an inverse relationship with PP value. In another study including 25 healthy volunteers, whose aortic strain, distensibility, and stiffness index were measured by echocardiography, heart rate response to deep breathing, characterizing parasympathetic function, showed low to moderate correlations with aortic function [28]. In addition, in a more recent study of 356 hypertensive patients, office and ambulatory heart rate were directly associated with pulse wave velocity, while a lesser decrease in nocturnal heart rate was associated with increased arterial stiffness [29]. A possible explanation for this relationship is that the baroreceptor response to sustained pressure on the arterial side of the circulation produces an afferent connection to the vasomotor and cardioinhibitory areas, and the efferent pathways from these areas constitute a reflex feedback mechanism that operates to stabilize the BP and heart rate. When the arterial system is less compliant, this results in a continuous increased stretch of the baroreceptors, causing a downregulation, altering autonomic function by lowering parasympathetic modulation and increasing sympathetic outflow. On the other hand, Sonesson et al. [30], using sympathetic stimulation induced by lower body negative pressure and invasive evaluation of abdominal aorta distensibility in 19 healthy volunteers, failed to reveal any significant impact of sympathetic stimulation on elastic properties of the abdominal aorta.

In the elderly population without hypertension and cardiovascular disease from the Ikaria study, aortic distensibility, as measured by PP levels, was associated with HRV and diabetes mellitus. This finding is in accordance with those of previous studies, since diabetes mellitus has been shown to accelerate the atherosclerosis process and arterial aging [31, 32].

Inevitably, our study was subject to some limitations. The cross-sectional design limits one from making causal inferences about the relationship between PP and HRV. In addition, the measurement of arterial pressure was performed at only one visit and on the right arm, which may hide the risk of misdiagnosed hypertension in some individuals with right subclavian artery atherosclerosis. As subclinical atherosclerosis is a common finding in elderly individuals (carotid and abdominal aorta atherosclerosis), in this study we focused only on those individuals without clinical evidence of cardiovascular disease. Finally, HRV was measured during only a 5-min ECG recording.

Conclusion

The results of this study documented a possible relationship between autonomic system dysfunction and mechanical properties of the aorta. It seems that decreased HRV confers aortic stiffness in elderly non-hypertensive individuals in the absence of known cardiovascular disease, indicating the role of sympathetic activation and elasticity of large arteries. These results may indicate a possible modulation of activation of the adrenergic system conferred through improvement of arterial elasticity, which may improve human longevity.

Acknowledgments We are particularly grateful to the men and women from the island of Ikaria, who participated in and collaborated on this survey. We would like to especially thank Konstantinos Chronakis for his technical support. We also wish to express our gratitude to the following: Mr Karoutsos (Mayor of Raches), Mr Stamoulos (Mayor of Evdilos), Mr Teskos (Mayor of St Kyrikos), Dr K. Katte, Dr B. Mylonakis, Mrs S. Spanou (Health Center of Eudilos), Dr S. Mamatas, Mr Skaros (General Hospital of St. Kyrikos), and the following field investigators: I. Andreou, D. Aragiannis, E. Christoforatou, K. Dimitriadis, N. Galiatsatos, E. Giakoumi, E. Gialafos, M. Kambaxis, P. Kourkouti, S. Kyvelou, G. Lazaros, D. Maragiannis, A. Margazas, G. Marinos, A. Patialiakas, S. Plytaria, E. Poulidakis, B. Psaroudaki, D. Roussos, G. Siasos, M. Striggou, C. Sykaras, G. Triantafyllou, G. Tsitsinakis, A. Valatsou, D. Vasiliou, G. Vogiatzi, S. Vogiatzoglou, M. Xynogala, M. Zaromytidou, C. Zisimos, V. Zoulia.

References

1. Bader H (1963) Anatomy and physiology of the vascular wall. In: Hamilton WF, Dow P (eds) Handbook of physiology. Part II. Circulation. American Physiology Society, Washington DC, pp 875–876
2. Vlachopoulos C, Aznaouridis K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 55:1318–1327
3. Triantafyllidi H, Rizos I, Rallidis L, Tsikrikas S, Triantafyllis A, Ikonomidis I, Panou F, Rigopoulos A, Kremastinos DT (2010) Aortic distensibility associates with increased ascending thoracic aorta diameter and left ventricular diastolic dysfunction in patients with coronary artery ectasia. Heart Vessels 25:187–194
4. van den Hoogen PC, Feskens EJ, Nagelkerke NJ, Menotti A, Nissinen A, Kromhout D (2000) The relation between blood pressure and mortality due to coronary heart disease among men in different parts of the world. Seven Countries Study Research Group. N Engl J Med 342:1–8
5. O'Rourke M (1990) Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. Hypertension 15:339–347
6. Franklin SS, Khan SA, Wong ND, Larson MG, Levy D (1999) Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. Circulation 100:354–360
7. Benetos A, Safar M, Rudnichi A, Smulyan H, Richard JL, Ducimetieere P, Guize L (1997) Pulse pressure: a predictor of long-term cardiovascular mortality in a French male population. Hypertension 30:1410–1415
8. Oishi Y, Miyoshi H, Iuchi A, Nagase N, Ara N, Oki T (2012) Vascular aging of common carotid artery and abdominal aorta in

clinically normal individuals and preclinical patients with cardiovascular risk factors: diagnostic value of two-dimensional speckle-tracking echocardiography. Heart Vessels. doi:10.1007/s00380-011-0229-y
9. Dobrin P (1983) Vascular mechanics. In: Shepard JT, Abbound FM (eds) Handbook of physiology. Part I. Peripheral circulation and organ blood flow. Williams and Wilkins, Baltimore, pp 65–102
10. Galinier M, Pathak A, Fourcade J, Androdias C, Curnier D, Varnous S, Boveda S, Massabuau P, Fauvel M, Senard JM, Bounhoure JP (2000) Depressed low frequency power of heart rate variability as an independent predictor of sudden death in chronic heart failure. Eur Heart J 21:475–482
11. Malik M, Camm AJ (eds) (1995) Heart rate variability. Futura, Armonk, p 543
12. Kasamaki Y, Izumi Y, Ozawa Y, Ohta M, Tano A, Watanabe I, Hirayama A, Nakayama T, Kawamura H, Himit D, Mahemuti M, Sezai A (2012) Relationship between status of plasma atrial natriuretic peptide and heart rate variability in human subjects. Heart Vessels. doi:10.1007/s00380-012-0237-6
13. Stefanadis CI (2011) Unveiling the secrets of longevity: the Ikaria study. Hellenic J Cardiol 52:479–480
14. The Blue Zones. http://www.bluezones.com. Accessed 31 May 2011
15. Panagiotakos DB, Chrysohoou C, Siasos G, Zisimos K, Skoumas J, Pitsavos C, Stefanadis C (2011) Sociodemographic and lifestyle statistics of oldest old people (>80 years) living in Ikaria island: the Ikaria study. Cardiol Res Pract 2011:679187
16. Chrysohoou C, Skoumas J, Pitsavos C, Masoura C, Siasos G, Galiatsatos N, Psaltopoulou T, Mylonakis C, Margazas A, Kyvelou S, Mamatas S, Panagiotakos D, Stefanadis C (2011) Long-term adherence to the Mediterranean diet reduces the prevalence of hyperuricaemia in elderly individuals, without known cardiovascular disease: the Ikaria study. Maturitas 70:58–64
17. Tsiachris D, Chrysohoou C, Oikonomou E, Lazaros G, Dimitriadis K, Maragiannis D, Roussos D, Andreou I, Tsantilas A, Christoforatou E, Pitsavos C, Panagiotakos D, Stefanadis C (2011) Distinct role of electrocardiographic criteria in echocardiographic diagnosis of left ventricular hypertrophy according to age, in the general population: the Ikaria Study. J Hypertens 29:1624–1632
18. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Eur Heart J 17:354–381
19. Nussinovitch U, Elishkevitz KP, Kaminer K, Nussinovitch M, Segev S, Volovitz B, Nussinovitch N (2011) The efficiency of 10-second resting heart rate for the evaluation of short-term heart rate variability indices. Pacing Clin Electrophysiol 34:1498–1502
20. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P (2003) International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35:1381–1395
21. Schnell O, Otter W, Standl E (2009) The Munich Myocardial Infarction Registry: translating the European Society of Cardiology (ESC) and European Association for the Study of Diabetes (EASD) guidelines on diabetes, pre-diabetes, and cardiovascular disease into clinical practice. Diabetes Care 32(Suppl 2):S326–S330
22. Chrysohoou C, Stefanadis C, Pitsavos C, Panagiotakos D, Das UN, Giugliano D (2011) Cardiovascular disease-related lifestyle factors and longevity. Cardiol Res Pract 2011:386892
23. O'Rourke M (1995) Mechanical principles in arterial disease. Hypertension 26:2–9
24. Kawasaki T, Sasayama S, Yagi S, Asakawa T, Hirai T (1987) Non-invasive assessment of the age related changes in stiffness of major branches of the human arteries. Cardiovasc Res 21:678–687
25. Benetos A, Laurent S, Hoeks AP, Boutouyrie PH, Safar ME (1993) Arterial alterations with aging and high blood pressure. A noninvasive study of carotid and femoral arteries. Arterioscler Thromb 13:90–97
26. Stefanadis C, Tsiamis E, Dernellis J, Toutouzas P (1999) Effect of estrogen on aortic function in postmenopausal women. Am J Physiol 276:H658–H662
27. Zion AS, Bond V, Adams RG, Williams D, Fullilove RE, Sloan RP, Bartels MN, Downey JA, De Meersman RE (2003) Low arterial compliance in young African–American males. Am J Physiol Heart Circ Physiol 285:H457–H462
28. Nemes A, Takacs R, Gavaller H, Varkonyi TT, Wittmann T, Forster T, Lengyel C (2010) Correlations between aortic stiffness and parasympathetic autonomic function in healthy volunteers. Can J Physiol Pharmacol 88:1166–1171
29. Garcia-Ortiz L, Garcia-Garcia A, Ramos-Delgado E, Patino-Alonso MC, Recio-Rodriguez JI, Rodriguez-Sanchez E, Gomez-Marcos MA (2011) Relationships of night/day heart rate ratio with carotid intima media thickness and markers of arterial stiffness. Atherosclerosis 217:420–426
30. Sonesson B, Vernersson E, Hansen F, Lanne T (1997) Influence of sympathetic stimulation on the mechanical properties of the aorta in humans. Acta Physiol Scand 159:139–145
31. Payvandi L, Dyer A, McPherson D, Ades P, Stein J, Liu K, Ferrucci L, Criqui MH, Guralnik JM, Lloyd-Jones D, Kibbe MR, Liang ST, Kane B, Pearce WH, Verta M, McCarthy WJ, Schneider JR, Shroff A, McDermott MM (2009) Physical activity during daily life and brachial artery flow-mediated dilation in peripheral arterial disease. Vasc Med 14:193–201
32. Oikonomou E, Chrysohoou C, Tsiachris D, Vogiatzi G, Gialafos E, Marinos G, Tsitsinakis G, Dimitriadis K, Tousoulis D, Pitsavos C, Stefanadis C (2011) Gender variation of exercise-induced anti-arrhythmic protection: the Ikaria Study. QJM 104:1035–1043