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Common and emergent factors associated with hypertension control in Romania. Data from SEPHAR II Study

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Abstract

Romania is an East European country with high mortality rates for ischemic heart and cerebrovascular diseases largely attributable to an increased level of uncontrolled hypertension. We aimed to analyze the data of SEPHAR II epidemiological study in order to identify the factors associated with treatment control in Romanian hypertensives. A total of 1975 subjects, selected on the base of stratified proportional sampling and consented to participate in the study, were evaluated during the two study visits. Hypertension was diagnosed according to current ESH-ESC guidelines (≥140/80 mmHg). High blood pressure (BP) variability was defined as visit-to-visit standard deviation (s.d.) of systolic blood pressure (SBP) situated in the 4th percentile with values ≥8.49 mmHg (Q4_SBP_s.d.). Arterial stiffness recordings were realized with an oscillometric device (Medexpert Arteriograph IrDA). According to the multivariate analysis for the validation of parameters associated with lack of BP control were found significant: a low level of education [OR=2.86; 95% confidence interval (CI) 1.84-4.45, p<0.0001] or income [OR=1.04; 95% CI 1.03-1.05, p<0.0001], increased aortic pulse wave velocity (PWVao) [OR=1.32; 95% CI 1.23-1.43, p<0.0001], high BP variability [OR=0.15; 95% CI 0.07-0.33, p<0.0001] and treatment with less than 3 antihypertensive or with ≥ 3 drugs, not including a diuretic [OR=1.91; 95% CI 0.95-3.84, p<0.031]. These results are confirming the association of uncontrolled hypertension with a low level of education or income, are highlighting the efficiency of ≥ 3 drug associations including a diuretic and are launching the attention of the effects of arterial stiffness and SBP variability on BP levels under antihypertensive treatment.

Keywords: arterial hypertension, blood pressure control, survey

Introduction

Arterial hypertension was assigned the leading risk factor by Global Burden of Disease Study in 2010, responsible for 9.4 million deaths each year [1, 2]. Despite an impressive arsenal of drugs for this condition the therapeutic control of arterial

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hypertension remains unsatisfactory [3]. Persistence of high blood pressure under antihypertensive treatment is associated with increased cardiovascular risk [4] and uncontrolled hypertension remains the main cause of fatal stroke, as it was reconfirmed in PREV-ICTUS study [5].

Romania is an East European country with high mortality rates for ischemic heart and cerebrovascular diseases [6]. This feature is largely attributable to an increased level of uncontrolled hypertension. SEPHAR (**S**tudy for the **E**valuation of **P**revalence of **H**ypertension and C**a**rdiovascular **R**isk in Romania) and SEPHAR II surveys are two epidemiological studies conducted in Romania in 2005 and 2011-2012 respectively, addressing the prevalence of arterial hypertension and of the associated risk factors in a representative sample for the adult population of this country. These studies revealed an important improvement in the proportion of treated hypertensives - from 39% to 59%, while the rate of treatment control rose only from 20% to 25% in these seven years [7]. Therefore, we aimed to analyze the data of SEPHAR II study in order to identify the factors associated with hypertension control in treated hypertensives.

Methods

SEPHAR II is a cross-sectional national survey, approved by the local Ethics Committee.

According to the last census data, reported by the National Institute of Statistics, the adult stable population in Romania accounted 16 833 541 people in 2011 [7]. With a previously estimated 40% prevalence of arterial hypertension and a maximum error of ±2.18% at a confidence level of 95% the minimum required sample size for SEPHAR II study had to include 1942 individuals [8].

The sample selection was based on the multi stratified proportional sampling procedure and it is detailed elsewhere [9, 10]. At the end of the study 1975 individuals selected and consented to participate in the study had eligible data for analysis. These individuals have been evaluated between 2011- 2012 in two study visits with a 76 item questionnaire, anthropometric parameters and three blood pressure (BP) measurements recorded on visit 1 and with laboratory workup, BP, electrocardiography (ECG) and arterial stiffness measurements on visit 2.

BP measurements were realized with an automatic oscillometric device model A&D UA 95 Plus, certified by the Association for the Advancement of Medical Instrumentation and European Society of Hypertension. At each study visit three consecutive BP measurements were taken at time interval of at least 1 min, with a cuff size adapted to arm circumference. Hypertension was defined as systolic blood pressure (SBP) at least 140 mmHg and or diastolic blood pressure (DBP) at least 90 mmHg at both study visits, using the arithmetic mean of the second and third BP measurements of each study visit or previously diagnosed hypertension. Hypertension control was considered for SBP less than 140 mmHg and DPB less than 90 mmHg in subjects under current treatment, recording the maximum value between the two SBP/DBP values from each visit. Visit-to-visit BP variability was assessed as the standard deviation (SD) of the mean SBP [11-13]. The ECG recording was performed with a General Electric CardioSoft MAC600 1.02 device and the arterial stiffness parameters – aortic augmentation index (AIXao) and aortic pulse wave velocity (PWVao) – were evaluated using Medexpert Arteriograph IrDA system.

Diabetes mellitus (DM) was stated in conformity with the current definition of the American Diabetes Association at the time of database analysis [14]. Obesity was recorded as a body mass index ≥30 kg/m^2 and visceral obesity when a waist-to-hip ratio was >0.95 in males and >0.85 in females. Metabolic syndrome and the reference values for lipids were defined according to NCEP ATP III criteria [15]. Left ventricular hypertrophy was assessed by Cornell product ≥2440 mm x ms on 12-lead ECG. Renal impairment was affirmed and classified based on eGFR$_{MDRD}$ and the presence or absence of albuminuria. Cardiovascular risk categories were evaluated according to the current ESH/ESC risk stratification chart [3].

A large variety of factors have been associated with hypertension control in different populational studies. Our data allowed us to evaluate the following parameters in regard with hypertension control: age, gender, level of education and income, area of residence, medical insurance status, conventional risk factors or emerging risk factors - arterial stiffness parameters or BP variability, target organ damage, history of overt cardiovascular disease, reported lifestyle changes and the characteristics of antihypertensive treatment.

A descriptive analysis (means, medians, standard deviations, and range for continuous data and frequency analysis for categorical data) was performed for all the target variables. Kolmogorov-Smirnov test was used to analyze continuous data distribution, according to which independent samples T test or Mann-Whitney U test were further used in analysis for differences between means of 2 independent

Table 1. Distribution of variables between patients with controlled blood pressure in comparison with those with uncontrolled blood pressure.

	Controlled BP values N = 118	Uncontrolled BP values N = 354	p value for differences	r_s for correlation with BP control	p value for correlation with BP control
SOCIODEMOGRAPHIC CHARACTERISTICS					
Age (years)	60.05 ± 12.25	61.39 ± 11.16	NS*		NS
Gender				-0.043	NS
• Female	69 (58.8)	224 (63.3)	NS**		
• Male	49 (41.5)	130 (36.7)	NS**		
Income (RON)	800 (200-5000)	700 (0-8472)	0.021**	-0.110	0.021
Area of residence				-0.169	<0.0001
• Rural	21 (17.8)	127 (35.9)	<0.0001		
• Urban	97 (82.2)	227 (64.1)	<0.0001		
Level of education				-0.141	0.002
• No education	3 (2.5)	11 (3.1)	0.003		
• Primary	24 (20.3)	99 (28)	0.003		
• Secondary	59 (50)	199 (56.2)	0.003		
• High	32 (27.1)	45 (12.7)	0.003		
CONVENTIONAL CV RISK FACTORS					
Obesity					
• by BMI	52 (44.4)	174 (49.9)	NS**	0.047	NS
• by WC	78 (66.7)	241 (68.3)	NS**	0.015	NS
Smoking	19 (26.4)	53 (15.1)	NS**	0.014	NS
DM	31 (26.3)	89 (25.2)	NS**	0.011	NS
Hypercholesterolemia	50 (42.4)	219 (81.4)	<0.0001**	0.174	<0.0001
High LDL-cholesterol	51 (43.2)	203 (57.7)	0.006**	0.126	0.006
Hypertriglyceridemia	3 (30)	7 (70)	NS**	0.017	NS
Mixed dyslipidemia	37 (31.4)	116 (33)	NS**	0.015	NS
EMERGING CV RISK FACTORS					
Target organ damage					
• LVH on ECG	4 (3.7)	13 (4.5)	NS**	0.016	NS
• UACR: 30-300mg/g	9 (7.6)	29 (8.3)	NS**	0.011	NS
• PWVao	9.94±2.15	10.53±2.37	0.049*	-0.135	0.026
• PWVao >10m/s	34 (47.9)	104 (52.5)	NS**	0.041	NS
• Q4_SBP_s.d	19 (16.1)	155 (43.8)	<0.0001**	0.248	<0.0001
OTHER FACTORS					
Antihypertensive treatment ≥3 drugs (D)	44 (37.3)	98 (27.2)	0.033**	-0.191	0.049
Self-evaluation of BP values				0.217	<0.0001
• Normal/low	62 (56.9)	101 (32)	<0.0001**		
• High	39 (35.8)	196 (62)	<0.0001**		
• Don't know	8 (7.3)	19 (6)	<0.0001**		

Values are presented as mean±s.d. for parametric continuous variable, median (range) for nonparametric continuous variables, and total number (percent) for categorical variables; *independent samples t test; **chi square test; ***Mann-Whitney U test; NS: non statistical significant (p >0,05); rs: Sperman correlation coefficient; BP: blood pressure; BMI: body mass index;, WC: waist circumference; DM: diabetes mellitus; LVH: left ventricular hypertrophy; ECG: electrocardiogram; UACR: urinary albumin to creatinine ratio; PWVao: aortic puls-wave velocity; Q4_SBP_s.d.: 4th quartile of SBP s.d. distribution (SBP' s.d values > 8.49mmHg); D: diuretic; CV: cardiovascular

study subgroups. Chi-square test was used to analyze differences between categorical data.

Bivariate correlation analysis (Spearman correlation coefficient calculation) was used to validate the association between BP control and variables for which statistically significant differences between the 2 study subgroups.

Binary logistic regression using a stepwise Likelihood ratio method including multicolliniarity testing (tolerance less than 0.1 and VIF value greater than 10) was used for validation of predictors of BP control in treated hypertensive patients (as dependent variable).

Performance of the prediction model was assessed by ROC curve (Receiver Operating Characteristics).

Statistical analysis was performed using IBM SPSS Statistics 20.0 software at a chosen significance threshold of $p < 0.05$.

Results

Distribution of variables between patients with controlled in comparison with those with uncontrolled hypertension are presented in Table 1. Two remarks are worth making. Firstly, *BP control was not correlated* with age, gender, associated cardiovascular risk factors (except for dyslipidemia), left ventricular hypertrophy on ECG or microalbuminuria (UACR=30-300 mg/g). Secondly, *uncontrolled blood pressure was positively correlated* with rural area of residence, a lower level of education or income, hypercholesterolemia consisting in high concentrations of plasmatic LDL-cholesterol, increased PWVao, high BP variability defined as visit-to-visit standard deviation of SBP situated in the 4th percentile, more precisely ≥8.49 mmHg (Q4_SBP_s.d.) and self-estimation of BP values as being high, whereas *was inversely correlated* with antihypertensive treatment based on ≥3 drugs, including a diuretic.

After multivariate analysis for the validation of parameters associated with lack of BP control remained significant only: a low level of education or income, increased PWVao or Q4-_SBP_s.d., treatment with less than 3 antihypertensive or with ≥3 drugs, not including a diuretic and self-estimation of BP as being high (Table 2). The model has 75.9% power of correctly predicting uncontrolled hypertension (Figure 1).

Discussion

It is difficult to compare BP control in different countries due to a high disparity between studies: variable age groups and categories of subjects, different blood pressure measurement methodologies, and, from the previous to the current ESH Guidelines for the management of arterial hypertension, different thresholds of control depending on risk category [3, 16-17].

SEPHAR II study, conducted on a representative sample for the Romanian adult population during 2011-2012, showed that only 24% of patients are attending target blood pressure values under antihypertensive treatment [3]. Similar results have been previously reported by BP-CARE survey, but on treated hypertensives evaluated in outpatient offices from nine Central and Eastern European countries, indicating a rate of 26% for hypertension control in Romania [18]. The most appropriate comparison of BP control

Predictors	B	Wald	P value	OR	95% CI for OR
Income	0.03	47.19	<0.0001	1.04	1.03-1.05
Area of residence	0.37	0.82	0.365	1.45	0.65 – 3.25
ED_cat	1.05	21.74	< 0.0001	2.86	1.84-4.45
Hypercholesterolemia	0.59	1.69	0.193	0.56	0.23-1.34
High LDLcholesterol	0.23	0.27	0.602	1.26	0.53-2.97
Q4_SBP_sd	-1.91	21.67	< 0.0001	0.15	0.07-0.33
PWVao	-0.28	55.53	<0.0001	1.32	1.23-1.43
3_AHT_D	0.644	3.257	0.031	1.91	0.95-3.84
EV_BP	0.150	3.964	0.046	0.86	0.74-0.99
Constant	1.492	1.673	<0.0001	4.445	

Table 2. Model for prediction of BP control in treated hypertensive patients.

Ed_cat: level of education; Q4_SBP_sd: 4th quartile of systolic blood pressure' standard deviation; PWVao: aortic pulse weave velocity, 3_AHT_D: at least 3 antihypertensive drugs including 1 diuretic; EV_BP: self-assessment of BP values; OR: odds ratio; 95% CI: 95% confidence interval; ns: no statistical significant ($p > 0.05$); The model has 75.9% power of correctly predicting high and very high total CV risk

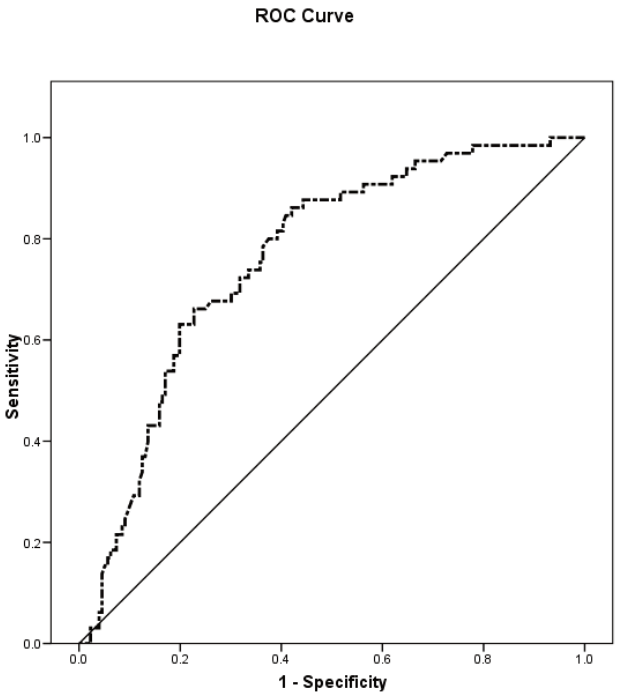

Figure 1. ROC Curve for prediction model of BP control in treated hypertensives. ROC: Receiver Operating Characteristic. Model 1: -2 Loglikelihood = 241.51; R2 = 0.151 (Cox&Snell); 0.220 (Nagelkerke), model $\chi 2$ = 42.97; Variables in equation: Income; Ed_cat; PWVao; Q4_SBP_sd; E_BP; 3_AHT_D; constant; 75.9% power of correctly predicting BP control in treated hypertensives. Ed_cat: level of education; Q4_SBP_sd: 4th quartile of systolic blood pressure' standard deviation; PWVao: aortic pulse weave velocity, 3_AHT_D: at least 3 antihypertensive drugs including 1 diuretic; EV_BP: self-assessment of BP values.

rates in Romania should be done with Poland, because the main surveys addressing hypertension and associated risk factors realized in the last years in those countries - SEPHAR and NATPOL – are based on the same methodology [9]. The available data from Poland are indicating also a low rate of treatment control in hypertension – 21%, but they were collected in different periods of time, almost ten years before SEPHAR II study [19]. Studies conducted more recently are showing higher trends of BP control in certain countries from western Europe: 37% in Italy [20], 22% for men and 38% for women in France – the MONA LISA study [21] and 49% in Switzerland - 2009 Swiss Hypertension Survey (SWISSHYPE) [22].

In our study BP control was not associated with age, as in BP-CARE study [18], while other studies have opposite results, from a better [23] to a worst control among older hypertensives [21].

We did not found a correlation of BP control with other risk factors, except for LDL-cholesterol. These were unexpected results taking into account that a series of studies have found a lower BP control in the presence of additional cardiovascular risk factors, including smoking, obesity or dyslipidemia [22, 24-26]. However, for certain conditions the association with blood pressure control remains controversial, as for diabetes mellitus. Despite a well-recognized difficulty to control hypertension in patients with diabetes mellitus [21, 27], some surveys have revealed the presence of this pathology as a predictor for a higher therapeutic control in hypertension [23, 28]. The association of BP control with subclinical organ damage was emphasized in other studies, but we have to mention that some of them have been conducted on individuals having a higher profile of cardiovascular risk, like in BP-CARE survey, than that including a general population of a country [18].

The results of SEPHAR II study are in line with previously reported associations of BP control with high educational level and mean income per family, being better in urban as compared with rural area of residence [21, 29-31]. Also, BP at goal prevailed significantly under three or more drugs, including a diuretic, compared with less than two or three or more drugs without a diuretic. This data are converging with the recent assumption that three-drug combinations can control hypertension in about 90% of patients with the condition of an active identification of patients and affordable access to therapy [32]. The lack of arterial hypertension control in individuals with self-estimation of BP values as being high worth a special attention. They are aware of their condition, but could be without resources or determination to take care of their own or might be the subjects of inappropriate medical care.

Our study revealed a significant correlation of BP control with emergent factors of cardiovascular risk prediction - blood pressure variability and aortic stiffness (evaluated by PWVao). Both, BP variability (high versus low standard deviation) and PWVao, are independent predictors of cardiovascular morbidity and mortality [33-38]. Moreover, data from ASCOT-BPLA showed that residual visit-to-visit variability of systolic BP was a strong predictor of stroke or coronary events in treated hypertensives [39]. In a previous analysis of SEPHAR II study we have found a significant correlation between BP variability and PWVao [40], and the current data are supporting the hypothesis that aortic stiffness induces high BP variability through sympathetic nerve activations and impaired barorefelex sensitivity [41]. Finally, in a retrospective study PWV was a highly sensitive marker

of the effective BP control throughout all decades of age, but the authors have concluded that this observation was needing confirmation from other studies [42]. We have to notice that the lack of BP control increased with PWVao throughout the values of arterial stiffness parameter and not delimited by the current cut-off for abnormal PWV established at >10m/sec [43].

The limits of this study consists in the fact that we have analyzed only a part of the factors related to the patient that could influence BP control and none of those related to medical care characteristics, due to the specific methodology of a populational study. Moreover, we did not evaluate the efficacy of antihypertensive treatment through 24-hour blood pressure monitoring which is a better tool for BP control assessment. Impact of variables like stress, anxiety and depression, the duration and quality of sleep or the level of salt consumption will be addressed in the upcoming survey SEPHAR III for the prevalence of arterial hypertension and associated risk factors in Romania. The results of this study are waited also in order to find out if the intensive program of continuing medical education developed by the Romanian Society of Hypertension during 2012-2015 have contributed to the improvement of blood pressure control in our country.

Conclusions

According to binary logistic regression the lack of BP control was correlated with low levels of education or income, increased PWVao or high blood SBP variability and treatment with less than 3 antihypertensive or with ≥ 3 drugs not including a diuretic. These results are confirming the association of uncontrolled hypertension with a low level of education or income, are highlighting the efficiency of ≥ 3 drug associations including a diuretic and are launching the attention of the effects of arterial stiffness and SBP variability on BP levels under antihypertensive treatment.

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List of abbreviations

AIXao – aortic augmentation index; BP – blood pressure; DBP – diastolic blood pressure; DM - diabetes mellitus; ECG – electrocardiography; Ed_cat – level of education; EV_BP – self-assessment of blood pressure values; OR – odds ratio; PWVao – aortic pulse wave velocity; Q4_SBP_s.d. – 4th quartile of systolic blood pressure' standard deviation; SBP – systolic blood pressure; SD – standard deviation; 3_AHT_D – at least 3 antihypertensive drugs including a diuretic; 95% CI – 95% confidence interval

References

1. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380: 2224-60.doi: 10.1016/S0140-6736(61766-8.12)
2. Poulter NR, Prabhakaran D, Caulfield M. Hypertension. Lancet. 2015; 386: 801-12. doi: 10.1016/S0140-6736(14)61468-9.
3. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A et al. 2013 Practice guidelines of Hypertension(ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of Arterial Hypertension. J Hypertens. 2013; 31: 1925-38. doi: 10.1097/HJH.0b013e328364ca4c.
4. Benetos A, Thomas F, Bean KE, Guize L. Why cardiovascular mortality is higher in treated hypertensives versus subjects of the same age, in the general population. J Hypertens. 2003; 21:1635-40
5. Redón J, Cea-Calvo L, Lozano JV, Martí-Canales JC, Llisterri JL et al. Blood pressure and estimated risk of stroke in the elderly population of Spain: the PREV-ICTUS study. Stroke. 2007; 38: 1167-73
6. Müller-Nordhorn J, Binting S, Roll S, Willich SN. An update on regional variation in cardiovascular mortality within Europe. Eur Heart J. 2008; 29: 1316-26. doi: 10.1093/eurheartj/ehm604
7. http://www.recensamantromania.ro/wp-content/uploads/2013/07/REZULTATE-DEFINITIVE-RPL_2011.pdf
8. Dorobantu M, Darabont RO, Badila E, Ghiorghe S. Prevalence, awareness, treatment, and control of hypertension in Romania. Results of the SEPHAR Study. Int J Hypertens. 2010; doi: 10.4061/2010/970694
9. Dorobanțu M, Darabont R, Ghiorghe S, Arsenescu-Georgescu C, Macarie C et al. Hypertension prevalence and control in Romania at a seven-year interval. Comparison of SEPHAR I and II surveys. J Hypertens. 2014; 32: 39-47. doi: 10.1097/01.hjh.0000434937.62412.24

10. Dorobantu M, Tautu OF, Darabont RO, Ghiorghe S, Badila E et al. Objectives and methodology of Romanian SEPHAR II Survey. Project for comparing the prevalence and control of cardiovascular risk factors in two East-European countries: Romania and Poland. Arch Med Sci. 2015; 11: 715–723 doi: 10.5114/aoms.2015.53290
11. Kikuya M, Ohkubo T, Metoki H, Asayama K, Hara A et al. Day-by-day variability of blood pressure and heart rate at home as a novel predictor of prognosis: the Ohasama study. Hypertension. 2008; 52: 1045-1050 doi: 10.1161/HYPERTENSIONAHA.107.104620
12. Rothwell PM, Howard SC, Dolan E, O'Brian E, Dobson JE et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet. 2010; 375: 895-905 doi: 10.1016/S0140-6736(10)60308-X
13. Nagai M, Hoshide S, Ishikawa J, Shimada K, Kario K. Visit to-visit blood pressure variations: new independent determinants for cognitive function in the elderly at high risk of cardiovascular disease, J Hypertens. 2012; 30: 1556-1563 doi: 10.1097/HJH.0b013e3283552735
14. Standards of medical care in diabetes–2013. Diabetes Care. 2013; 36 Suppl 1: S11-66
15. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106: 3143-3421
16. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R eta al. 2007 Guidelines for the Management of Arterial Hypertension. J. Hypertens., 2007; 25: 1751-62
17. Mancia G. Blood pressure control in the hypertensive population. Is the trend favourable? J Hypertens. 2013;31: 1094-5. doi: 10.1097/HJH.0b013e32836184cf
18. Grassi G, Cifkova R, Laurent S, Narkiewicz K, Redon J et al. Blood pressure control and cardiovascular risk profile in hypertensive patients from central and eastern European countries: results of the BP-CARE study. Eur Heart J. 2011; 32: 218-25. doi: 10.1093/eurheartj/ehq394
19. Zdrojewski T, Wyrzykowski B, Szczech R, Wierucki L, Naruszewicz M et al. Epidemiology and prevention of arterial hypertension in Poland. Blood Press Suppl. 2005; 2:10-6
20. Tocci G, Rosei EA, Ambrosioni E, Borghi C, Ferri C et al. Blood pressure control in Italy: analysis of clinical data from 2005-2011 surveys on hypertension. J. Hypertens, 2012; 30: 1065-74. Doi: 10.1097/HJH.0b013e3283535993
21. Wagner A, Sadoun A, Dallongeville J, Ferrières J, Amouyel Ph et al. High blood pressure prevalence and control in a middle-aged French population and their associated factors: the MONA LISA study. J. Hypertens, 2011; 29: 43-50. Doi: 101097/HJH.0b013e32833f9c4d
22. Brenner R, Waeber B, Allemann Y. Medical treatment in hypertension in Switzerland. The 2009 Swiss Hypertension Survey (SWISSHYPE). Swiss Med Wkly, 2011; 141.w13169. doi: 10.4414/smw.2011.13169
23. Petrella RJ, Merikle EP, Jones J. Prevalence, treatment, and control of hypertension in primary care: gaps, trends, and opportunities. J Clin Hypertens (Greenwich). 2007; 9:28-35
24. Arcucci O, de Simone G, Izzo R, Rozza F, Chinali M et al. Association of suboptimal blood pressure control with body size and metabolic abnormalities. J Hypertens. 2007 Nov; 25(11): 2296-300
25. Danon-Hersch N, Marques-Vidal P, Bovet P, Chiolero A, Paccaud F et al. Prevalence, awareness, treatment and control of high blood pressure in a Swiss city general population: the CoLaus study. Eur J Cardiovasc Prev Rehabil. 2009;16: 66-72. doi: 10.1097/HJR.0b013e32831e9511
26. Chmiel C, Wang M, Senn O, Del Prete V, Zoller M et al. Uncontrolled arterial hypertension in primary care--patient characteristics and associated factors. Swiss Med Wkly. 2012;142:w13693. doi: 10.4414/smw.2012.13693
27. Nilsson P, Cifkova R, Kjeldesen SE. Treatment of hypertension in patients with type 2 diabetes mellitus. ESH Scientific Newsletter. 2010; 11: No.1R (revised version)
28. Foguet Q, Marti H, Elosua R, Sala J, Masià R et al. Hypertension confirmation and blood pressure control rates in epidemiological surveys. Eur J Cardiovasc Prev Rehab. 2008; 15: 263-9. Doi: 10.1097/HJR.0b013e3282f3ec2f
29. Grotto I, Huerta M, Sharabi Y. Hypertension and socioeconomic status. Curr Opin Cardiol. 2008; 23:335-9. doi: 10.1097/HCO.0b013e3283021c70
30. Minor D, Wofford M, Wyatt SB. Does socioeconomic status affect blood pressure goal achievement? Curr Hypertens Rep. 2008;10:390-7
31. Kiely DK, Gross AL, Kim DH, Lipsitz LA. The association of educational attainment and SBP among older community-living adults: the Maintenance of Balance, Independent Living, Intellect and Zest in the Elderly (MOBILIZE) Boston Study. J Hypertens. 2012; 30:1518-25. doi: 10.1097/HJH.0b013e3283 550fc0.
32. Poulter NR, Prabhakaran D, Caulfield M. Hypertension. Lancet. 2015; 386: 801-12. doi: 10.1016/S0140-6736(14)61468-9
33. Muntner P, Shimbo D, Tonelli M, Reynolds K, Arnett DK, Oparil S. The relationship between visit-to-visit variability in systolic blood pressure and all-cause mortality in the general population: findings from NHANES III, 1988 to 1994. Hypertension. 2011; 57: 160-166. doi: 10.1161/HYPERTENSIONAHA.110.162255.
34. Laurent S, Boutouyrie P. Arterial stiffness as an early marker of organ damage. In: Berbari AE, Mancia G, editors. Special issues in hypertension. Italia: Springer-Verlag; 2012. p. 9-18.
35. Willum-Hansen T, Staessen JA, Torp-Pedersen C, et al. Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. Circulation. 2006; 113: 664-670

36. Mitchell GF, Hwang SJ, Vasan RS, et al. Arterial stiffness and cardiovascular events: the Framingham Heart Study. Circulation. 2010; 121: 505-511. doi: 10.1161/CIRCULATIONAHA.109.886655
37. Sutton-Tyrrell K, Najjar SS, Boudreau RM, et al. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation. 2005; 111: 3384-3390
38. Wang KL, Cheng HM, Sung SH, et al. Wave reflection and arterial stiffness in the prediction of 15-year all-cause and cardiovascular mortalities: a community-based study. Hypertension. 2010; 55: 799-805. doi: 10.1161/HYPERTENSIONAHA.109. 139964
39. Rothwell PM, Howard SC, Dolan E, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet. 2010; 375: 895-905. doi: 10.1016/S0140-6736(10)60308-X
40. Darabont RO, Tautu OF, Pop D, Fruntelata A, Deaconu A et al. Visit-to-Visit Blood Pressure variability and arterial stiffness independently predict cardiovascular risk vategory in a general population: results from the SEPHAR II study. Hellenic J Cardiol 2015; 56: 208-216.
41. Mancia G, Parati G, Pomidossi G, Casadei R, Di Rienzo M, Zanchetti A. Arterial baroreflexes and blood pressure and heart rate variabilities in humans. Hypertension. 1986; 8: 147-153
42. Safar ME1, Blacher J, Protogerou A, Achimastos A. Arterial stiffness and central hemodynamics in treated hypertensive subjects according to brachial blood pressure classification. J Hypertens. 2008;26:130-7
43. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'. Eur Heart J. 2010; 31: 2338-2350. doi: 10.1093/eurheartj/ehq165