GENERAL

OBESITY RELATED HYPERTENSION – PHARMACOTHERAPY REGIMEN AND BLOOD PRESSURE CONTROL AMONG YOUNG ADULT PATIENTS IN POLAND AND GERMANY

ANNA PACZKOWSKA^{1*}, KAROLINA HOFFMANN², WIESŁAW BRYL²,
KINGA MARZEC¹, JONAS RAAKOW³, MATTHIAS PROSS⁴, DOROTA KOPCIUCH¹,
TOMASZ ZAPRUTKO¹, PIOTR RATAJCZAK¹, ELŻBIETA NOWAKOWSKA¹
and KRZYSZTOF KUS¹

¹Department of Pharmacoeconomics and Social Pharmacy,
Poznan University of Medical Sciences,
Rokietnicka 7 St., 60-806 Poznan, Poland

²Department of Internal Diseases, Metabolic Disorders and Arterial Hypertension,
Poznan University of Medical Sciences,
Szamarzewskiego 84 St., 60-569 Poznan, Poland

³Department of Surgery, Campus Charité Mitte and Campus Virchow Klinikum,
Charite – Universitätsmedizin Berlin, 1 Charitepl St., 10117 Berlin, Germany

⁴Department of Surgery, DRK Kliniken Berlin, Kopenick, 2-8 Salvador-Allende St.,
12559 Berlin, Germany

Abstract: The aim of this study was to analyze the pharmacotherapy regimen and evaluate the blood pressure control in obese inpatients in Poland and Germany. The cross-sectional international multicenter study was conducted at selected health care facilities in Germany and Poland. The target group consisted of 256 patients (120 patients from Germany and 136 patients from Poland) aged 18–40 years, hospitalized for obesity-related hypertension in the year 2019. The number of hypertensive drugs used for obesity-related hypertension treatment was comparable in both study groups of patients (2.76 ± 1.24 patients from Germany, 2.59 ± 1.44 patients from Poland). ACEIs were significantly more frequently used by patients from Germany ($p < 0.001$). The following antihypertensive drugs: diuretics, calcium channel antagonists, fixed-dose combination drugs, and α -blockers, were significantly more frequently used by Polish patients ($p < 0.001$). As a result of the applied treatment, 52.5% of patients from Germany and 60.3% from Poland achieved the desired degree of blood pressure normalization. Systolic and diastolic blood pressure values, number of antihypertensive drugs used, duration of hospitalization due to uncontrolled hypertension and blood pressure control were associated with body mass index. Blood pressure control rates in obese patients are improving with the progress of hypertension pharmacotherapy and with the patient's better access to newer generation drugs.

Keywords: hypertension, obesity, inpatients, blood pressure control, pharmacotherapy regimen

The prevalence of obesity and obesity-related diseases, such as hypertension, is currently considered one of the major public health issues in most areas of the world. Numerous epidemiological studies found a positive correlation between body mass and the occurrence of hypertension (1, 2). Hypertension was found to be one and a half to five times more common in obese patients than in people with normal body weight, and as much as seven times more common in people with BMI above 40 kg/m²

(3, 4). Among overweight and obese patients, the prevalence of hypertension is reported to be around 50% and to increase further with higher grades of obesity (5). Obesity-related hypertension is increasingly affecting young people, posing the risk of occurrence of life-threatening complications. The aim of antihypertensive treatment in obese patients is to reduce arterial pressure to below 130/80 mmHg. Results of clinical studies found that obese patients with hypertension were twice as likely to be

* Corresponding author: e-mail: aniapaczkowska@ump.edu.pl

resistant to antihypertensive treatment than people with normal body weight which makes that some patients are hospitalized for intensive treatment. A significant share of obese patients with hypertension requires simultaneous therapy with two or more antihypertensive drugs in order to achieve the therapeutic objective (6-8). Yet, little is known about pharmacotherapy regimen and blood pressure control in obese young inpatients in developing countries. The aim of the study was to analyze the course of treatment (recommended pharmacotherapy) of obese patients with uncontrolled hypertension. This paper also evaluates the blood pressure control in obese young patients in Poland and Germany.

EXPERIMENTAL

Study population

The cross-sectional international multicenter study was conducted in a selected health care facility in Germany (Berlin) and in Poland (Poznan). In the

study, 411 consecutive patients (all patients hospitalized for obesity-related hypertension in the studied time horizon -from 1 January 2019 to 31 December 2019, who agreed to participate in the study) were taken into consideration. However, based on the inclusion and exclusion criteria of the study, 256 patients (120 patients from Germany and 136 patients from Poland) aged 18-40 years, hospitalized for obesity-related hypertension were finally included in the study. The decision to include a patient in the study was made by their attending physician. Prior to surveying, each of the eligible study subjects was informed about the study objective and conditions and gave their written informed consent to participation in the study. The study protocol was approved by the Ethics Committee of the Poznan University of Medical Sciences and by the Ethics Committee of the Charité – Universitätsmedizin Berlin.

The main criteria of patient inclusion in the study were as follows: age of 18-40 years, obesity-related hypertension diagnosed according to the

Table 1. Characteristics of obesity-related hypertension patients from Poland and Germany n=256.

		Poland	Germany
Group size	Total	136	120
	Female (%)	109 (80.1)	93 (77.5)
	Male (%)	27 (19.9)	27 (22.5)
Age (years)	Total $\bar{x} \pm (SD)^*$	30.96 $\pm$ 8.88	31.73 $\pm$ 6.60 NS
	Female $\bar{x} \pm (SD)$	32.12 $\pm$ 5.08	32.78 $\pm$ 4.12 NS
	Male $\bar{x} \pm (SD)$	29.05 $\pm$ 6.15	30.66 $\pm$ 5.12* SS $p < 0.05$
Body mass index - BMI [kg/m ²]	Total $\bar{x} \pm (SD)^*$	36.84 $\pm$ 7.45	38.30 $\pm$ 8.98 NS
	Overweight (%) (25-29.9 kg/m ²)	16.1	18.3 NS
	I degree of obesity (%) (30-34.9 kg/m ²)	28.7	25.8 NS
	II degree of obesity (%) (35-39.9 kg/m ²)	24.3	17.5 NS
	III degree of obesity (%) (≥ 40 kg/m ²)	30.9	38.3 NS
Duration of hypertension (years)	Total $\bar{x} \pm (SD)^*$	17.05 $\pm$ 11.50	16.10 $\pm$ 10.08 NS
Most common comorbidities	Diabetes type 2 (%)	51.5	52.5 NS
	Angina pectoris (%)	5.9	10.0 NS
	Heart failure (%)	5.1	4.2 NS

$\bar{x} (SD)^*$ - average (standard deviation); *-Statistically significant difference: Germany versus Poland for $p < 0.05$; NS- no significance, SS- statistically significant.

ICD-10 classification, hospitalization due to uncontrolled obesity-related hypertension in the 2019 year, patient's consent to participation in the study. On the other hand, the main criteria of patient exclusion from the study included: lack of the patient's consent to participation in the study, age under 18 and above 40 years, pending diagnosis of obesity-related hypertension.

Study technique

The survey relied on the analysis of medical records of hospitalized obesity-related hypertensive patients. Data collected from these medical records concerned a range of variables including details on hypertension pharmacotherapy regimen and metabolic disease history. Information on the patient's demographic data (age, gender, location of medical care provision), course of the disease (duration, presence of comorbid diseases), as well as a medical assessment of metabolic disease or blood pressure control was also collected. Evaluation of the blood pressure control in the hospital environment was based on the patient's medical data: percentage of patients whose blood pressure values were normalized with the medical procedures and pharmacotherapy type used, and based on average daily blood pressure values (24-Hour Ambulatory Blood Pressure Monitoring) of the patients upon discharge from the hospital. In accordance with the latest guidelines of the American Heart Association / American College of Cardiology 2017 (AHA / ACC 2017) and European guidelines ESC / ESH 2018 values below 130/80 mm Hg were adopted as target blood pressure values (7). The BMI was calculated from weight and height information taken from the patient's medical records (body weight in kilograms/height in meters squared) and classified according to international conventions: overweight (25-29.9 kg/m²), obesity (=30 kg/m²), grade 1 obesity (30-34.9 kg/m²), grade 2 obesity (35-39.9 kg/m²), and grade 3 obesity (≥ 40 kg/m²).

Statistical analysis

The obtained test results were analyzed statistically. Values of the analyzed measurable parameters were presented using average, median, and standard deviation, while immeasurable values were presented using sample size and proportion. Differences between unrelated quality characteristics in comparable groups were identified using the chi-square test of homogeneity.

A p-value of < 0.05 was considered statistically significant and test probability of $p < 0.01$ was considered highly significant. The database and sta-

tistical tests were performed based on the STATISTICA 12.0 software (StatSoft, Polska).

RESULTS

Characteristics of the study group

Based on the adopted study inclusion and exclusion criteria, the target group of 256 inpatients (120 patients from Germany and 136 patients from Poland) aged 18-40 years, treated for uncontrolled obesity-related hypertension in the 2019 year was selected to participate in the study. In both groups of patients from Germany and Poland with obesity-related hypertension, most of the patients were female – 77.5% and 80.1% respectively. The average age of the study subjects was 31.73 ± 6.60 years in the German group and 30.96 ± 8.88 in the Polish group. Mean BMI value in the German group was 38.30 ± 8.98 , and in the Polish group – 36.84 ± 7.45 . In the German group of patients with obesity-related hypertension, 25.8% of the patients had grade 1 obesity, 17.5% grade 2 obesity, 38.3% grade 3 obesity, and 18.3% of the patients were overweight as a consequence of the treatment applied. In the Polish group of patients with obesity-related hypertension, 28.7% of the patients had grade 1 obesity, 24.3% grade 2 obesity, 30.9% grade 3 obesity, and 16.2% of the patients were overweight as a consequence of the treatment applied (Table 1)

Antihypertensive medication

Analysis of medical records has shown that the average duration of hospitalization due to uncontrolled hypertension among obese patients from Poland was 6.80 ± 1.54 days, whereas among obese patients from Germany was 6.55 ± 1.31 days (NS). Analysis of medical records has shown that the number of hypertensive drugs used in the treatment of obesity-related hypertension was 2.76 ± 1.24 and 2.59 ± 1.44 on average in the German and Polish group of patients respectively (NS) (Table 3). Of the whole group of patients, a vast majority would receive three or more hypertensive drugs during their hypertension treatment (51.9%). 28.1% of the patients were treated with two hypertensive drugs while monotherapy was being administered to 19.9% of the patients.

Among patients from Germany undergoing hypertension treatment, 66.7% were receiving ACEIs, 51.7% – β -blockers, 36.7% – diuretics, 33.3% – ARBs, 24.2% – a calcium channel antagonist, and 2.5% – a fixed-dose combination drug. Among patients from Poland undergoing hypertension treatment, 88.2% were receiving diuretics,

62.5% – β -blockers, 41.9% – a calcium channel antagonist, 37.5% – ACEIs, 36.0% – ARBs, 20.6% – α -blockers, and 13.3% – a fixed-dose combination drug (Fig. 1). Comparative analysis of the type of antihypertensive drugs used by obese patients from Poland and Germany has shown that ACEIs were significantly more frequently used by patients from Germany ($p < 0.001$). The following antihypertensive drugs: diuretics, calcium channel antagonists, fixed-dose combination drugs, and α -blockers, on the other hand, were significantly more frequently used by Polish patients ($p < 0.001$) (Table 2).

Detailed analysis of pharmacotherapy administered to obesity-related hypertension patients in both groups has shown that the most frequently recorded bitherapy was a combination of two hypertensive drugs – a calcium channel antagonist and an ACEI (29.3% of subjects). Of polytherapy, the most frequently recorded one was a combination of three hypertensive drugs: a β -blocker, a diuretic, and an ARB (27.0%), and a combination of an ACEI, a diuretic, and a calcium channel antagonist (23.4%).

Blood pressure control

In both groups of patients, statistical analysis has shown a significant relationship between the degree of obesity and all analyzed variables: systolic and diastolic blood pressure values, the number of antihypertensive drugs used, duration of hospitalization due to uncontrolled hypertension and blood pressure control ($p < 0.001$). The higher degree of obesity of the study subjects, the higher was the systolic and diastolic blood pressure values and greater was the number of antihypertensive drugs taken by obese patients with comorbid hypertension.

Similarly, the higher the body mass index of the study subjects, the lower was the desired degree of blood pressure normalization ($\leq 130/80$ mmHg) of obese patients with comorbid hypertension (Table 3).

As a result of the applied treatment, 52.5% of patients from Germany and 60.3% from Poland achieved the desired degree of blood pressure normalization ($\leq 130/80$ mmHg). No statistically significant differences were found in obesity-related hypertension treatment efficacy between the study groups (NS) (Table 3).

DISCUSSION AND CONCLUSION

The global prevalence of obesity has been increasing for several decades. World Health Organization (WHO) estimates that 500 mn people worldwide are obese ($\text{BMI} > 30 \text{ kg/m}^2$), and another 900 mn are overweight ($\text{BMI} 25\text{--}30 \text{ kg/m}^2$) (9). The prevalence of obesity in Poland is 16.7% and in Germany is 23.6% (10).

This study has shown an additional correlation between body mass and both systolic and diastolic blood pressure values. Many epidemiological studies found hypertension to be one and a half to five times more common in obese patients than in people with normal body weight, and as much as seven times more common in people with BMI above 40 kg/m^2 (3, 4). The Framingham Heart Study (11), upon a division of the population into BMI quintiles, found that the people in the top quintile had systolic blood pressure lower by 16 mmHg and diastolic blood pressure 9 mmHg higher than the people in the bottom quintile. Analysis of the data from the Framingham Heart Study led to an estimation that the development of hypertension is directly associ-

Figure 1. Pharmacotherapy regimen among obesity-related hypertension patients from Poland and Germany.

Table 2. Antihypertensive drug class used for the treatment of obesity-related hypertension patients from Poland and Germany n = 256.

Antihypertensive drug class	Active substance	Poland [%]	Germany [%]
Angiotensin-converting enzyme inhibitors (ACEI)	Overall	37.5	66.7* SS p < 0.001
	Ramipril	21.3	36.7* SS p < 0.01
	Captopril	11.0	25.8* SS p < 0.01
β -blockers	Overall	62.5	51.7 NS
	Carvedilol	20.6	15.0 NS
	Metoprolol	27.2	20.8 NS
Diuretics	Overall	88.2	36.7* SS p < 0.001
	Furosemid	48.5	12.5* SS p < 0.001
	Spironolactone	42.7	28.3* SS > 0.001
Calcium channel antagonist	Overall	41.9	24.2* SS p < 0.01
	Amlodipine	36.7	23.3* SS p < 0.05
	Lercanidipine	21.3	11.7* SS p < 0.05
Angiotensin II receptor antagonists (ARBs)	Overall	36.0	33.3 NS
	Telmisartan	22.1	20.8 NS
	Candesrtan	36.0	33.3 NS
α -adrenolytics	Overall	20.6	0.0* SS p < 0.001
	Doxasosin	13.2	0.00* SS p < 0.001
Fixed-dose combination drug	Overall	13.7	2.5* SS p < 0.01
	Perindopril + amlodipine + indapamid	5.1	2.5 NS
	Ramipril + amlodipine	2.2	0.0 NS

*-Statistically significant difference: Germany versus Poland for p < 0.05; NS- no significance, SS- statistically significant.

ated with obesity in as many as 78% of men and 65% of women. The Physicians' Health Study (12) has been observing 13,563 healthy male subjects for fifteen years and found that body mass increase by 10% increases the risk of developing hypertension by as much as 70%.

Among Polish and German groups of obesity-related hypertension patients, the most common comorbidity was diabetes type 2, which occurred

among 51.5% of patients from Poland and 52.5% from Germany. The above data is consistent with the literature data. The prevalence of diabetes is rising at an alarming rate throughout the world. By 2030 it is expected that more than 360 million people will have diabetes (13). The dramatic rise in diabetes prevalence is mainly due to the increase in the number of people with type 2 diabetes, amounting to 85-95% of all cases. Direct causes of increased dia-

Table 3. Evaluation of efficacy of hypertension treatment among obesity-related hypertension patients from Poland and Germany n = 256.

Variables	General PL n = 136, D n = 120	Overweight PL n = 20, D n = 19	I degree of obesity PL n = 41, D n = 33	II degree of obesity PL n = 33, D n = 22	III degree of obesity PL n = 42, D n = 46
Duration of hospitalization (SEM ± SD) Poland (PL) Germany (D) P-value	6.80 ± 1.54 6.55 ± 1.31 NS	6.15 ± 1.35 5.37 ± 0.96* SS p < 0.05	6.34 ± 1.37 5.97 ± 1.16 NS	6.67 ± 1.38 6.45 ± 1.22 NS	7.67 ± 1.57 7.50 ± 0.86 NS
Number of hypertensive drugs (Mean ± SD) Poland (PL) Germany (D) P-value	2.59 ± 1.44 2.76 ± 1.24 NS	1.35 ± 0.49 1.16 ± 0.37 NS	1.73 ± 0.55 1.88 ± 0.42 NS	2.70 ± 0.47 2.82 ± 0.66 NS	3.93 ± 0.64 4.02 ± 0.65 NS
Systolic blood pressure (mmHg) (Mean ± SD) Poland (PL) Germany (D) P-value	127.66 ± 14.08 130.22 ± 13.95 NS	116.20 ± 9.61 116.68 ± 9.74 NS	122.10 ± 11.02 124.03 ± 10.70 NS	129.61 ± 12.83 131.36 ± 12.05 NS	137.02 ± 13.24 139.70 ± 11.40 NS
Diastolic blood pressure (mmHg) (Mean ± SD) Poland (PL) Germany (D) P-value	81.08 ± 9.16 83.51 ± 9.30* SS p<0.05	75.00 ± 7.07 75.79 ± 6.92 NS	77.63 ± 8.03 80.30 ± 5.81 NS	81.70 ± 7.41 82.64 ± 7.03 NS	86.86 ± 9.10 89.41 ± 9.70 NS
Controlled blood pressure (<130/80 mmHg) (%) Poland (PL) Germany (D) P-value	60.3% 52.5% NS	90.0% 84.2% NS	75.6% 72.7% NS	51.5% 40.9% NS	38.1% 30.4% NS

P-value - level of statistical significance; p < 0.05 was considered statistically significant; SS - statistically significant; NS - no significance; SD - standard deviation; *Statistically significant difference; D versus PL for p < 0.05.

betes-related morbidity include increased life expectancy, obesity, high-calorie diet, and sedentary lifestyle. Obesity and type 2 diabetes affect more frequently children and young adults (14).

Scientific literature still offers an insufficient number of scientific reports on international comparisons of resistant obesity-related hypertension treatment regimens and blood pressure control in hospital conditions. Results obtained in our study are innovative and are the first reports in the scientific literature concerning the comparative analysis of the type of pharmacotherapy used and efficacy of resistant obesity-related hypertension treatment in selected highly developed EU member states (Poland vs. Germany).

Analysis of medical records has shown that the number of hypertensive drugs used in the treatment of obesity-related hypertension was 2.76 ± 1.24 and 2.59 ± 1.44 on average in the German and Polish groups of patients respectively. Of the whole group of patients, a vast majority would receive three or more hypertensive drugs during their hypertension treatment (51.9%). 28.1% of the patients were treated with two hypertensive drugs while monotherapy was being administered to 19.9% of the patients. Many clinicians in the field of obesity and comorbid diseases are of an opinion that hypertension is frequently resistant to treatment. For a significant share of obese patients with hypertension, monotherapy is insufficient and such patients require simultaneous therapy with two or more antihypertensive drugs in order to achieve the therapeutic objective (15).

This study has shown an additional correlation between the degree of obesity and the number of antihypertensive drugs taken. These results are consistent with those in HYDRA – a cross-sectional study conducted on a sample of 38,875 primary care attendees with obesity-related hypertension in Germany (1). The HYDRA study found a strong relationship between BMI increase and both systolic and diastolic BP and also increasing the use of combination therapy in patients who were overweight or obese (1).

Among patients from Germany undergoing hypertension treatment, the most commonly used groups of antihypertensive drugs included: ACEI (66.7% of patients) and β -blockers (51.7% of patients). Among patients from Poland undergoing hypertension treatment, the most commonly used groups of antihypertensive drugs included: diuretics (88.2% of patients) and β -blockers (62.5%). Comparative analysis of the type of antihypertensive drugs used by obese patients from Poland and Germany has shown that ACEIs were significantly

more frequently used by patients from Germany. The following antihypertensive drugs: diuretics, calcium channel antagonists, α -blocker, and fixed-dose combination drugs, on the other hand, were significantly more frequently used by Polish patients. These results corroborate with references on this issue (15, 16). In the HYDRA study, a clear preference of antihypertensive drug classes in obese patients was only apparent for diuretics and angiotensin-converting enzyme inhibitors, with their use progressively increasing with higher BMI classes. Moreover, in the HYDRA study, the use of β -blockers was a significant predictor of good blood pressure control (1).

Detailed analysis of pharmacotherapy administered to obesity-related hypertension patients in both groups has shown that the most frequently recorded bitherapy was a combination of two hypertensive drugs – a calcium channel antagonist and an ACEI (29.3% of subjects). Of polytherapy, the most frequently recorded one was a combination of three hypertensive drugs: a β -blocker, a diuretic, and an ARB (26.9%), and a combination of an ACEI, a diuretic, and a calcium channel antagonist (23.4%). The above results are consistent with those of the HOS study (the Hypertension-Obesity-Sibutramine Study) (17). The HOS study demonstrates that antihypertensive combination therapy with ACE inhibitors and calcium channel blockers is more advantageous than a β -blocker/diuretic-based regimen in supporting the weight-reducing actions and concomitant metabolic changes induced by sibutramine in obese hypertensive patients. The β -blocker/diuretic therapy attenuated the sibutramine-induced reduction of visceral obesity and abrogated the sibutramine-mediated improvement in glucose tolerance and the decrease in triglyceride levels.

As a result of the applied treatment, 52.5% of patients from Germany and 60.3% from Poland achieved the desired degree of blood pressure normalization ($\leq 130/80$ mmHg). The results of the analyses revealed that the degree of obesity has a significant impact on blood pressure normalization. The proportion of patients with blood pressure normalization was the lowest in patients with III degree of obesity (38.1% patients from Poland and 30.4% of patients from Germany with blood pressure below 130/80 mmHg). The above findings are consistent with the results from the Polish survey WOBASZ II. The highest control rate of hypertension was observed in overweight and with I degree of obesity patients (44%) compare to patients with II and III degree of obesity (40.9%) (18).

The above results are consistent with a wide-range DETECT study conducted in Germany on over 50,000 primary care patients (5). DETECT study indicated that treatment and control rates were 56.0% and 20.3% in 2003, and improved from 55.3% and 18% in 2001 according to HYDRA study (1). Results of the German Health Examination Survey 2008-2011 has shown that among obese patients aware of their hypertensive status 36.6% were uncontrolled. Previous population-based studies suggest that the probability of insufficient blood pressure control in obese patients is about 50% higher than in hypertensive patients with normal weight (19, 20).

Our study has some limitations though. The study population was relatively small ($n = 256$) and may be difficult to be generalized. Considering an insufficient number of studies related to pharmacotherapy regimen and blood pressure control in obese young inpatients in developed countries, this study might be recognized as an important contribution in the field.

To conclude, a pharmacotherapy regimen for obesity-related hypertension in developed countries is based on the use of polytherapy. The following antihypertensive drugs: ACEI, β -blockers and diuretics are the most commonly used in obesity-related hypertension pharmacotherapy. Body mass index significantly impacts the value of blood pressure, pharmacotherapy regimen and control rate of hypertension. The vast majority of patients with obesity-related hypertension in developed countries achieved the desired degree of blood pressure normalization as a result of the applied treatment.

Conflicts of interest

The authors declare no conflict of interest.

REFERENCES

1. Bramlage P., Pittrow D., Hofler M., Wittchen H., Kirch W., Sharma AM.: *Int. J. Obes.* 27, P8 (2003).
2. Adamczak M., Gojowy D., Więcek A.: *Arterial Hypertension* 18, 224 (2014).
3. Tsujimoto T, Sairenchi T, Iso H, Irie F., Yamagishi K., et al.: *J. Hypertens.* 30, 1122 (2012).
4. Mokdad A.H., Ford E.S., Bowman B.A., Dietz W.H., Vinicor F., et al.: *JAMA* 289, 76 (2003).
5. Labeit A.M., Klotsche J., Pieper L., Pittrow D., Einsle F., et al.: *PloS One* 7, 1 (2012).
6. Egan B.M., Zhao Y., Axon R.N., Brzezinski W.A., Ferdinand K.C.: *Circulation* 124, 1046 (2011).
7. Williams B., Mancia G., Spiering W., Rosei E.A., Azizi M., et al.: *Eur. Heart J.* 39, 3021 (2018).
8. Graudal N.A., Hubeck-Graudal T., Jurgens G.: *Am. J. Hypertens* 25, 1 (2012).
9. Marques A., Peralta M., Naia A., Loureiro N., Gaspar de Matos M.: *European Journal of Public Health*. 28, 2 (2018).
10. <http://www.oecd.org/health/obesity-update.htm>
11. Garrison R.J., Kannel W.B., Stokes J., Castelli W.P.: *Prev. Med.* 16, 235 (1987).
12. Gelber R.P., Gaziano J.M., Manson J.E., Buring J.E., Sesso H.D.: *Am. J. Hypertens.* 20, 370 (2007).
13. Wild S., Roglic G., Green A., Sicree R., King H.: *Diabetes Care* 27, 1047 (2004).
14. Kozek E., Podolec P., Kopeć G., Pająk A., Tykarski A., et al.: *Kardiol. Pol.* 66, 1020 (2008).
15. Landsberg L., Aronne L.J., Beilin L.J., Burke V., Igel L.I., et al.: *J. Clin. Hypertens.* 15, 14 (2013).
16. Sarganas G., Neuhauser H.K.: *J. Clin. Hypertens.* 18, 1146 (2016).
17. Scholze J., Grimm E., Herrmann D., Unger T., Kintscher U.: *Circulation* 115, 1991 (2007).
18. Niklas A., Marcinkowska J., Kozela M., Pająk A., Zdrojewski T., et al.: *Pol. Arch. Intern. Med* 129, 864 (2019).
19. Moore L.L., VISIONI A.J., Qureshi M.M., Bradlee M.L., Ellison R.C., et al.: *Arch. Intern. Med.* 165, 1298 (2005).
20. Allcock D.M., Sowers J.R.: *Curr. Diab. Rep.* 10, 139 (2010).