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Treatment of arterial hypertension in patients with severe obesity

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Abstract

Introduction: Obesity is one of the most important cardiovascular risk factors for mortality. It increases the risk of developing hypertension and influences the response to antihypertensive drugs. Ambulatory blood pressure measurement (ABPM) is a tool for a detailed analysis of mean blood pressure values and assessing the blood pressure (BP) profile during the night with the daily values and optimal treatment determination.

Aim: The study aimed to evaluation the type of antihypertensive drugs and control assessment of hypertension based on ABPM in patients with severe obesity.

Material and methods: The study group consisted of 129 overweight and obese patients (group 1: BMI < 40 kg/m^2; group 2: BMI ≥ 40 kg/m^2).They were interviewed, taking into account the antihypertensive drugs taken. We divided drugs into 5 groups: beta-blockers, angiotensin converting enzyme inhibitors (ACE-I) / angiotensin II receptor blockers (ARB), diuretics, calcium channel blockers and others. Mean systolic BP and diastolic BP from the day, day and night, mean heart rate from day to day was assessed based on ABPM.

Results and discussion: The most frequently administered drugs in both groups were ACE-I/ARB. The second most often taken drug was β-blocker and diuretics. Group 1 was significantly older than group 2. Based on the analysis, HR level was significantly dependent on age, BMI, and diabetes. The systolic BP and diastolic BP level was dependent on age and sex.

Conclusions: Only a combination of individually designed pharmacological therapy with personalized dietary interventions, regular exercise, cognitive behavioral therapy, and bariatric interventions, when needed, could guarantee the final success. ABPM should be used routinely in every patients to control assessment of hypertension.

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1. Introduction

Obesity is one of the most important cardiovascular risk factors. According to the World Health Organization (WHO), in 2016, more than 1.9 billion adults aged 18 and over were overweight. Of these, more than 650 million were obese.[1] Recent studies show that about 14% of obese patients are severely obese.[2] By 2030, nearly two-thirds of the world's adult population is projected to be overweight or obese.[3] According to the American Society of Endocrinology, the guidelines of 2016 proposed a division of obesity, taking into account the increased metabolic and cardiovascular risk in overweight people and a coexisting complication of obesity.[4] Numerous studies have confirmed that the higher the body mass index (BMI), the greater the risk of many diseases and the higher the mortality rate.[5] Not only obesity but being overweight is associated with a higher risk of death.[6,7]

The existence of a positive relationship between body weight and the development of arterial hypertension has already been confirmed by numerous epidemiological studies.[8–10] Today it is known that obesity increases the risk of developing hypertension and influences the response to antihypertensive drugs. Ambulatory blood pressure measurement (ABPM) seems to be a beneficial tool. It allows a detailed analysis of mean blood pressure values throughout the day and the assessment of the blood pressure (BP) profile during the night in relation to the daily values and optimal treatment determination. There are no separate guidelines for antihypertensive treatment in obese patients, and we use the same groups of drugs. However, it is known that treating these patients is complex and insufficient.

2. Aim

The study aimed to evaluation the type of antihypertensive drugs and control assessment of hypertension based on ABPM in patients with severe obesity.

3. Material and methods

The study included 129 overweight and obese patients (BMI ≥ 25 kg/m^2) hospitalized at the Department of Cardiology and Internal Diseases of the University Clinical Hospital in Olsztyn (Poland) from 2017–2021. Patients with recent infection, fever, cancer, liver, and lung diseases were excluded. The inclusion criterion was treated and recognized hypertension at least 3 months earlier. Each patient was precisely interviewed, taking into account the antihypertensive drugs taken. Drugs are divided into 5 groups: beta-blockers, angiotensin converting enzyme inhibitors (ACE-I) / angiotensin II receptor blockers (ARB), diuretics, calcium channel blockers, and others (centrally acting drugs, alpha-blockers). The BMI was calculated according to the Quetelet formula: body weight (kg) / height (m^2). Obesity was diagnosed based on BMI according to WHO criteria.[11] The patients were divided into two groups:

(1) Group 1 – patients with BMI < 40kg/m^2,

(2) Group 2 – patients with BMI ≥ 40kg/m^2.

Laboratory tests were performed on the patients, including C-reactive protein (CRP), glucose, liver enzymes, thyroid-stimulating hormone (TSH), creatinine, uric acid, and lipid profile. Each patient had a 24/7 BP measurement (ABPM) using the IEM Mobil-O-Graph NG PWA. Before inserting the device, each subject had BP measured on both upper limbs. Measurements were made in a sitting position after a minimum 5-minute rest. When the differences between systolic BP (SBP) and diastolic BP (DBP) measured on the upper limbs were less than 10 mmHg, the ABPM cuff was applied to the dominant limb. The cuff was applied to the upper BP arm if the BP difference was greater than 10 mmHg. The cuff size was adjusted according to the arm circumference according to the ABPM protocol. The device took SBP, DBP, and heart rate (HR) measurements automatically every 30 minutes during the night (22.00–6.00) in a silent mode and every 15 minutes during the day (6.00–22.00). Arterial hypertension was diagnosed at BP values of more than 135/85 mmHg throughout the day based on the European Society of Hypertension (ESH) guidelines.[12] The device was installed on the first or second day of hospitalization. Mean SBP and DBP from the day, day and night, mean HR from day to day, and the amount of BP drop during the night was assessed.

Statistical Analysis

The median, first quartile (Q1), and third quartile (Q3) of various factors were estimated. The distribution of variables was compared with the theoretical normal distribution using the Shapiro–Wilk test. The differences between BMI of less than 40 kg/m^2 and equal to or more than 40 kg/m^2 due to various predictors were analyzed with the Mann–Whitney test. The correlation between the HR level and SBP vs. BMI was analyzed using the Spearman correlation coefficient (*r*). The generalized linear model (GLM), with the Akaike information criterion (AIC) for normal distribution and logarithmic function, was used to determine the relationship between the HR/SBP/DBP levels and a set of predictor variables. The proportions of the categorical data were tested using the X^2 test. A P value of less than 0.05 was considered to be significant. The analysis was conducted using Statistica software (v. 13.3) (StatSoft, Kraków, Poland).

4. Results

The study group consisted of 129 patients with overweight and obesity (BMI ≥ 25 kg/m^2), with an average age of 52 years (44–61 years), including 76 males and 53 females.

Group 1 was significantly older than group 2 (57 years vs. 48 years old, P < 0.001). Smoking and diabetes were more often in group 2 but without statistical significance (Table 1).

The lipid profile analysis revealed abnormalities in high-density lipoprotein (HDL) levels, which were significantly higher in group 1. CRP levels were higher in group 2 (2.8 mg/dL vs. 5.0 mg/dL; P = 0.003). There were no significant differences in other laboratory parameters (Table 2).

The analysis of ABPM parameters revealed that all BP values were significantly higher in group 2 (SBP: 24 h-median 128.5 vs. 134 mm Hg, respectively, P = 0.03; DBP 24 h-median 78.5 vs. 83.5 mm Hg, respectively, P = 0.009; SBP daytime-median 131.5 mm Hg vs. 136 mm Hg, respectively, P = 0.04; DBP daytime-median 81.5 mm Hg vs. 86 mm Hg, respectively, P = 0.007). All HR values were higher in group 2 (HR 24h-median 68 bpm vs. 74 bpm, respectively, P = 0.007; HR daytime-median 70 bpm vs. 76 bpm, respectively, P = 0.009; HR nighttime-median 63 bpm vs. 68 bpm, respectively, P = 0.007). Nocturnal dipping was more remarkable in group 2; however, there was no statistical significance (Table 3).

The most frequently administered drugs in both groups were ACE-I or ARB. The second most often taken drug was beta-blockers and diuretics. There were no statistical differences between patients from group 1 and 2 due to analyzed drugs (Table 4).

Table 1. Patient general characteristic.

Parameter	All (*n* = 129)	Group 1 (*n* = 53)	Group 2 (*n* = 76)	*P*
Age, years*	52.0 (44–61)	57.0 (49–68)	48.0 (39.5–58)	<0.001
Sex**				
Female	53 (41)	26 (49)	27 (36)	0.12
Male	76 (59)	27 (51)	49 (64)	
Smoking status				
Yes	38 (29)	13(25)	25(33)	0.31
No	91 (71)	40 (75)	51 (67)	
Diabetes				
Yes	37 (2)	14 (26)	23 (30)	0.63
No	92 (71)	39 (74)	53 (70)	

Comments: * numbers are given as median (25–75% IQR); ** numbers are given as *N* (%); IQR – interquartile range.

Table 2. Laboratory parameters.

Parameter	Group 1 (*n* = 53)	Group 2 (*n* = 76)	*P*
Total cholesterol, mg/dL	197.5 (166.0–226.0)	194.0 (165.0–217.0)	0.35
Low-density lipoprotein, mg/dL	115.0 (92.0–133.0)	117.5 (88.5–131.0)	0.60
HDL, mg/dL	48.0 (42.5–57.0)	45.0 (39.0–51.0)	0.03
Triglyceride, mg/dL	143.0 (108.0–180.0)	168.0 (128.0–228.0)	0.08
Uric acid, mg/dL	6.0 (5.2–7.0)	6.6 (5.9–7.3)	0.06
CRP, mg/L	2.8 (1.0–5.8)	5.0 (2.6–8.0)	0.003
Aspartate transaminase, U/L	22.5 (18.0–27.0)	23.0 (20.0–31.0)	0.25
Alanine transaminase, U/L	24.5 (18.0–35.5)	29.0 (24.0–47.0)	0.035
Thyroid-stimulating hormone, µIU/mL	1.5 (1.1–2.2)	1.5 (1.1–1.9)	0.76
Glucose, mg/dL	103.0 (96.5–130.0)	104.0 (92.0–132.0)	0.92
Creatinine, mg/dL	0.8 (0.7–0.9)	0.75 (0.6–0.9)	0.19

Comments: numbers are given as median (25–75% IQR); IQR – interquartile range.

Table 3. ABPM parameters.

Parameter	Group 1 (*n* = 53)	Group 2 (*n* = 76)	*P*
SBP 24-h, mm Hg	128.5 (119.0-135)	134.0 (124.0-142.0)	0.03
DBP 24-h, mm Hg	78.5 (72.0-85.0)	83.5 (76.0-90.0)	0.009
SBP daytime, mm Hg	131.5 (122.0-140.0)	136.0 (126.0-146.0)	0.04
DBP daytime, mm Hg	81.5 (75.0-86.0)	86.0 (78.0-92.0)	0.007
SBP nighttime, mm Hg	120.0 (108.0-127.0)	124.0 (114.0-137.0)	0.07
DBP nighttime, mm Hg	72.0 (64.0-79.0)	75.5 (66.0-83.0)	0.12
Dipping %	8.0 (3.7-12.0)	8.4 (2.4-13.1)	0.87
HR 24-h, bpm	68.0 (62.0-73.0)	74.0 (67.0-80.0)	0.007
HR daytime, bpm	70.0 (66.0-75.0)	76.0 (68.0-84.0)	0.009
HR nighttime, bpm	63.0 (56.0-70.0)	68.0 (61.0-74.0)	0.007

Comments: numbers are given as median (25–75% IQR); IQR – interquartile range.

Table 4. Taken antihypertensive drugs.

Drugs	Group 1 (*n* = 53)		Group 2 (*n* = 76)		*P*
	n	%	*n*	%	
β-blockers	26	49	47	62	0.15
ACE-I/ARB	45	85	67	88	0.59
Diuretics	31	59	54	71	0.14
Ca-blockers	28	53	40	53	0.98
Others	14	26	21	28	0.88

Table 5. Association between the predicted variables and the HR level using GLM.

Variables	*P*	Akaike Information Criterion (AIC)
aAge	0.09	
BMI	0.06	
Sex	0.40	886.1
Smoking	0.42	
Diabetes	0.02	

Table 6. Association between the predicted variables and SBP and DBP level using GLM.

Variables	*P*	Akaike Information Criterion (AIC)
SBP level		
age	0.17	
BMI	0.07	
sex	0.04	974.9
smoking	0.11	
diabetes	0.39	
pre-diabetes	0.91	
DSP Level		
age	0.006	
BMI	0.09	
sex	0.02	908.9
smoking	0.05	
diabetes	0.53	
pre-diabetes	0.69	

There was a linear correlation between HR and BMI (r = 0.3; P < 0.05) (Figure 1), whether they were taking beta-blockers or not (P < 0.05).

There was a linear correlation between SBP and BMI (r = 0.3; P < 0.05) (Figure 2).

Based on the multivariate analysis, HR level was significantly dependent on diabetes. The SBP and DBP level was dependent on age and sex (P < 0.05) (Tables 5 and 6).

5. Discussion

Obesity is a common and rapidly increasing problem in the western world and is linked directly to several diseases. Hypertension is one of the most prevalent and clinically important cardiovascular complications of obesity.[13] Consequently, not only the prevalence of obesity but also the prevalence of obesity hypertension is increasing worldwide. Regarding available antihypertensive treatment, data from clinical trials suggest that all first-line antihypertensive drugs should be of similar relevance in reducing SBP and hypertension-related organ damage in obese patients.[14] It is common knowledge that weight loss is essential in managing obesity-hypertension syndrome. Multiple methods like diet, exercise, medications, and a combination of these measures should be used. Although antihypertensives are considered important components in the holistic approach to managing this complex problem, their efficacy in the most obese patients compared with only overweight patients is questionable.[15]

Moreover, a significant difference in the definition of normal BP values between European (normal BP < 140/90 mm Hg) and American guidelines (normal BP < 130/80 mm Hg) leads to the simple explanation of why the percentage of resistant hypertension in obese patients is higher in the studies that used the American guidelines.[16,17] Based on this significant discrepancy, we have used the ABPM measurements to compare the BP values in the studied groups and to enable more universal conclusions. Interestingly Haddadin et al.[18] have found that the home BP measurement decreased the percentage of resistant hypertension by more than 50% compared to clinic measurement. However, on the other hand, the authors could not use the ABPM in the in- and out-clinic settings due to limited resources. In our study, we performed only in-clinic ABPM measurements, but the aim of the study was the comparison of BP treatment in obese patients and not the detection of refractory hypertension. Additionally, the authors

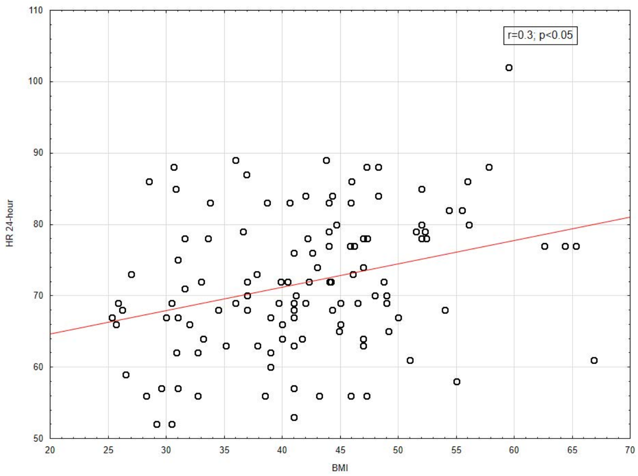

Figure 1. Linear correlation between HR and BMI.

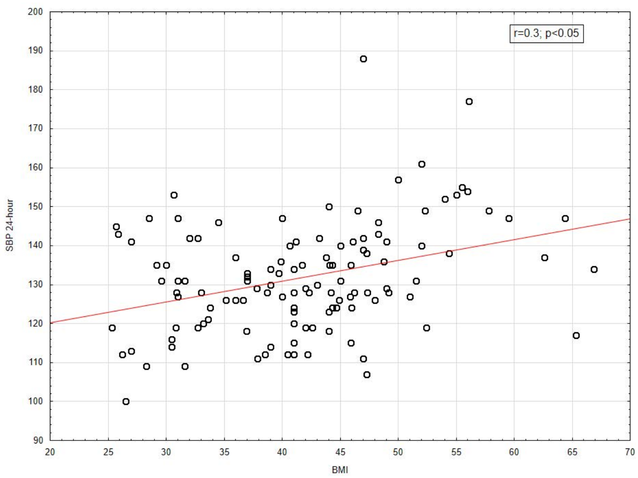

Figure 2. Linear correlation between SBP and BMI.

mentioned above reported 3 main reasons for pseudo-resistant hypertension: medication non-adherence (14%), suboptimal medical regimen (11%), and white coat hypertension (12%). Those factors were highly excluded in our study group, as we controlled the medication intake during the hospitalization and could detect the patients with 'white coat hypertension' based on ABPM. Various researchers have confirmed such attitudes, and the superiority of ABPM over in-office and home BP measurements has already been confirmed. Tepe et al. concluded that the prevalence of masked hypertension in obese adolescents is high and recommend ABPM even if in-office BP measurements were normal.[19] Moreover, Palatini et al. have shown in their study on ABPM in obese patients that any inaccuracy of individual measurements has little or no effect on the average of measurements over prolonged periods of ambulatory recording.[20] Furthermore, our research findings align with the US study that showed patients with advanced obesity tend to be younger, with an average age between 40-59 years old.[21]

Haddadin et al. showed that the prevalence of resistant hypertension gradually increased with BMI, from overweight patients, across class I and II obesity, to class II obesity patients. Our study population had a linear correlation between SBP and BMI, strengthening the findings. Moreover, there was also a statistically significant linear correlation between HR and BMI, independently of beta-blocker intake. According to Grassi et al.[22], sympathetic nervous activity gradually increased from normal-weight patients across overweight subjects to obese individuals, independently of sleep apnea syndrome, which confirms our findings. Interestingly, sympathetic nervous activity correlates directly with BMI and waist-to-hip ratio and with total cholesterol, low-density lipoprotein cholesterol, and triglycerides. A comparison of our study groups revealed a statistically significant difference in high-density lipoprotein and a similar tendency with low-density lipoprotein and triglycerides, although not statistically significant.

High BP treatment is much more complicated and challenging in most obese patients. According to Reisin et al., obese hypertensive patients require more antihypertensive medications. One-third of the patients' BP remained elevated, despite further treatment escalation.[23] In our study, the most frequently administered drugs in both groups were ACE-I or ARB, which, combined with diuretics, are thought to be more beneficial in achieving positive BP values in obese patients.[24,14] The second most often used drugs were beta-blockers and diuretics, without statistical significance between both groups. Despite comparable medication, SBPs and DBPs were significantly lower in patients with BMI less than 40 kg/m^2. In the study by Haddadin et al., apparent treatment-resistant hypertension ranged from 10.5% in overweight patients to 19.5% in patients with BMI equal to or more than 40 kg/m^2,[18] which reflects our findings. Unfortunately, many physicians do not differentiate antihypertensive use according to the obesity level or metabolic syndrome presence.[25] We observe a significant improvement in BP control after weight reduction in our daily practice. On the other hand, some essential data shows that lifestyle changes alone (e.g. diet and physical exercise) are insufficient for clinically significant weight loss.[26] Therefore it is sometimes necessary to discuss bariatric surgery with the patient, as it provides more constant BMI reduction with a greater probability of long-term BP decrease, according to Wilhelm et al.[27]

Study limitations

This study had a number of limitations, including its small sample size. Moreover, a long-term observation outside of the hospital would allow a better understanding of the hypertension impacts and treatments as well as their linkage to body weight. In addition, the ABPM assessment was based only on one measurement. Ideally, this would be done multiple times and using different equipment to confirm validity. Furthermore, the ABPM measure should be taken outside of the hospital setting to ensure it reflects the patient's lifestyle, but at the same time, the measurement conditions were very similar for all of the patients included in the study.

6. Conclusions

Obese patients with hypertension require a multidisciplinary approach to achieve satisfying BP levels. Weight loss is correlated with BP reduction. Only a combination of individually designed pharmacological therapy with personalized dietary interventions, regular exercise, cognitive behavioral therapy, and bariatric interventions, when needed, could guarantee the final success. ABPM should be used routinely in every patients to control assessment of hypertension. The obesity-focused international guidelines on hypertension treatment are still unsatisfactory.

CONFLICT OF INTEREST

Not declared.

FUNDING
Not declared.

ETHICS
The study was approved by the Bioethics Committee at the Faculty of Medical Sciences of the University of Warmia and Mazury in Olsztyn (Poland) on 22 June 2017.

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