CLINICAL FEATURES OF HYPERTENSION IN PATIENTS WITH NORMAL WEIGHT AND OVERWEIGHT

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V.I. BULDA
MD, professor, head of the Department of Internal Medicine, Educational and Scientific Centre "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
ORCID: 0000-0001-9003-8384

I.O. BERDNYK
PhD, assistant, Department of Internal Medicine, Educational and Scientific Centre "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
ORCID: 0000-0001-5918-3743

O.V. BARABANCHYK
PhD, associate professor, Department of Internal Medicine, Educational and Scientific Centre " Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
ORCID: 0000-0003-2670-8448

I.O. RODIONOVA
PhD, associate professor, Department of Internal Medicine, Educational and Scientific Centre "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
ORCID: 0000-0002-7893-8563

Contacts:
Berdnyk Inna Oleksandrivna,
01135, Kyiv, Ukraine
Hlibova Street, 7, Apartment 1.
Tel.: +38 063 261 53 14
Email: inna.berdnyk@knu.ua

INTRODUCTION

Hypertension is a major cause of cardiovascular disease and premature death worldwide. Despite the widespread use of antihypertensive drugs, the average blood pressure (BP) has remained unchanged or decreased slightly over the past four decades [1].

Being overweight is becoming an increasingly common condition worldwide. According to current data, at least 750 million people worldwide are overweight, as determined by a body mass index (BMI) of 25.0 to 29.9 kg/m^2, and another 320 million are obese with a BMI of 30.0 kg/m^2 and above. Recent data indicate that 69.4% of the adult population in the United States has overweight or obesity [2, 3]. In Eastern Europe in 2017, the percentage of adults with overweight did not differ significantly from the US and was 21%. A recent study in Germany found that 35.4% of the adult population suffered from overweight and another 21.3% from obesity [4].

In addition, it was found that increased activation of the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS) play a fundamental role in the physiopathology of hypertension [5, 6].

Increased adipose tissue deposition, regardless of whether it is assessed as overweight, obesity or increased waist circumference, is significantly associated with higher BP and the development of hypertension. In particular, the Nurses' Health Study showed that BMI has a direct strong association with high BP: the relative risk of hypertension in women who gained 5.0–9.9 kg was 1.7 and who gained ≥ 25.0 kg was 5.2 [7].

The relationship between body weight and BP was first established in the 1960s in the Framingham study [8]. However, the nature of this correlation remained unknown until the second half of the 1980s, when a number of studies highlighted the possible mechanisms that correlated the two conditions. Such studies were initiated by observation and noted that metabolic and cardiovascular complications are more common in patients with the "androgenic" obesity phenotype (most adipose tissue is localized in the upper part of the body). Consistently, other population-based studies have been conducted during the 1980s that used the lumbar-hip ratio as a quantitative indicator of visceral fat, demonstrating that the higher ratio correlated with a significant increase in cardiovascular risk [8, 9].

One of the key mechanisms for the development of elevated BP in patients with overweight is hyperactivation of the SNS. A key role in this mechanism plays the distribution of total body fat, as microneurography studies have shown that the degree of SNS activity is higher in patients with irrational distribution of visceral fat. It has previously been shown that there is a direct relationship between SNS activation and waist circumference [10–13].

Numerous studies have shown that overweight and obesity induce changes in arterial baroreceptor control of the SNS, which includes inhibitory and excitatory components. As a rule, in such situation there may be a decrease in parasympathetic tone with increasing sympathetic activity with decreasing heart rate variability. Conversely, with weight loss, parasympathetic tone and heart rate variability increase [14].

To determine the relationship between high BP and overweight and to study the effects of obesity on the course of hypertension, a population-based multicenter randomized study MESA was conducted, in which 3687 patients participated. BMI and waist circumference were used to assess obesity. In MESA patients who did not have baseline heart disease, diabetes and oncology were divided into groups with different combinations of BMI: waist circumference (normal, overweight, and obesity classes 1 and 2–3) and different ethnic and gender groups by waist circumference (optimal or suboptimal). The calculated absolute rates of cardiovascular events per 1000 people per year and the relative risks (95% confidence intervals (CI)) for cardiovascular disease for patients with hypertension compared with normal BP, calculated in the BMI groups were: 13.2 vs. 4.2 and 3.13 (0.99–9.86) for normal BMI/suboptimal waist circumference, 9.0 vs. 4.5 and 2.00 (1.19–3.36) for BMI/optimal waist circumference, 8.4 vs. 5.6 and 1.50 (0.88–2.54) for overweight /suboptimal waist circumference, 14.1 vs. 2.1 and 6.75 (0.69–65.57) for obesity/suboptimal waist circumference. This study found a high relative risk of cardiovascular disease associated with hypertension for patients with overweight and obesity compared to normal body weight.

Another factor involved in the stimulation of the SNS is leptin. It is an adipokine produced

by adipocytes, and its plasma concentration directly correlates with the amount of fat mass. Leptin suppresses appetite and stimulates the SNS [15]. There are gender differences in the concentration of leptin: women have higher hormone levels and greater expression of receptors compared to men. A plausible explanation for this phenomenon may be that subcutaneous adipose tissue in women produces more leptin than visceral adipose tissue [16].

Numerous studies have emphasized that the concentration of aldosterone in urine and plasma increases in patients with overweight compared with those with normal weight. In particular, the results of its plasma concentration are directly correlated with the amount of visceral adipose tissue. Various authors have shown how adipose tissue releases adipokines, which stimulate the adrenal glands to produce aldosterone, regardless of the plasma activity of renin [17]. Therefore, activation of RAAS is directly involved in the development of hypertension associated with obesity.

People with overweight, especially if they have significant amounts of visceral fat, often have increased plasma renin activity, along with increased angiotensin-converting enzyme (ACE), higher concentrations of aldosterone, angiotensinogen, and angiotensin II. RAAS activation in such patients is determined by a number of factors, some of which consist of physical renal compression induced by increased visceral fat, SNS hyperactivity, and local RAAS activation in adipose tissue [18]. Adipose tissue is able to produce angiotensin II. Even if the majority of angiotensinogen continues to be produced by the liver in obese individuals (as in healthy subjects), it has been shown that obese patients show an increase in the level of angiotensinogen produced by adipose tissue [19, 20].

To support this conclusion, an interesting study in mice deficient in adipocyte angiotensinogen (AgtaP2) showed that a high-fat diet caused an increase BP in wild-type rats, but did not cause an increase BP in AgtaP2 rats, even if both groups had an equal increase weight and fat mass. Moreover, it should be noted that RAAS of adipose tissue not only produces angiotensin II, due to the enzymatic activity of ACE inhibitors, but also uses a less common mechanism that relies on the enzymatic activity of cathepsins and chymases [21, 22].

Objective of the study: to determine the clinical features of hypertension in overweight patients.

MATERIALS AND METHODS

A total of 170 patients were included in the study and depending on body weight were divided into two groups:

- group I – 86 patients with normal body weight;
- group II – 84 patients with overweight.

Inclusion criteria were: patients aged 18 to 75 years; previously diagnosed with hypertension; prescribed antihypertensive therapy (no more than three drugs from the five main classes for treatment) more than 8 weeks before inclusion in the study; lack of achievement of target blood pressure levels (poorly controlled hypertension); BMI from 18.5 to 29.9 kg/m^2.

The diagnosis of hypertension and the distribution of respondents by its degree and stage was carried out in accordance with the recommendations of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) 2018 and the current classification of hypertension in Ukraine.

The study was approved by the Commission on bioethical expertise and ethics of scientific research at the Bogomolets National Medical University, protocol No. 144 of 29.03.2021. All participants signed an in-formed consent.

BMI is the most common and widely used and practical way to assess the degree of overweight. To determine it, it is necessary to divide body weight in kilograms by body height in square meters (kg/m^2). Indicators 17.0–18.4 are defined as insufficient body weight, indicators 18.5–24.9 is normal body weight, indicators 25.0–29.9 is overweight, and more than 30.0 is obesity, which also divided into 3 stages [23].

An important risk factor for a number of diseases associated with overweight and obesity is fat distribution. It is known that an increase amount of abdominal fat (central obesity or abdominal type) is also associated with a significant increase in metabolic cardiovascular risk. However, to accurately determine the latter requires expensive instrumental research methods, which are not always present in the clinical practice of the doctor. In this regard, waist circumference, thighs and their index are often used as a simple, inexpensive and universal way to determine central obesity [24]. The WHO report on obesity, as well as the conclusion of the obesity experts of the American Heart, Lung and Blood Institute, recommends the use of waist circumference as an additional indicator of metabolic risk factors, along with the allocation of BMI [25]. Measurements were performed standing without shoes, on the exhale, with emphasis on both feet and with arms freely lowered along the torso. We used the following guidelines: the middle of the distance between the lower rib and the iliac tubercle. Measurement of the length of the thigh circumference was performed at the level of the largest circumference of the buttocks parallel to the floor [26].

In Europe, the recommendations of WHO experts are used with two levels of waist circumference. The first one is a waist circumference > 94 cm in men and > 80 cm in women is a level above which should not be allowed. The second level is waist circumference > 102 cm in men and > 88 cm in women corresponds to body weight, which should be reduced [27].

RESULTS

There were slightly more women in the two groups (57.1% and 60.2%, respectively) by gender, which had no statistically significant difference ($p = 0.736$). The mean age of patients did not differ significantly and in group I was 48.9 ± 12.1 years, in group II – 52.4 ± 12.9 years ($p = 0.39$) (Table 1).

The total duration of hypertension in patients with normal weight was 5.2 ± 2.5 years, in patients with overweight – 5.9 ± 2.2 years ($p > 0.05$). By age, patients in both groups had a disease duration of 3 to 5 years (70.9% and 64.3% respectively), but a statistically higher proportion of patients in group II had a longer course (more than 5 years) – 20.3% ($p = 0.014$) in contrast to group I (8.2%), where the duration of up to 3 years was 20.9% against 15.4% of patients (Table 2).

The distribution by stage of hypertension was as follows: stage 0–I is present in 12 patients with overweight (14.3%),

Table 1. Gender and age characteristics of patients with normal weight and overweight

Indicators	Patients with normal weight (n = 86)	Patients with overweight (n = 84)	p
Men, n (%)	37 (41.9)	33 (39.8)	0.736[1]
Women, n (%)	49 (57.1)	51 (60.2)	
Average age (years)	48.9 ± 12.1	52.4 ± 12.9	0.39[2]

[1] assessment of the significant difference between groups by the chi-square (χ^2).
[2] comparison between groups by Student's t-test.

another 56 patients (66.7%) had stage II, which did not differ from similar indicators in group I (20.9% and 71% respectively, p = 0.068). However, a significantly higher percentage of patients in group II had stage III hypertension and amounted to 19% in contrast to patients with normal weight, where these data were only 8,1% (p = 0.044).

The majority of patients had grade 1 of BP (65.1% in group I and 58.2% in group II), slightly less grade 2 (32.6% and 32.1%, respectively) without statistical difference in the study groups. However, the number of patients with grade 3 hypertension with overweight was significantly higher than with normal weight (10.7% and 2.3% respectively, p = 0.039).

When comparing the data of office measurement of systolic BP (SBP) and diastolic BP (DBP) in patients with hypertension with normal weight and overweight, we did not find significant differences. Thus, in the group I the average values of SBP were 154.1 ± 23.9 mm Hg, in the group II – 155.8 ± 24.8 mm Hg (p > 0.05), and the average values of DBP was 96.1 ± 21 mm Hg and 95.4 ± 19.1 mm Hg respectively (p > 0.05). When comparing the average data of office BP measurement depending on the stage of hypertension, we found some differences (Table 3).

Thus, in group II with grade II hypertension, the level of SBP was significantly lower compared to the SBP in grade III (147.7 ± 24.1 mm Hg vs. 158.9 ± 25.5 mm Hg, p < 0.05). There were no differences in the level of DBP (96 ± 18.8 mm Hg and 97.1 ± 19.1 mm Hg respectively, p > 0.05). No statistical difference was found in group I (153 ± 24.9 vs. 154.2 ± 26.3 mm Hg, p > 0.05).

Regarding anthropometric indicators, the growth of patients in the two groups had no significant differences and amounted to 174.5 ± 62.2 cm and 172.5 ± 56.87 cm, respectively (p = 0.984). Body weight in patients of group II was 87.3 ± 21.4 kg, which significantly exceeded the corresponding figure in group I (72.9 ± 20.89 kg, p = 0.0034). Based on this, the BMI was also significantly higher in group II (28.3 ± 6.2 vs. 22.9 ± 6.1 kg/m^2, p < 0.001), as well as the average waist circumference (94 ± 18.45 cm vs. 85.3 ± 18.21 cm, p = 0.036) and the ratio of waist circumference to hip circumference (0.86 ± 0.2 vs. 0.81 ± 0.17,

Table 2. Characteristics of patients with normal weight and overweight by features of the course of hypertension, M ± SD

Indicators		Patients with normal weight (n = 86)	Patients with overweight (n = 84)
The total duration of the disease, years		5.2 ± 2.5	5.9 ± 2.2
Duration of the disease, years, abs (%)	up to 3 years	18 (20.9)	13 (15.4)
	3–5 years	61 (70.9)	54 (64.3)
	more than 5 years	7 (8.2)	17 (20.3)*
Stage of hypertension, abs (%)	I (uncomplicated)	18 (20.9)	12 (14.3)
	II (asymptomatic disease)	61 (71)	56 (66.7)
	III (established disease)	7 (8.1)	16 (19)*
Grade of hypertension (level of BP), abs (%)	1	56 (65.1)	49 (58.2)
	2	28 (32.6)	27 (32.1)
	3	2 (2.3)	9 (10.7)*

* p < 0,05

Table 3. The average SBP and DBP in patients with hypertension with normal weight and overweight at different stages of hypertension, M ± SD

BP	II grade	III grade
Patients with normal weight (n = 86)		
SBP, mmHg	153.0 ± 24.9	154.2 ± 26.3
DBP, mmHg	95 ± 18	95.9 ± 19.4
Patients with overweight (n = 84)		
SBP, mmHg	147.7 ± 24.1	158.9 ± 25.5*
DBP, mmHg	96 ± 18.8	97.1 ± 19.1

* p < 0,05

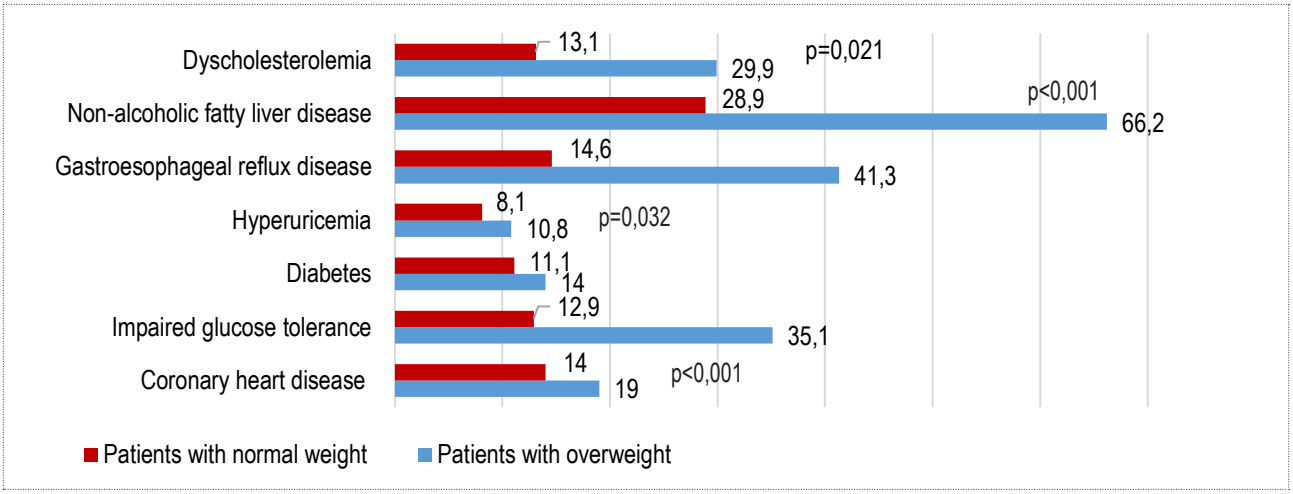

Figure. Frequency of comorbidities

p = 0.029). A correlation between body weight and waist circumference was found in overweight patients (r = 0.64, p < 0.05).

In addition, considering the increased risk of abdominal obesity in overweight patients and current ESH/ESC 2018 recommendations, we calculated the proportion of patients with abdominal obesity (waist circumference in men > 102 cm and in women > 88 cm) and in group II it was 38% (as opposed to 3.1% of group I), which has a statistically significant difference (p < 0.0001).

In our work we also analyzed a concomitant pathology according to the available medical documentation and anamnesis. The frequency of pathology and the results of statistical analysis are shown in Figure.

DISCUSSION

Concomitant diseases were found in patients of two groups. These include coronary heart disease, history of stroke/transient ischemic attack, impaired glucose tolerance, diabetes mellitus, asymptomatic hyperuricemia, gout and others. Thus, according to the above results, patients with overweight were statistically more likely to have impaired glucose tolerance (35.1% vs. 12.9% of patients, p < 0.001), nonalcoholic fatty liver disease (NAFLD) (66.2% vs. 28.9% of patients, p < 0.001), dyscholesterolemia (29.9% vs. 13.1% of patients, p = 0.021) and gastroesophageal reflux disease (GERD) (41.3% vs. 14.6% of patients, p = 0.0032). The incidence of coronary heart disease, history of stroke, diabetes mellitus, asymptomatic hyperuricemia, gout, gallstone disease, bronchial asthma, autoimmune thyroiditis did not differ statistically from patients with normal body weight (p > 0.05).

The most significant association was observed between patients with overweight and NAFLD (objective data (OD) 3.25; 95% CI 1.55–5.13) and with impaired glucose tolerance (odds ratio (OR) 3.54; 95% CI 1.12–5.68). The percentage of patients with dyscholesterolemia was also statistically higher, although slightly lower than in previous cases (OD 2.61; 95% CI 1.05–3.87) and with GERD (OD 3.14; 95% CI 1.56–5.99).

A direct correlation was found between patients with abdominal obesity and GERD (r = 0.56, p < 0.01), dyscholesterolemia (r = 0.53, p < 0.05) and with diabetes (r = 0, 45, p < 0.05).

In addition, patients who smoked significantly more often had coronary heart disease (p = 0.044), and those who drank more than 8 doses per month were more likely to suffer from gout (p < 0.01).

CONCLUSIONS

Overweight patients had a significantly longer course of the disease (in particular longer than 5 years, p < 0.005), in patients with grade 3 hypertension and stage II hypertension, the level of SBP was significantly lower compared to SBP in stage III (p < 0.05). In addition, it was found that more than a third of overweight patients have abdominal obesity, although the BMI is less than 30 kg/m2. Among the comorbidities there is a statistically significant association of overweight with NAFLD (OR 3.25; 95% CI 1.55-5.13), GERD (41.3% vs. 14.6% of patients, p = 0.0032), dyscholesterolemia (29.9% vs. 13.1% of patients, p = 0.021) and impaired glucose tolerance (35.1% vs. 12.9% of patients, p < 0.001).

Conflict of interest

All authors declare that there is no conflict of interest or financial obligations considering the publication of the article.

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V.I. Bulda, MD, professor, head of the Department of Internal Medicine, Educational and Scientific Centre «Institute of Biology and Medicine», Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
I.O. Berdnyk, PhD, assistant, Department of Internal Medicine, Educational and Scientific Centre «Institute of Biology and Medicine», Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
O.V. Barabanchyk, PhD, associate professor, Department of Internal Medicine, Educational and Scientific Centre «Institute of Biology and Medicine», Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
I.O. Rodionova, PhD, associate professor, Department of Internal Medicine, Educational and Scientific Centre «Institute of Biology and Medicine», Taras Shevchenko National University of Kyiv, Kyiv, Ukraine

Objective of the study: To determine the clinical features of arterial hypertension in overweight patients.
Materials and methods. There were 170 patients included in the study and depending on body weight were divided into two groups: group I – 86 patients with normal body weight and group II – 84 patients with overweight. In our work we calculated the proportion of patients with abdominal obesity and also analyzed concomitant pathology according to the available medical documentation and anamnesis.
Results. There were slightly more women in the two groups. Comparing the data of office measurement of systolic and diastolic blood pressure in patients with hypertension with normal weight and overweight didn't show significant differences. The most significant association was observed between patients with overweight and nonalcoholic fatty liver disease (objective data (OD) 3.25; 95% confidence interval (CI) 1.55–5.13) and with impaired glucose tolerance (OR 3.54; 95% CI 1.12–5.68). The percentage of patients with dyscholesterolemia was also statistically higher, although slightly lower than in previous cases (OD 2.61; 95% CI 1.05–3.87) and with gastroesophageal reflux disease (OD 3.14; 95% CI 1.56–5.99). A direct correlation was found between patients with abdominal obesity and the presence of gastroesophageal reflux disease ($r = 0.56$, $p < 0.01$), dyscholesterolemia ($r = 0.53$, $p < 0.05$) and with diabetes ($r = 0.45$, $p < 0.05$). In addition, patients who smoked significantly more often had coronary heart disease ($p = 0.044$).
Conclusions. The article summarizes information on the clinical features of arterial hypertension in overweight patients. The prevalence of hypertension among the adult population is 30-45%, with overweight and obesity continuing to occupy leading positions among young and mature people in the developed world and in middle-income countries. Determining the features of the course, duration of the disease, the distribution between stage and degree in this category of patients will help to develop optimal algorithms for patient management.

Keywords: arterial hypertension, overweight, obesity, coronary heart disease, dyscholesterolemia.

КЛІНІЧНІ ОСОБЛИВОСТІ АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ У ХВОРИХ ІЗ НОРМАЛЬНОЮ ТА НАДЛИШКОВОЮ ВАГОЮ

В.І. Бульда, д. мед. н., професор, завідувач кафедри внутрішньої медицини Навчально-наукового центру «Інститут біології та медицини» Київського національного університету ім. Тараса Шевченка, Київ, Україна
І.О. Бердник, к. мед. н., асистент кафедри внутрішньої медицини Навчально-наукового центру «Інститут біології та медицини» Київського національного університету ім. Тараса Шевченка, Київ, Україна
О.В. Барабанчик, к. мед. н., доцентка кафедри внутрішньої медицини Навчально-наукового центру «Інститут біології та медицини» Київського національного університету ім. Тараса Шевченка, Київ, Україна
І.О. Родіонова, к. мед. н., доцентка кафедри внутрішньої медицини Навчально-наукового центру «Інститут біології та медицини» Київського національного університету ім. Тараса Шевченка, Київ, Україна

Мета дослідження: визначити клінічні особливості артеріальної гіпертензії у хворих із надлишковою масою тіла.
Матеріали та методи. Дослідження охоплювало 170 пацієнтів, які залежно від маси тіла були розподілені на дві групи: I група – 86 хворих з нормальною масою тіла, та II група – 84 пацієнти з надлишковою масою тіла. У запропонованій роботі автори визначили кількість пацієнтів, які мають абдомінальне ожиріння, а також провели аналіз супутньої патології за наявною медичною документацією та анамнезом.
Результати. Виявлено, що в обох групах переважали жінки. При порівнянні даних офісного вимірювання систолічного й діастолічного артеріального тиску у хворих на артеріальну гіпертензію з нормальною та надлишковою масою тіла достовірних відмінностей не виявлено. Найбільш значущий зв'язок спостерігався в пацієнтів між надлишковою вагою та неалкогольною жировою хворобою печінки (objective data (OD) 3,25; 0,95% довірчий інтервал (ДІ) 1,55–5,13) і порушенням толерантності до глюкози (відносний ризик 3,54; 0,95% ДІ 1,12–5,68). Відсоток пацієнтів із дисхолестеринемією також був статистично вищим, хоча й дещо нижчим, ніж у попередніх випадках (OD 2,61; 0,95% ДІ 1,05–3,87), а також у пацієнтів з гастроезофагеальною рефлюксною хворобою (OD 3,14; 0,95% ДІ 1,56–5,99). Встановлено прямий кореляційний зв'язок у пацієнтів між абдомінальним ожирінням і наявністю гастроезофагеальної рефлюксної хвороби ($r = 0,56$, $p < 0,01$), дисхолестеринемією ($r = 0,53$, $p < 0,05$) та цукровим діабетом ($r = 0,45$, $p < 0,05$). Крім того, пацієнти, які палили, значно частіше мали ішемічну хворобу серця ($p = 0,044$).
Висновки. У статті узагальнено відомості про клінічні особливості артеріальної гіпертензії в пацієнтів із надлишковою масою тіла. Поширеність артеріальної гіпертензії серед дорослого населення становить 30–45%, водночас надлишкова вага та ожиріння продовжують посідати провідні позиції серед молодого та зрілого населення розвинених країн світу та країн, що розвиваються. Визначення особливостей перебігу, тривалості захворювання, розподілу між його стадією та ступенем у даної категорії хворих допоможе розробити оптимальні алгоритми ведення хворого.

Ключові слова: артеріальна гіпертензія, надлишкова маса тіла, ожиріння, ішемічна хвороба серця, дисхолестеринемія.