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## CENTRAL AORTIC PRESSURE INDICES IN YOUNG WOMEN WITH EXCESSIVE BODY WEIGHT AND ARTERIAL HYPERTENSION

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This study aimed to investigate changes in central aortic pressure and central hemodynamics, as well as tumor necrosis factor- $\alpha$  and C-reactive protein, in young women with arterial hypertension and excess body weight. The study included 43 young women, aged 18-40 (mean age 36.7 $\pm$ 2.3 years), who were referred for an examination due to the detection of elevated blood pressure. Based on office and blood pressure measurements, individuals with persistent stage 1 arterial hypertension were divided into two groups: 20 women with normal body weight (group 1) and 23 women with excess body weight (group 2). The control group consisted of 20 women (mean age 36.5 $\pm$ 2.7 years) with normal blood pressure and body weight. Young women with stage 1 arterial hypertension showed significantly greater increases in vascular stiffness and central aortic pressure than the control group. In women with stage 1 arterial hypertension and excess body weight, significantly higher values of central haemodynamic parameters were observed: systolic aortic pressure, diastolic aortic pressure, mean aortic pressure and pulse aortic pressure, as well as pulse wave velocity, compared to a group of patients with arterial hypertension and normal body weight. An increase in serum concentrations of tumor necrosis factor- $\alpha$  and C-reactive protein was observed in female patients with grade 1 hypertension, which was more pronounced in those with excess body weight, which confirms the role of inflammation in the pathogenesis of hypertension in the examined cohort of young women.

**Key words:** central aortic pressure, tumor necrosis factor- $\alpha$ , C-reactive protein, arterial hypertension, excess body weight, young women.

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## СТАН ПОКАЗНИКІВ ЦЕНТРАЛЬНОГО АОРТАЛЬНОГО ТИСКУ У МОЛОДИХ ЖІНОК ІЗ НАДЛИШКОВОЮ МАСОЮ ТІЛА ТА АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

Метою дослідження було вивчити особливості змін параметрів центрального аортального тиску та центральної геодинаміки, а також фактора некрозу пухлин- $\alpha$  та С-реактивного протеїну у молодих жінок з артеріальною гіпертензією та надлишковою масою тіла. В дослідження включено 43 молоді жінки 18-40 років (середній вік 36,7 $\pm$ 2,3 роки), що були направлені на обстеження в зв'язку з виявленням підвищеного артеріального тиску. За результатами офісного та добового вимірювання артеріального тиску обстежені особи зі стійкою артеріальною гіпертензією 1 ступеня були розподілені на 2 групи: 20 жінок (1-а група) з нормальною масою тіла та 23 (2-а група) з надлишковою масою тіла. Контрольну групу склали 20 жінок (середній вік 36,5 $\pm$ 2,7 роки, з нормальними артеріальним тиском та масою тіла. Встановлено, що у жінок молодого віку з артеріальною гіпертензією 1 ступеня відмічено значиміше підвищення параметрів судинної жорсткості і центрального аортального тиску порівняно з особами контрольної групи. При артеріальній гіпертензії 1 ступеня та надлишкової масі тіла у жінок визначено достовірно вищі значення показників центральної гемодинаміки – систолічний аортальний тиск, діастолічний аортальний тиск, середній аортальний тиск і пульсовий аортальний тиск та швидкості поширення пульсової хвилі відносно групи пацієток з АГ та нормальною масою тіла, що свідчить про підвищення артеріальної ригідності у жінок молодого віку з артеріальною гіпертензією 1 ступеня та надлишковою масою тіла. У пацієток з артеріальною гіпертензією 1 ступеня визначається підвищення концентрації у сироватці крові фактора некрозу пухлин- $\alpha$  та С-реактивного протеїну, більш виражене у пацієток з надлишковою масою тіла, що підтверджує роль запалення в патогенезі артеріальної гіпертензії в дослідженій когорті молодих жінок.

**Ключові слова:** центральний аортальний тиск, фактор некрозу пухлин- $\alpha$ , С-реактивний протеїн, артеріальна гіпертензія, надлишкова маса тіла, молоді жінки.

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Cardiovascular disease (CVD) is the leading cause of disability and premature death in the European Region, accounting for over 42.5 % of all deaths [6]. The most significant risk factors for CVD are high blood pressure (BP), dyslipidaemia, being overweight or obese, low physical activity and smoking [2].

Hypertension (AH) is the most common form of CVD worldwide. According to World Health Organization (WHO) data from 2023, 1.28 billion adults aged 30–79 suffered from this disease [6]. AH is linked to many other risk factors and is associated with most chronic non-communicable diseases.

Excess weight and obesity are among the leading causes of mortality and disability in the European region. Annually, these conditions cause more than 1.2 million deaths, accounting for over 13 % of total

mortality in the region [11]. Obesity is a global problem of modern society due to its prevalence and the high risk of developing comorbid conditions, including hypertension, ischemic heart disease, and diabetes mellitus, which decrease quality of life and lifespan.

The increase in cardiovascular disease (CVD) risk factors among young adults is particularly concerning. Over the past few decades, obesity has increased worldwide regardless of gender, race, or age, and the associated health risks have simultaneously increased in children and adolescents.

The prognosis for patients with AH depends primarily on blood pressure levels and target organ damage. Arterial stiffness is one of the criteria for subclinical target organ damage [7]. However, there is not enough research on the mechanisms of development and progression from risk factors to disease manifestation. The relationship between excess weight, obesity, and arterial stiffness as predictors of cardiovascular disease development in women of different ages remains unclear.

**The purpose** of the study was to investigate changes in central aortic pressure and central hemodynamics, as well as tumor necrosis factor- $\alpha$  and C-reactive protein, in young women with arterial hypertension and excess body weight.

**Materials and methods.** The study included 43 young women, aged 18–40 (mean age  $36.7 \pm 2.3$  years), who were referred for an examination at the GI L.T. Malaya National Institute of Therapy of the National Academy of Medical Sciences of Ukraine due to the detection of elevated blood pressure. Informed consent was a condition for participation in the study. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Excess body weight was defined as a body mass index (BMI) of at least  $25 \text{ kg/m}^2$ , obesity as a BMI of at least  $30 \text{ kg/m}^2$ , and abdominal obesity as a waist circumference greater than 80 cm in women.

Based on office and BP measurements, individuals with persistent stage 1 hypertension were divided into two groups: 20 women with normal body weight (BMI  $24.3 \pm 0.5 \text{ kg/m}^2$ ) (group 1) and 23 women with excess body weight (BMI  $28.9 \pm 0.6 \text{ kg/m}^2$ ) (group 2).

The control group consisted of 20 women (mean age  $36.5 \pm 2.7$  years) with normal blood pressure and body weight (BMI  $24.1 \pm 0.5 \text{ kg/m}^2$ ).

Exclusion criteria: history of taking antihypertensive drugs for less than three months before inclusion in the study, secondary forms of AH, professional athletes, pregnancy, long-term stage 3 AH, history of coronary heart disease, angina pectoris, or myocardial infarction, history of stroke, transient ischemic attack, history of chronic heart failure, history of chronic renal failure, diabetes mellitus, heart rhythm disturbances, severe concomitant diseases of the respiratory or endocrine systems, or oncological diseases.

All participants underwent a general clinical examination, which included a questionnaire to identify risk factors for cardiovascular disease, a physical examination, and anthropometric measurements to determine body mass index (BMI) and waist circumference. The examination also included a physical examination by a physician, a complete blood count, a urinalysis with a microalbuminuria (MAU) test strip, and a biochemical blood analysis with fasting glucose, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and creatinine. The creatinine test included a calculation of the glomerular filtration rate (GFR) using the CKD-EPI formula. The examination also included an electrocardiogram (ECG) in 12 standard leads using an ECG600G device (Heaco Ltd., UK) and daily blood pressure monitoring (DBPM) using an ABPM-04 device (Meditech, Hungary).

Clinical blood pressure (BP) measurements were performed using validated oscillometric devices three times at one-minute intervals by the same physician over a period of five days in the morning between 9 and 11 a.m., with the participant sitting after resting for ten minutes on the same arm. The arm for BP measurement was selected upon admission based on higher BP compared to measurements on the right and left arms.

Central aortic pressure and arterial stiffness were measured using applanation tonometry with a SphygmoCor-PVx device (AtCor Medical Pty Ltd., Australia). A sensor was used to record the pulse wave in the radial artery, and the pulse wave in the ascending aorta was determined using the inverse transfer function method. The following levels were measured in the aorta: SBP (cSBP), DBP (cDBP), and PP (cPP), as well as the main characteristics of the central pulse wave: augmentation pressure (AP), amplitudes of systolic peaks (P1 and P2), augmentation index ( $AI_x = TP/PT \text{ P2/P1}$ ), and pulse wave velocity (PWV), all of which were normalized to a heart rate (HR) of 75 beats per minute (bpm).

We determined the concentrations of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and C-reactive protein (CRP) using enzyme-linked immunosorbent assay (ELISA) kits from DRG (USA). The ELISA tests were performed using a LabLine-90 ELISA analyzer from Austria.

The results were statistically analyzed using Statistica 10.0 software (StatSoft, Inc., USA). For quantitative indicators measured on an interval scale, we calculated the mean value, standard deviation, and mean error. For "qualitative" and "ordinal" indicators, the frequency of indicator detection was determined as a percentage or the frequency of different rank assessments, respectively. To analyze intergroup differences in indicators, Student's t-test value was calculated. For indicators measured on a nominal scale, the reliability of the difference in indicator frequency between the two groups was assessed using a t-test with Fisher's transformation. Linear and rank correlation coefficients were also calculated. Differences in mean values and correlation relationships were considered reliable at a significance level of  $p < 0.05$ .

**Results of the study and their discussion.** An analysis of central aortic pressure parameters revealed that the following indicators were significantly higher in young women with grade 1 AH than in the control group: cSBP, cDBP, cPP, and central pulse wave characteristics (AR, AIx, AIx@HR 75, and PWP). Additionally, an increase in SBP, DBP, and pulse pressure (PT) in the aorta was observed in patients with stage 1 hypertension and excess body weight compared to those with hypertension and normal body weight ( $p < 0.05$ ). The dynamics of central aortic pressure parameters is presented in Table 1.

Table 1

Characteristics of the central pulse wave in the examined individuals

Parameter	Control group (n=20)	Group 1 (n=20)	Group 2 (n=23)
cSBP, mmHg	108.8±1.8	120.3 ± 2.1***	130.8 ± 2.3*** °
cDBP, mmHg	75.1±1.5	81.3±2.0*	88.9±2.3*** °
cPP, mmHg	33.5±1.5	36.7±1.1***	39.9±1.1*** °
AP, mmHg	5.3±0.5	7.3±0.7*	13.6±2.5**
AIx, %	14.3±1.8	23.0±2.5*	27.1±3.1**
AIx@HR 75, %	11.5±1.7	19.1±2.1**	23.1±2.5***
PWV, m/s	7.5±0.3	8.3±0.2*	9.1±0.2*** °

Notes: \* – significance of differences compared to the control group ( $p < 0.05$ ); \*\* –  $p < 0.01$ ; \*\*\* –  $p < 0.001$ ; ° – significance of differences compared to group 1 ( $p < 0.05$ ).

When we analyzed the PWV in the examined individuals, we found that, on average, the PWV was  $8.3 \pm 0.3$  m/s in young women with stage 1 hypertension and normal body weight. This value was 10.7 % ( $p < 0.05$ ) higher than in the control group and 9.6 % ( $p < 0.05$ ) higher than in patients with grade 1 arterial hypertension (AH) and excessive weight.

A comparative assessment of TNF- $\alpha$  levels in the study groups revealed that TNF- $\alpha$  levels in women with stage 1 hypertension and normal or excessive weight were significantly higher ( $p < 0.05$ ) than in the control group (Fig. 1). At the same time, patients who were overweight had statistically significantly higher TNF- $\alpha$  values than patients with hypertension and a normal body weight ( $p < 0.05$ ).

Analysis of CRP concentration in the blood revealed higher levels of this indicator in patients with stage 1 AH and excess weight compared to the group of women with stage 1 AH and normal body weight ( $p < 0.05$ ) (Fig. 2).

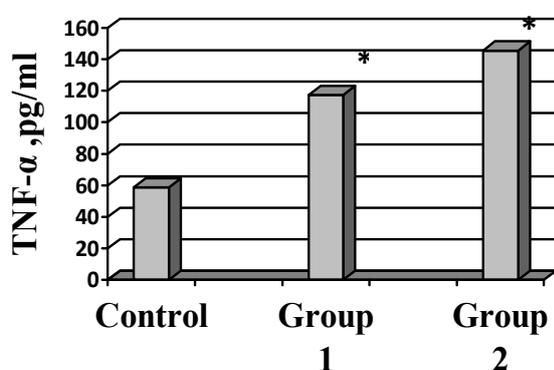


Fig. 1. Patterns of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) changes in young people with stage 1 hypertension with normal body weight (group 1) and overweight (group 2) and the control group.

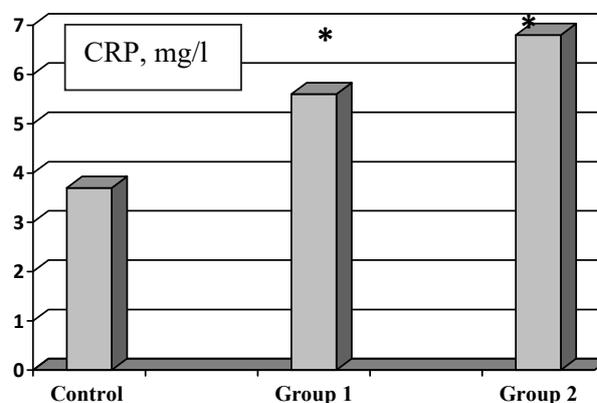


Fig. 2. Specific features of C-reactive protein (CRP) changes in young individuals with stage 1 AH with normal body weight (group 1) and overweight (group 2) and the control group.

Pulse wave velocity (PWV) is widely accepted as the gold standard for assessing arterial stiffness. According to the 2023 ESC/ESH recommendations, a PWV value greater than 10 m/s indicates target organ damage [3].

Arterial stiffness is a significant prognostic factor in patients with cardiovascular disease, regardless of traditional risk factors. Determining vascular stiffness is valuable for diagnosing arterial hypertension (AH) and cardiovascular morbidity and mortality in healthy elderly individuals and patients with AH, as well as overall mortality. Additionally, it is valuable for diagnosing cardiovascular and overall mortality in patients with diabetes mellitus and impaired glucose tolerance, as well as other pathological conditions [4, 5].

Arterial stiffness, a known cardiovascular risk factor, is associated with aging and atherosclerosis. It is also important to note that determining vascular stiffness in young adults is of significant importance, as it would contribute to the development of preventive strategies aimed at preventing cardiovascular diseases, primarily hypertension, and reducing cardiovascular mortality [11].

In a systematic review conducted by Lan Y.S. et al. [9], it was shown that arterial stiffness increases with age in healthy women and has an inverse relationship with exercise intensity. In another study [7], it was shown that arterial stiffness in men increases progressively across all age groups, whereas in women it does not increase significantly annually until the age of 50, but shows a more rapid increase after that age. In another systematic review [14], it was shown that higher pulse wave velocity, systolic blood pressure, and diastolic blood pressure are associated with the onset of hypertension.

Currently, many researchers are focusing on studying the formation mechanisms of arterial stiffness, including the roles of endothelial dysfunction and systemic inflammation in the development of this pathology [10]. However, most studies focus on investigating this problem in individuals with established CVD at the stage of clinical manifestations.

Vascular rigidity and endothelial dysfunction significantly impact the dynamics of AH progression and the risk of cardiovascular complications [13].

Recent studies have focused on the role of inflammation as a key factor in the pathogenesis of arterial hypertension. It has been established that immune mediators, including cytokines and cells of the innate and adaptive immune systems, play an important role in the pathogenesis of arterial hypertension and target organ damage [3]. It has been demonstrated that cells of the innate and adaptive immune systems contribute to cytokine production, influence neighboring cells, and carry out pro- and anti-inflammatory effects. The studies have established the important pathogenetic role of cytokines such as IL-1 $\beta$ , IL-6, and TNF- $\alpha$ . Moreover, it is possible to analyze circulating cytokines to assess the risk of inflammation in arterial hypertension [1].

It has been shown that higher levels of IL-1 $\beta$ , TNF- $\alpha$ , and IFN- $\gamma$ , which are involved in different inflammatory pathways, increase even before the onset of hypertension [3]. Also, the results of clinical studies in women before and after the onset of hypertension indicate the involvement of immune cells in increasing blood pressure [8].

The increase in TNF- $\alpha$  content with increasing body weight may be due to the fact that this pro-inflammatory cytokine enhances lipolysis processes in adipocytes and hepatocytes, increasing the concentration of free fatty acids in adipose and liver tissues [12].

Clinical studies have shown that C-reactive protein (CRP), as a marker of inflammation, increases in arterial hypertension and is also associated with increased cardiovascular risk. CRP is an acute phase protein that is mainly produced by hepatocytes and also synthesized by vascular smooth muscle cells and macrophages. Research results indicate that CRP levels are significantly higher in patients with hypertension compared to the patients with normal blood pressure [12]. These data confirm the influence of the inflammatory component in the pathogenesis of arterial hypertension, as well as its association with arterial wall rigidity and damage to target organs. In this regard, it is suggested that CRP may also serve as a predictor of cardiovascular health. In addition, with normal blood pressure, an increase in CRP may predict the future development of hypertension [15].

Elevated CRP levels in patients with AH and excess weight indicate systemic inflammation. [12].

The data obtained suggest that immunological mechanisms, mediated by increased levels of the pro-inflammatory cytokines TNF- $\alpha$  and CRP, play an important role in the development of vascular rigidity.

At the same time, in order to confirm the study results, additional large-scale studies are needed, as well as an analysis of the influence of other cardiovascular risk factors, such as physical activity and smoking, on arterial stiffness parameters in young women with increased body weight and arterial hypertension.

## Conclusions

1. Young women with stage 1 AH showed significantly greater increases in vascular stiffness and central aortic pressure than the control group.

2. In women with stage 1 AH and excess body weight, significantly higher values of central haemodynamic parameters were observed: systolic aortic pressure, diastolic aortic pressure, mean aortic pressure and pulse aortic pressure, as well as pulse wave velocity, compared to a group of patients with AH and normal body weight. The obtained data indicates an increase of arterial rigidity in young women with grade 1 arterial hypertension and excess body weight.

3. An increase in serum concentrations of tumor necrosis factor- $\alpha$  and C-reactive protein was observed in female patients with grade 1 hypertension, which was more pronounced in those with excess body weight, which confirms the role of inflammation in the pathogenesis of hypertension in the examined cohort of young women.

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