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CHANGES IN CENTRAL AORTIC PRESSURE AND ARTERIAL STIFFNESS IN YOUNG MEN WITH ARTERIAL HYPERTENSION AND CHRONIC KIDNEY DISEASE

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The purpose of the study was to investigate changes in central aortic pressure and arterial stiffness in young patients with hypertension and chronic kidney disease and to identify factors influencing these changes. We examined 74 men (mean age 27.3±3.6 years) with hypertension of the 1st and 2nd degree. Depending on the presence of chronic kidney disease, 2 groups were identified: 20 patients without chronic kidney disease (group 1) and 54 patients with chronic kidney disease of stages 1-3 (group 2). The control group included 20 men (mean age 27.1±2.3 years). It was found that in young patients with hypertension, central aortic pressure and pulse wave velocity in elastic arteries are increased compared to the control group; moreover, they are more pronounced in the presence of chronic kidney disease. It was also shown that the daily non-dipper profile and left ventricular hypertrophy were significantly more common in young patients with hypertension and chronic kidney disease compared to the group without renal disease and the control group.

Key words: arterial hypertension in young people, central aortic pressure, pulse wave velocity, daily blood pressure monitoring, left ventricular hypertrophy.

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ЗМІНИ ЦЕНТРАЛЬНОГО АОРТАЛЬНОГО ТИСКУ ТА АРТЕРІАЛЬНОЇ РИГІДНОСТІ У ЧОЛОВІКІВ МОЛОДОГО ВІКУ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ ТА ХРОНІЧНОЮ ХВОРОБОЮ НИРОК

Метою дослідження було вивчити особливості змін показників центрального аортального тиску та артеріальної ригідності у пацієнтів молодого віку з артеріальною гіпертензією та хронічною хворобою нирок і визначити фактори, що впливають на ці зміни. Обстежено 74 чоловіків (середній вік 27,3±3,6 років) з артеріальною гіпертензією 1 та 2 ступеня. В залежності від наявності хронічної хвороби нирок було виділено 2 групи: без хронічної хвороби нирок – 20 пацієнтів (1 група) та з хронічною хворобою нирок 1–3 стадії – 54 пацієнта (2 група). Групу контролю склали 20 чоловіків (середній вік 27,1±2,3 років). Встановлено, що у пацієнтів з артеріальною гіпертензією молодого віку показники центрального аортального тиску і швидкість поширення пульсової хвилі по артеріях еластичного типу збільшуються в порівнянні з групою контролю; причому більш виражено при наявності хронічної хвороби нирок. Встановлено, що добовий профіль «нон-диппер» та гіпертрофія лівого шлуночка зустрічались достовірно частіше у пацієнтів молодого віку з артеріальною гіпертензією та хронічною хворобою нирок в порівнянні з групою без ураження нирок та контрольною групою.

Ключові слова: артеріальна гіпертензія в осіб молодого віку, центральний аортальний тиск, швидкість поширення пульсової хвилі, добовий моніторинг артеріального тиску, гіпертрофія лівого шлуночка.

The work is a fragment of the research project "To determine the features of immunocytokine imbalance in comorbid patients with hypertension and type 2 diabetes and cardiovascular and renal complications", state registration No. 0123U101711.

The prognosis of hypertension is determined by both the degree of elevation of blood pressure (BP) and the severity of structural and functional changes in the target organs of the heart, brain, kidneys, and blood vessels [1]. It has been established that the presence of target organ damage in hypertension increases the risk of cardiovascular complications at any level of BP [3]. Various cardiovascular risk factors can have a harmful effect already in adolescence and young adulthood and contribute to the occurrence of adverse consequences later, in adulthood.

Clinical trial data have shown that central aortic pressure is a better predictor of cardiovascular events than peripheral pressure [6]. Elevated central SBP and central PP have been shown to be associated with a significant increase in the risk of cardiovascular events and all-cause mortality [9]. It is suggested that indices of elevated central aortic pressure have a greater prognostic value than those of peripheral BP [5].

The kidneys are a component and a significant part of the microcirculatory system of the body, an important organ of metabolism and humoral regulation of various processes. Undoubtedly, the kidneys affect the formation of cardiovascular pathology and suffer from various cardiovascular diseases. A decrease in glomerular filtration rate (GFR) is considered as a marker of unfavorable prognosis of cardiovascular diseases common in the population, which is fully consistent with the established concept of cardiorenal relationships [8]. However, studies describing the relationship between BP and the main

cardiovascular risk factors for the development of chronic kidney disease (CKD) in young people at the onset of hypertension are limited.

The purpose of the study was to investigate the features of changes in central aortic pressure and arterial stiffness in young patients with arterial hypertension and chronic kidney disease and to identify factors leading to increased arterial stiffness.

Materials and methods. An open controlled study was conducted, which included 74 men aged 18–35 years (mean age 27.3±3.6 years) with grade 1 and 2 hypertension who did not receive regular drug therapy. Among the examined patients, grade 1 hypertension was detected in 66 and grade 2 – in 8 people. The duration of hypertension was 3.2±1.3 years.

Patients were divided into two clinical groups. The first group included 20 patients with hypertension stage 1 and 2 without chronic kidney disease (CKD). The second group consisted of 54 patients with hypertension stage 1 and 2 and CKD stage 1–3, of which 48 patients had eGFR 60–89 ml/min/m² and 6 patients had eGFR 30–59 ml/min/m². The control group consisted of 20 patients aged 18-35 years (mean age 27.1±2.3 years). The clinical characteristics of the examined individuals are presented in Table 1.

Table 1

Clinical characteristics of the examined individuals

Parameters	Control (n=20)	Group 1 (n=20)	Group 2 (n=54)
Average age, years	27.1±2.3	26.9±2.1	27.3±2.3
Duration of hypertension, years		3.1±1.1	3.3±1.3
Smoking, n (%)	10 (50 %)	7 (35 %)	26 (48.1 %)*
Hypertension family history, n (%)	8 (40 %)	9 (45 %)	29 (53.7 %)*
Family history of early cardiovascular events, n (%)	2 (10 %)	3 (15 %)	18 (33.3 %)
BMI, kg/m²	23.1±0.5	24.5±0.5	27.9±0.6*
Abdominal obesity, n (%)	4 (20 %)	4 (20 %)	23 (42.6 %)*
Dyslipidemia, n (%)	3 (15 %)	4 (20 %)	31 (57.4 %)*
SBP, mm Hg	119.7±2.2	150,4±3.3	153.0±3.4
DBP, mm Hg	73.4±1.7	92.8±3.4	94.4±3.4

Notes: * – $p < 0.05$ between groups 1 and 2.

All participants signed informed consent to participate in the study. Patients were screened in accordance with the recommendations of the European Society of Hypertension and the European Society of Cardiology (ESH/ESC, 2018).

Exclusion criteria: history of regular use of antihypertensive drugs, professional athletes, secondary hypertension, cardiac arrhythmias, inflammatory diseases, autoimmune and endocrine diseases (including type 2 diabetes mellitus).

All examined individuals underwent a general clinical examination, which included a survey to identify risk factors for cardiovascular diseases, examination, anthropometric measurements, physical examination, measurement of office blood pressure, heart rate, general blood and urine analysis (with determination of microalbuminuria), iochemical blood test with determination of fasting glucose, lipid metabolism indicators, creatinine with calculation of glomerular filtration rate (eGFR) according to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula. Chronic kidney disease (CKD) was defined according to the Clinical Practice Guideline for Evaluation and Management Chronic Kidney Disease (KGIGO 2012).

The criterion for overweight was considered to be 25 kg/m²≤BMI<30 kg/m², the criterion for obesity was BMI≥30 kg/m², and for abdominal obesity: waist circumference (WC) in men ≥94 cm; for WC/WC≥0.94 in men.

When analyzing metabolic factors, it was found that BMI in the control group and patients with hypertension without CKD was significantly lower than in patients with hypertension and CKD ($p<0.05$). Abdominal obesity was significantly more common in patients with hypertension and CKD compared to patients with hypertension without CKD and the control group.

To assess kidney function in patients with hypertension, our study evaluated the UIA index, serum creatinine level, and glomerular filtration rate (GFR)

24–hour BP monitoring (BPM) was performed using the "ABPM–02" device (Meditech, Hungary). The following were assessed: mean values of SBP, DBP, pulse pressure (PP), mean BP per day (24 hours), day and night, time index (TI) of hypertension: % of measurements of SBP ≥140 and DBP ≥90

mm Hg. during the period of alertness and, respectively, ≥120 and ≥70 mm Hg. during sleep. The severity of the day–night biphasic BP rhythm was assessed by the diurnal index (DI), which was calculated by the formula:

DI = 100 % x (BPd – BPn) / BPd,

here BPd is the average BP during wakefulness; BPn is the average BP during sleep.

Four groups of patients were distinguished by the value of the DI:

– "dipper" (DI – 10–20 %) – optimal nocturnal decrease in BP;

– "non-dipper" (DI – 0–10 %) – insufficient nocturnal decrease in BP;

– "night picker" (DI <0) – persistent increase in nocturnal BP;

– "over-dipper" (DI >20 %) – excessive nocturnal decrease in BP.

Central aortic pressure and arterial stiffness were measured by applanation tonometry with pulse wave contour analysis on the carotid-femoral segment using the SphygmoCor-PVx device (AtCor Medical Pty Ltd, Australia) according to standard methods recommended by experts in the assessment of arterial stiffness (Laurent S., 2006). The program automatically calculated the levels of systolic, diastolic, and aortic pressure and pulse wave velocity (PWV).

Structural and functional parameters of the heart were determined by echocardiography using the diagnostic system "GE Medical Systems" (Germany) with a phased array sensor with a modulated frequency of 2.25–3 MHz in M- and B-modes in accordance with the recommendations of the American Society of Echocardiography (ASE, 2016). The LV myocardial mass (LVMM) and LVMM index (LVMMI) were calculated according to the recommendations of the ASE (2016). According to the recommendations of the European Society of Cardiology in 2018, 95 g/m² and 115 g/m² for women and men, respectively, were used as the threshold values, when reached or exceeded, the presence of LVH can be determined.

Mathematical computer processing of the research results was carried out using the Statistica 10.0 software package using standard algorithms of variation statistics. For quantitative indicators measured on an interval scale, the mean value, standard deviation and error of the mean were calculated. For "qualitative" and "ordinal" indicators, the frequency of detection of the indicator in percent or the frequency of registration of different rank estimates of the indicator, respectively, was determined. When analyzing intergroup differences in indicators, the value of the Student's t-test was calculated. In the case of indicators measured on a nominal scale, the reliability of differences in the frequency of detection of the indicator in the two compared groups was assessed by the Student's t-test using Fisher's transformation, linear correlation coefficients and rank correlations were calculated. Differences in mean values and correlations were considered reliable at a significance level of $p < 0.05$.

Results of the study and their discussion. The results of the renal functional state are presented in Table 2.

Table 2

Parameters of the functional state of the kidneys in the examined patients

Parameters	Group 1 (n=20)	Group 2 (n=54)
Creatinine, μmol/l	78.6±5.7	84.6±6.3
Albuminuria, mg/day	9.12±10.7	25.13±25.1
GFR, ml/min/1.73 m²	92.9±11.6	71.5±10.8

It was noted that the serum creatinine level in all groups of patients did not exceed the threshold values and did not differ significantly between groups ($p>0.05$).

Determination of the level of albumin in the urine, according to quantitative analysis, made it possible to establish that in the examined patients with AH 1 and 2 stages of young age, the presence of MAU >30 mg/l as a criterion for target organ damage is not typical and was detected only in 8 (11.6 %) patients. Thus, MAU >30 mg/l was detected in 1 (5 %) patient out of 20 people in the 1st group, in the 2nd group with AH and CKD stages 1 and 2, MAU >30 mg/l was detected in 5 (10.4 %) out of 48 patients, and in patients with CKD stage 3 in 2 (33.3 %) out of 6 patients. Thus, a tendency towards an increase in the frequency of detection of MAU with an increase in the stage of CKD was established.

Among all examined patients, an increase in total cholesterol (TC) levels of more than 5.0 mmol/l was noted in 3 (15 %) of the control group, 4 (20 %) of group 1 and 31 (57.4 %) of group 2 patients. In group 2, an increase in TG levels ≥1.7 mmol/l was determined in 19 patients (35.1 %), and a decrease in HDL-C levels in men ≤ 1.0 mmol/l was detected in 23 (42.6 %) patients.

According to the DMBP data, the average daily values of systolic and diastolic BP did not differ between the groups of examined patients, which was explained by the inclusion criteria for patients with stage 1 and 2 hypertension. The results of the DMBP analysis did not allow us to determine the influence

of these DMBP indicators on the presence and stage of CKD. Analysis of the types of daily blood pressure curves according to the DMBP data showed that in all groups of examined patients with stage 1 and 2 hypertension, a high prevalence of the "non-dipper" daily profile (72.9 %) was recorded. At the same time, the maximum percentage of people with a violation of the daily profile ("non-dipper") was registered in the 2nd group with CKD stages 1, 2, 3 – in 41 (75.9 %) patients, while in the group with hypertension without CKD – in 9 (45.0 %) patients. Central aortic pressure values are shown in Fig. 1.

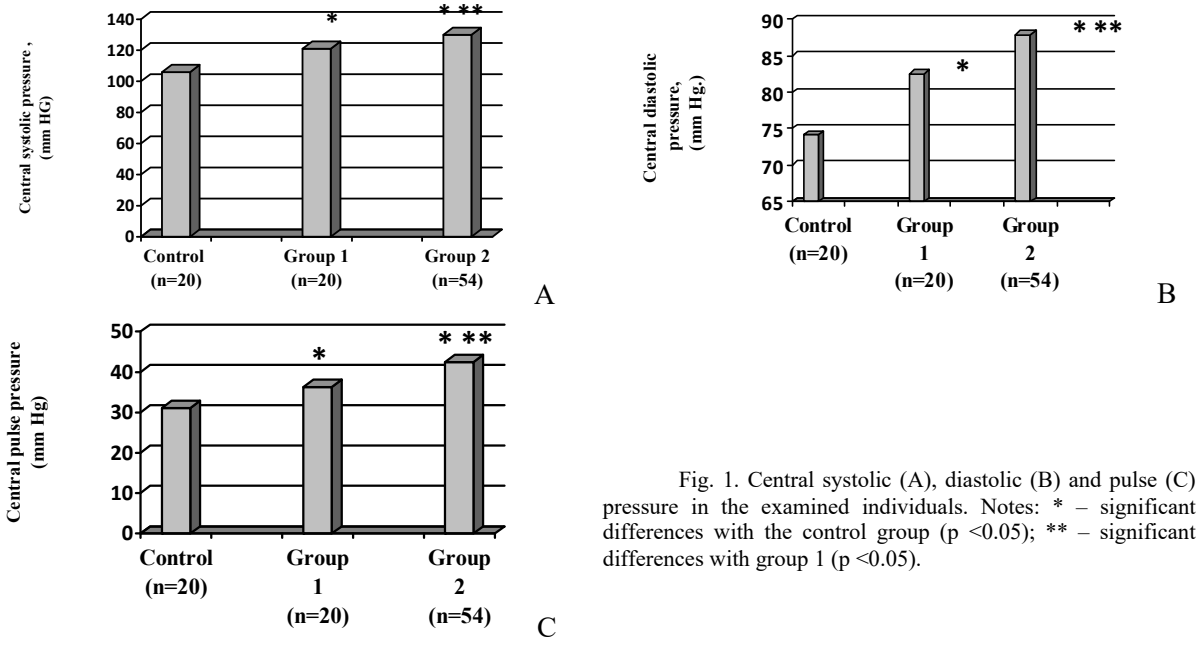

Fig. 1. Central systolic (A), diastolic (B) and pulse (C) pressure in the examined individuals. Notes: * – significant differences with the control group (p <0.05); ** – significant differences with group 1 (p <0.05).

It was found that the central systolic pressure increased in the group 1 by 14.2 % and in the group 2 by 22.6 % (all p<0.05). In patients with hypertension and CKD, an increase in central systolic pressure was found by 7.4 % (p<0.05) compared to patients with hypertension without CKD and by 22.6 % (p<0.05) compared to the control group. Diastolic pressure in the aorta increased in the group with hypertension by 11.3 % and in the group with hypertension and CKD by 18.6 % (all p<0.05) compared to the control group. When analyzing the changes in this indicator between the groups of examined patients, it was found that in the group 2 there was an increase compared to group 1 by 6.5 %, which did not reach a significant difference. Changes in central pulse pressure were as follows. According to the study, it was found that compared with the control group, this indicator increased by 16.7% in patients with hypertension without CKD and by 36.7% in patients with hypertension and CKD (all p<0.05). Central pulse pressure in the 1st group exceeded the control group by 13.1 % (p<0.05) and was lower by 17.1 % (p<0.05) compared with the data of the 2nd group. The pulse wave propagation velocity (PWV) measured on the carotid-femoral segment in patients with hypertension and CKD was 9.6 % higher (p<0.05) compared to patients with hypertension without CKD (Fig. 2).

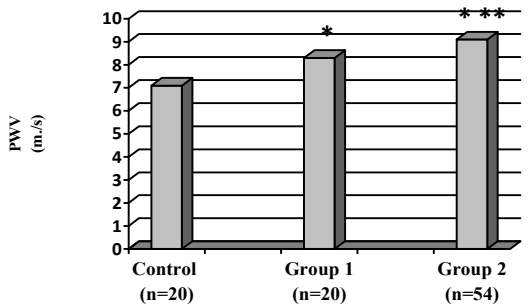

Fig. 2. Changes in PWV in the examined individuals. Notes: * – significance of differences with the control group (p <0.05); ** – significance of differences with group 1 (p <0.05).

In our study, elevated PWV was registered in 42 (77.8 %) patients with hypertension and CKD and 8 (40 %) patients with hypertension without CKD. In patients with hypertension and CKD, PWV was 28.2 % (p<0.05) higher than in the control group, while in patients with hypertension – by 16.9 % (p<0.05).

When analyzing the structural and functional parameters of the heart, it was noted that all indicators did not differ from normal values (Fig. 3).

In the absence of significant differences in the volume of the LV in systole and diastole in the groups of examined patients, a significant decrease in ejection fraction (EF) LV was found in patients with CKD stage 3 compared to patients with hypertension without CKD (by 20.3 %) and in individuals with hypertension and CKD stages 1 and 2 – by 19.2 % (p<0.05). Thickening of the posterior wall of the LV and the interventricular septum was found in the group of patients with stage 3 CKD compared with the data of patients in group 1 and patients with hypertension and stage 1–2 CKD.

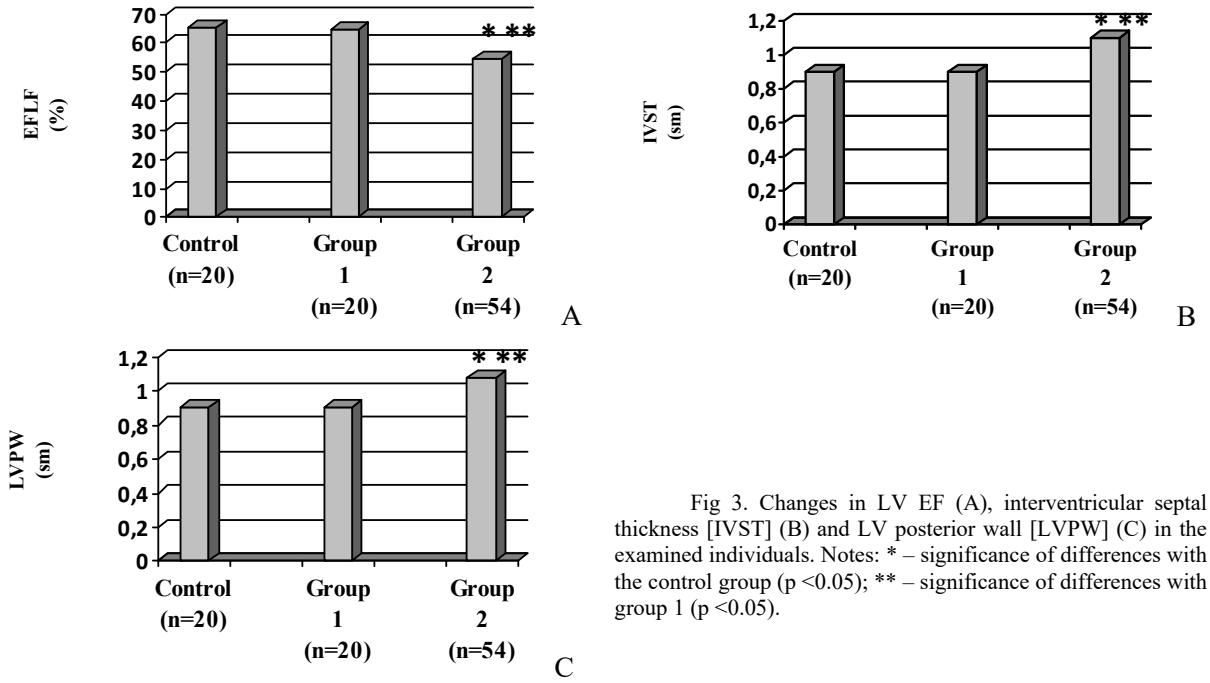

Fig 3. Changes in LV EF (A), interventricular septal thickness [IVST] (B) and LV posterior wall [LVPW] (C) in the examined individuals. Notes: * – significance of differences with the control group ($p < 0.05$); ** – significance of differences with group 1 ($p < 0.05$).

In young people, a persistent and prolonged increase in blood pressure to stage 1 and 2 hypertension is accompanied by an increase in the mass of the LV myocardium, which may indicate the initial manifestations of myocardial remodeling. To determine the presence of LVH in the examined individuals, LVMMI was calculated. It was found that in general, LVH was detected in 14 individuals in the examined patients. It was noted that significantly ($p<0.05$) higher LVMMI was determined in the group of patients with hypertension and CKD (104.6±4.2 g/m²), compared to patients with hypertension without CKD (89.6±2.1 g/m²). Moreover, in individuals with hypertension and CKD stage 3, this indicator was – 139.8±5.3 g/m² and exceeded the values of patients in group 1 and individuals with hypertension and CKD stage 1-2 (all $p<0.05$). Intragroup analysis showed that LVH was detected in 5 % of patients without CKD, in 20.8 % of patients with CKD stages 1 and 2, and in 66.7 % of patients with CKD stage 3.

We found that overweight and abdominal obesity, dyslipidemia were significantly more common in group 2. It has been previously shown that with increasing body weight, the prevalence of hypertension increases significantly [10]. These data support the idea that increased body weight due to a high proportion of visceral adipose tissue is significantly associated with the development of hypertension and other metabolic risk factors for cardiovascular diseases [2].

CKD is commonly associated with lipid metabolism disorders, which may contribute to morbidity and premature mortality associated with renal dysfunction. Dyslipidemia often occurs early in the disease and gradually worsens with disease severity and progression to end-stage renal disease (ESRD) [11]. Our study found lipid abnormalities in patients in group 2, which is consistent with previous studies.

It has been proven that patients with a “monotonic” diurnal BP profile (non-dipper, night-picker type) are at increased risk of developing LVH, myocardial infarction, and stroke [12]. Our study identified a higher prevalence of the “non-dipper” diurnal profile in group 2 of patients, which may be associated with a short history of hypertension, which is also confirmed by other researchers [7].

In young people, a persistent and prolonged increase in blood pressure to grades 1 and 2 hypertension is accompanied by an increase in the mass of the LV myocardium, which may indicate the initial manifestations of myocardial remodeling. The data obtained by us naturally reflect the process of the emergence and development of LVH as a target organ damage with increased blood pressure and are confirmed by the data of numerous studies of the structural and functional state of the LV in patients with hypertension [14].

Arterial stiffness is considered an independent predictor of cardiovascular risk and mortality [8]. According to the literature, increased arterial stiffness is reflected in changes in its structural and functional state. Structural changes include an increase in the content of extracellular matrix, the index of proliferation of smooth cells, degradation of the internal elastic membrane and collagen deposition [13]. We assessed the elastic properties of the aorta, parameters of central aortic pressure, and the nature of the formation of the reflected wave. The classic marker of vascular stiffness is the PWV [8]. In our study, it was found that the PWV in patients with hypertension with CKD was significantly higher ($p<0.05$) compared with patients with hypertension without CKD.

Central aortic pressure has previously been shown to be an independent predictor of cardiovascular mortality [13]. We show that central systolic pressure, aortic diastolic pressure, and central pulse pressure increased in both groups of patients with hypertension, but more significantly in the group with hypertension and CKD.

Conclusions

1. In young people with hypertension of stages 1 and 2, the central aortic pressure and the velocity of the pulse wave propagation along the elastic arteries increased compared to healthy individuals; more pronounced changes were observed in patients with hypertension and CKD stages 1-3.

2. In young patients with stage 1 and 2 hypertension, a relationship has been established between the stages of CKD and cardiovascular risk factors, such as abdominal obesity, dyslipidemia, and albuminuria. A high prevalence of a non-dipper daily blood pressure profile according to DMBP data has been established in young patients with stage 1 and 2 hypertension who did not receive systematic drug therapy. In patients with hypertension and CKD stages 1-3, the frequency of a non-dipper daily blood pressure profile is higher than in patients with hypertension without CKD.

3. In young men with stage 1 and 2 hypertension who did not receive systematic drug therapy, a statistically significant relationship was found between the presence and stage of CKD and LVMMI, as well as the presence of left ventricular hypertrophy. In the presence of stage 1 and 2 CKD, LVH was detected in 20.8 % and in stage 3 CKD – in 66.7 % of cases. For patients with stage 1 and 2 hypertension without CKD, the presence of LVH was not characteristic and occurred only in 5 % of cases.

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