



## Clinical and Functional State of the Kidneys in Middle-Age Patients with Arterial Hypertension

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**Abstract:** *Purpose of the study*– assessment of the functional state of the kidneys and the formation of chronic kidney disease in middle-aged patients with arterial hypertension without associated diseases. **Material and methods.** 58 patients aged 38 to 60 years with a diagnosis of arterial hypertension were examined. A clinical diagnostic examination was carried out in the hospital: examination and history taking, biochemical blood test, general urine test, determination of glomerular filtration rate, monitoring of the clinical condition and tests during the hospital stay after 3 and 6 months. The study did not include patients with associated diseases or severe diseases of internal organs. **Results and its discussion.** In patients with arterial hypertension and without associated cardiovascular diseases, the main factors influencing the formation of renal dysfunction, manifested by hyposthenuria, albuminuria and proteinuria, are smoking, obesity, dyslipidemia and arterial hypertension. When arterial hypertension lasted more than 10 years, hypertensive nephropathy and chronic kidney disease were diagnosed in 67% of cases. **Conclusions.** The results of the study confirm that smoking, obesity, dyslipidemia and arterial hypertension influence the formation of kidney dysfunction, manifested by albuminuria/proteinuria. The risk of developing hypertensive nephropathy with a duration of arterial hypertension of more than 10 years is 13 times higher than the risk of developing renal dysfunction with a duration of arterial hypertension of less than 5 years (RR=13.3, CI 95% 1.92–92.61;  $p<0.001$ ). Nephroprotective antihypertensive therapy promotes reverse regression of albuminuria.

**Key words:** arterial hypertension, nephropathy, risk factors, albuminuria, chronic kidney disease.

Arterial hypertension (AH) is the most common disease in the adult population. With the onset of the disease, vital organs are involved in the pathological process - the heart, blood vessels, kidneys, brain, while the clinical manifestations of target organ damage are often determined only with advanced changes [1, 2,11,12,15, 28, 30.] . At the initial stages of hypertension, only hemodynamic changes occur in the kidneys, which may not affect its function for a long time and may not be accompanied by structural changes. The kidneys, on the one hand, are the target organs for hypertension, on the other, they are involved in the maintenance and progression of hypertension [3-23]. Kidney damage in hypertension is manifested by the development of hypertensive nephropathy and chronic kidney disease [6]. An early marker of kidney involvement in the pathological process is albuminuria, and a late marker is proteinuria [22-36]. The development of kidney damage in middle-aged patients with hypertension is of interest, since initially there is a lower likelihood of having associated cardiovascular diseases and, accordingly, a lower degree of target organ damage [7,34,35, 36].

**Purpose of the study**– assessment of the functional state of the kidneys and the formation of chronic kidney disease in middle-aged patients with arterial hypertension and without associated diseases.

**Material and methods.** The study included 58 patients with hypertension (main group) aged from 38 to 60 years [average age ( $M \pm m$ ) – ( $49.5 \pm 3.7$ ) years; 46 men and 12 women] who underwent examination and treatment in the cardiology department. The exclusion criteria from the study were acute diseases and/or exacerbation of chronic diseases of internal organs during the observation period, a history of acute and/or chronic kidney disease, cerebrovascular pathology, combined cardiovascular diseases, including coronary heart disease, atherosclerotic lesions of the central and peripheral arteries. The control group included 32 practically healthy people, comparable in age and gender with the main group [average age – ( $39.1 \pm 4.1$ ) years;  $p=0.108$ ; 22 men and 10 women,  $\chi^2=1.8$ ;  $p=0.178$ ]. Anamnesis was studied with an assessment of smoking status, a clinical examination was performed [body mass index (BMI), assessment of systolic (SBP) and diastolic (DBP) blood pressure], biochemical examination of blood (creatinine, cholesterol, triglycerides, albumin) and urine (albumin, protein, relative density). Glomerular filtration rate (GFR) was calculated using the CKD-EPI formula (NKF, 2009). The observation period and assessment of parameters (SBP, DBP, GFR, urine albumin) over time ( $\Delta$ ) was 6 months. Statistical analysis was carried out using parametric and non-parametric statistics methods: mean value ( $M$ ), standard error ( $m$ ), relative risk (RR) and confidence interval (CI),  $\chi^2$  test, Student t test ( $t$ ) with Bonferroni correction. Differences between samples were considered statistically significant at  $p < 0.05$ . Results and its discussion. The results of clinical and laboratory examination are presented in table. 1. The duration of hypertension was ( $7.4 \pm 0.8$ ) years. All examined patients irregularly took or did not take antihypertensive therapy before hospitalization, which caused the initially high levels of SBP [ $(153.8 \pm 5.5)$  mmHg;  $p=0.000$ ] and DBP [ $(95.3 \pm 1.4)$  mmHg;  $p=0.000$ ] compared to the control group [respectively ( $120.2 \pm 6.1$ ) mmHg. and ( $76.1 \pm 0.7$ ) mmHg]. BMI was higher ( $p=0.000$ ) in the main group [ $(30.6 \pm 1.1)$  kg/m<sup>2</sup>] than in the control group [ $(22.3 \pm 0.6)$  kg/m<sup>2</sup>]. 34 patients with hypertension (58%) smoked. The lipid spectrum in patients with hypertension was also characterized by high cholesterol levels [ $(5.9 \pm 0.2)$  mmol/l;  $p=0.002$ ] and triglycerides [ $(3.6 \pm 0.6)$  mmol/l;  $p=0.017$ ] in the blood compared to the control group ( $4.8 \pm 0.3$  and  $1.5 \pm 0.4$ , respectively). The data obtained allow us to conclude that there are unity of risk factors for cardiovascular and kidney diseases. There were no differences between the groups in the levels of creatinine and blood albumin. However less in patients with hypertension, a lower GFR was determined [ $(82.1 \pm 3.1)$  ml/min/1.73 m<sup>2</sup>] compared to the group of healthy individuals ( $112.1 \pm 1.9$ ;  $p=0.000$ ), a decrease in relative density urine ( $1.016 \pm 0.001$ ;  $p=0.049$ ), a “high” increase in the level of albumin in urine was detected [ $(45.6 \pm 10.2)$  mg/g;  $p=0.004$ ] and proteinuria [ $(158.2 \pm 15.4)$  mg/day;  $p=0.000$ ]. Thus, the smoking factor [3, 8], obesity, dyslipidemia [9] and hypertension [3, 10] influence the formation of renal dysfunction, manifested by hyposthenuria, albuminuria and proteinuria. Albuminuria more than 30 mg/g was detected in 29 (50%) people, respectively, the risk of developing moderate albuminuria with

blood pressure above 140/90 mm Hg. 16 times higher than in the control group with blood pressure less than 140/90 mm Hg. (RR=16.0, CI 95% 2.28–112.03;  $p=0.001$ ). Smoking in patients with hypertension increases the risk of kidney dysfunction with the development of moderate albuminuria by 24 times compared with healthy individuals (RR=24.5, CI 95% 2.52–169.97;  $p=0.000$ ). Depending on the duration of hypertension, the main group was divided into 3 groups; the functional state of the kidneys was assessed prospectively (over 6 months). The 1st group included 20 people with a duration of hypertension up to 5 years, the 2nd group included 20 people with a duration of hypertension from 5 to 10 years, and the 3rd group included 15 patients suffering from hypertension for more than 10 years. Data of clinical and laboratory parameters are presented in table. 2. As can be seen from those presented in table. 2 data, the groups did not differ from each other ( $p>0.05$ ) in gender, degree of hypertension, SBP and DBP levels, blood creatinine level. Overweight (BMI>25 kg/m<sup>2</sup>) was detected in all groups. There were no differences ( $p>0.05$ ) between the groups in the level of GFR and relative density of urine, however, in the 3rd group of patients a lower GFR and hyposthenuria were determined. With the duration of hypertension, albuminuria ( $p = 0.002$ ) increases to the “high” level and proteinuria ( $p = 0.000$ ). Thus, markers of kidney dysfunction are most pronounced in patients suffering from hypertension for more than 10 years. All patients received 2-component antihypertensive therapy (the main drug is an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker) in accordance with accepted recommendations [2, 10]. Assessment of SBP and DBP, GFR and urine albumin levels are presented over time after 3 and 6 months (Table 3). In all groups of patients, the effectiveness of antihypertensive therapy was revealed in achieving target levels of SBP ( $p = 0.000$ ) and DBP ( $p = 0.000$ ) after 6 months, with the greatest rate of decrease in SBP determined in the 1st group of patients [ $\Delta = (-4.8)$  mmHg/month] and DBP in group 3 [ $\Delta=(-2.5)$  mm Hg/month]. According to the rate of decrease in SBP/DBP less than 140/90 mm Hg. There were no differences between groups ( $p>0.05$ ). By the 6th month of observation, there was a trend towards an increase in GFR without any significant changes in all observed patients with hypertension. Against the background of stable antihypertensive therapy in patients with a duration of hypertension of less than 5 years, the level of urine albumin after 6 months did not change and remained at the “highly normal” level ( $p = 0.609$ ). Regression of albuminuria without significant changes to the initial level ( $p>0.05$ ) was detected in the 2nd group of patients (from “high” to “highly normal”)

**Table 1 Clinical and laboratory characteristics of the examined patients with arterial hypertension**

Index	Main group $n=58$ (M $\pm$ m)	Control group, $n=32$ (M $\pm$ m)	R
Age, years	49.5 $\pm$ 3.7	39.1 $\pm$ 4.1	0.108
Men	46	22	$\chi^2=1.8$ 0.178
Women	12	10	
Duration of hypertension, years	7.4 $\pm$ 0.8	—	—
Smoking, number of smokers, %	34(58)	—	—
BMI, kg/m <sup>2</sup>	30.6 $\pm$ 1.1	22.3 $\pm$ 0.6	0.000
SBP, mmHg	153.8 $\pm$ 5.5	120.2 $\pm$ 6.1	0.000
DBP, mm Hg.	95.3 $\pm$ 1.4	76.1 $\pm$ 0.7	0.000
Cholesterol, mmol/l	5.9 $\pm$ 0.2	4.8 $\pm$ 0.3	0.002
Triglycerides, mmol/l	3.6 $\pm$ 0.6	1.5 $\pm$ 0.4	0.017
Blood creatinine, $\mu$ mol/l	93.1 $\pm$ 3.4	91.5 $\pm$ 1.8	0.739
GFR, ml/min/m <sup>2</sup>	82.1 $\pm$ 3.1	112.1 $\pm$ 1.9	0.000
Blood albumin, g	52.6 $\pm$ 0.6	51.4 $\pm$ 0.5	0.181
Urine albumin, mg/g	45.6 $\pm$ 10.2	5.0 $\pm$ 0.1	0.004
Protein, mg/day	158.2 $\pm$ 15.4	0.00	—
Relative density of urine	1.016 $\pm$ 0.001	1.020 $\pm$ 0.002	0.049

Note: *p*– reliability when comparing groups using analysis of variance.

### Clinical and laboratory characteristics of patients depending on the duration of arterial hypertension

Table 2

Index	1st group, <i>n</i> =20 ( <i>M</i> ± <i>m</i> )	2nd group, <i>n</i> =20 ( <i>M</i> ± <i>m</i> )	3rd group, <i>n</i> =18 ( <i>M</i> ± <i>m</i> )	<i>R</i>
Age, years	46.2±1.7	49.9±1.2	53.1±1.6*	0.009
Men	16	15	15	$\chi^2=0.047$ 0.977
Women	4	5	3	
Duration of hypertension, years	3.3±0.4	7.3±0.5*	12.7±1.3*^	0.000
BMI, kg/m <sup>2</sup>	31.3±1.4	29.7±2.3	30.6±1.9	0.833
SBP, mmHg	156.0±3.4	159.5±4.2	153.8±8.5	0.778
DBP, mm Hg.	95.5±1.6	94.0±2.3	96.9±3.4	0.715
AG degree:				$\chi^2=1.586$ 0.452
I	12	8	4	
II	6	8	10	
III	2	4	4	
Blood creatinine, μmol/l	90.3±4.4	91.8±8.1	98.4±3.7	0.596
GFR, ml/min/m <sup>2</sup>	86.1±4.7	82.2±6.9	71.6±3.8	0.082
Urine albumin, mg/g	12.2±2.0	42.1±15.9	92.3±21.9*	0.002
Protein, mg/day	34.1±1.1	118.2±2.3*	192.0±3.7*^	0.000
Relative density of urine	1.018±0.002	1.016±0.001	1.014±0.001	0.057

Note: *p*– reliability for multiple comparisons of groups using analysis of variance; \*significant (*p*<0.05) difference with group 1 (Student's *t* test with Bonferroni correction); ^significant (*p*<0.05) difference with group 2 (Student's *t* test with Bonferroni correction).

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level [ $\Delta$ =(-2.25) mg/g/month; *p*=0.415] and group 3 remained at the “high” level [ $\Delta$ =(-5.7) mg/g/month; *p*=0.175]. At the same time, the rate of decline

Table 3 Dynamics of clinical and laboratory parameters during regular antihypertensive therapy

Index	1st group, <i>n</i> =20 ( <i>M</i> ± <i>m</i> )	2nd group, <i>n</i> =20 ( <i>M</i> ± <i>m</i> )	3rd group, <i>n</i> =18 ( <i>M</i> ± <i>m</i> )	<i>R</i>
SBP, mmHg, baseline	156.0±3.4	159.5±4.2	153.8±8.5	
SBP, mmHg, 3rd month	129.5±2.3	133.5±1.5	132.5±2.8	
SBP, mmHg, 6th month	126.8±2.1	131.5±1.8	130.2±3.8	0.420
$\Delta$ SBP, mm Hg/month	-4.8	-4.6	-3.9	
Rto the original	0.000	0.000	0.016	
DBP, mmHg, baseline	95.5±1.6	94.0±2.3	96.9±3.4	
DBP, mm Hg, 3rd month	81.2±2.7	84.5±1.6	88.9±1.7	
DBP, mm Hg, 6th month	81.8±2.9	83.8±1.9	81.9±2.3	0.601
$\Delta$ DBP, mmHg/day	-2.3	-1.7	-2.5	
Rto the original	0.000	0.002	0.000	
Urine albumin, mg/g, initially	12.2±2.0	42.1±15.9	92.3±21.9	
Urine albumin, mg/g, 3rd month	15.1±4.8	36.8±4.7	76.3±14.1	

Urine albumin, mg/g, 6th month	13.1±3.1	28.6±3.9	58.9±10.1*^	0.000
<b>Δ urine albumin, mg/g/month</b>	0.15	-2.25*	-5.7*^	
<b>Rto the original</b>	0.609	0.415	0.175	
GFR, ml/min/m2, baseline	86.1±4.7	82.2±6.9	71.6±3.8	
GFR, ml/min/m2, 3rd month	88.9±3.9	83.1±7.9	71.9±5.7	
GFR, ml/min/m2, 6th month	91.4±3.7	83.4±8.0	78.6±6.1	0.348
<b>Δ GFR, ml/min/m2/month</b>	0.88	0.2	1.17	
<b>Rto the original</b>	0.381	0.910	0.337	

Note: \*significant ( $p < 0.05$ ) difference with group 1 (Student's *t* test with Bonferroni correction);

^significant ( $p < 0.05$ ) difference with group 2 (Student's *t* test with Bonferroni correction).

albuminuria was highest in patients with hypertension for more than 10 years compared with the group of patients with hypertension for less than 5 years ( $p < 0.05$ ). Persistent albuminuria of more than 30 mg/g for 6 months in 12 (67%) patients with hypertension duration of more than 10 years allowed us to establish stage II chronic kidney disease due to the development of hypertensive nephropathy. Analysis of the risks of kidney dysfunction with the development of albuminuria was determined to be highest in patients with a duration of hypertension of more than 10 years and 13 times higher than that with a duration of hypertension of less than 5 years (RR = 13.3, CI 95% 1.92–92.61;  $p < 0.001$ ).

## Conclusions

Thus, the results of our study confirm that smoking, obesity, dyslipidemia and hypertension influence the formation of kidney dysfunction, manifested by albuminuria/proteinuria. When hypertension lasted more than 10 years, the development of hypertensive nephropathy and chronic kidney disease was detected in 67% of cases. The risk of developing hypertensive nephropathy with a duration of hypertension of more than 10 years is 13 times higher than the risk of developing kidney dysfunction with a duration of hypertension of less than 5 years (RR=13.3, CI 95% 1.92–92.61;  $p < 0.001$ ). Nephroprotective antihypertensive therapy promotes reverse regression of albuminuria.

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