

Role of modifiable risk factors in the development of cognitive impairment in hypertensive patients

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Abstract

Background. The prevalence of all types of cognitive impairment, including dementia, is increasing but knowledge of aetiological factors is still evolving. This study aimed to analyze the state of cognitive functions in hypertensive patients and evaluate the role of risk factors in their occurrence.

Materials and methods. We examined 89 patients (1-st group; middle age of patients was $51,1 \pm 7,3$ years; 53,9% of men) with stage 2 hypertension and 30 practically healthy people (2-nd group; middle age of individuals was $41,4 \pm 10,1$ years; 56,7% of men) with normal level of blood pressure. Cognitive tests included the General Practitioner assessment of Cognition (GPCOG), the Mini-Mental State Examination (MMSE), Schulte tables.

Results. The average MMSE score was 26.5 ± 1.8 in the 1st group and 28.9 ± 1.0 in the 2nd group, that indicates a significant cognitive decline in hypertensive patients ($p < 0.01$). Obese and hypertensive patients performed more poorly than nonobese hypertensives, their average MMSE score was significantly lower (26.4 ± 1.4 and 28.0 ± 1.2 , respectively, $p < 0.01$). The level of total cholesterol and LDL-C was also associated with cognitive decline (MMSE score was 26.1 ± 1.8 and 27.5 ± 1.4 , respectively, $p < 0.01$). Smoking was negatively associated with attention and sensomotor reactions rate.

Conclusions. Cognitive performance was significantly lower in hypertensive patients compared to the control group. Factors that definitely affect the development of cognitive impairment in hypertensive patients are increased BMI, hypercholesterolemia and smoking.

Keywords: hypertension, cognition, smoking, cholesterol, body mass index

Introduction. There is no doubt that dementia is an urgent medical and social problem. There are about 50 million people with dementia worldwide, about 10 million new cases are reported each year. The total number of people with dementia is predicted to be about 82 million in 2030 and will almost double by 2050 [1].

The onset of dementia is always preceded by cognitive impairment. So, in a year dementia will occur in 5-15% of patients with moderate cognitive disorders (for comparison - in the general population the probability of its development is 1-5%), and in 4 years such patients will be already 70%, accordingly in 5 years 100% of patients with cognitive impairment will suffer from dementia.

It is also known that cardiovascular disease, especially arterial hypertension, is a major risk factor of cognitive impairment. The connection between high arterial blood pressure (BP) and cognitive impairment in older patients has been established in large epidemiological studies: The Framingham Heart Study, Hoorn Study, Uppsala Longitudinal Study of Adult Men, ARIC, Honolulu-Asia Aging Study. Subclinical brain damages (as a target organ at hypertension) are observed in 44% of patients, which is approximately double the prevalence of heart and kidney lesions [2].

But, unfortunately, the standard plan of examination of a hypertensive patient does not include the examination of the brain, so in clinical practice doctors state its lesions already at the stage of development of complications. [3]. The pathophysiology of dementia is complicated and still poorly studied, and there is no cure that can stop the disease from progressing. Taking into consideration the fact that age and genetic disposition are uncontrolled, it is important to study the risk factors of dementia that can be modified.

The goal of work is to analyze the state of cognitive functions in hypertensive patients and evaluate the role of risk factors (overweight, hypercholesterolemia, smoking) in their occurrence.

Materials and methods of investigation. We examined 89 patients (1-st group; middle age of patients was $51,1 \pm 7,3$ years; 53,9% of men) with stage 2 hypertension and 30 practically healthy people (2-nd group; middle age of individuals was $41,4 \pm 10,1$ years; 56,7% of men) with normal level of blood pressure in Chervonograd Central City Hospital.

All patients underwent clinical and anamnestic examination during which BP was measured and body mass index (BMI) was determined, laboratory tests (level of total cholesterol (TC), high and low density lipoprotein cholesterol (LDL-C), triglycerides, glucose, creatinine and calculating glomerular filtrate rate, electrolytes of blood) were done and instrumental methods of investigation (24-hour monitoring of BP, electrocardiography, ultrasound examination of the heart) were used.

According to ESC/EAS recommendations, levels of TC>4.9 mmol/l and LDL-C>3 mmol/l were considered as elevated.

BMI was evaluated by the formula: $BMI = \text{body weight}/\text{height}^2$, kg/m². The diagnosis of overweight or obesity was determined according to WHO criteria (1997). Overweight was determined at BMI of 25 to 29.9 kg/m², first-degree obesity - from 30 to 34.9 kg/m², second-degree obesity - from 35 to 39.9 kg/m², third-degree obesity - BMI more than 40,0 kg/m².

According to standardized guidelines for measurement of smoking, a smoker is a person who, at the time of the survey, smokes any tobacco product either daily or occasionally and has smoked 100 or more cigarettes in his/her lifetime; an ex-smoker is a person who currently does not smoke at all but who has smoked 100 or more cigarettes in his/her lifetime; a non-smoker is a person who has smoked less than 100 cigarettes in his/her lifetime.

Neuropsychological testing was used to objectify cognitive impairment: the General Practitioner assessment of Cognition (*GPCOG*), the Mini-Mental State Examination (MMSE) – tests of orientation, attention, memory, language and visual-spatial skills. 29-30 scores were regarded as absence of cognitive impairment, 27-28 scores - as mild cognitive impairment, 24-26 scores - as moderate cognitive impairment, 20-23 scores - as initial dementia, <20 scores - as marked (evident) stage of dementia. Stability of attention and sensomotor reactions rate was evaluated using Schulte tables.

Received results were processed using the program "STATISTICS FOR WINDOWS". The probability of difference between the average quantitative values of two samples was determined by the Mann-Whitney test.

Results. The base characteristics of the patients included in the study are presented in Table 1.

Table 1. Characteristics of the patients included in the study

Index	1 group Hypertensive patients (n=89)	2 group Patients without hypertension (n=30)
Age	51, 1 ± 7,3*	41,4 ± 10,1
Males, %	53,9 (48)	56,7 (17)
Females, %	46,1 (41)	43,3 (13)
Smokers, %	38,2% (34)	46,7% (14)
Median SBP, mm. Hg	168,4 ± 13,7*	128,1 ± 9,7
Median DBP, mm. Hg	97,6 ± 10,4*	78,6 ± 8,1
BMI, kg/m ²	25,6 ± 2,0*	23,8 ± 1,9
TC, mmol/L	5,6 ± 0,8*	4,2 ± 0,6
LDL-C, mmol/L	4,3 ± 1,6*	3,2 ± 0,8
GPCOG, scores	6,9 ± 1,4*	8,3 ± 0,7
MMSE, scores	26,5 ± 1,8*	28,9 ± 1,0
Schulte tables, sec	52,3 ± 10,7*	33,4 ± 4,2

Note: * - $p < 0,01$

The table shows that the patients of group 1 were older, among them males predominated. The level of blood pressure, both systolic and diastolic, in patients in group 1 was significantly higher than in group 2. There was also a significantly higher number of overweight and hypercholesterolemic patients in group 1.

The main complaints among hypertensive patients were: headache (92%), dizziness (81%), tinnitus (70%), sleep disorders (63%), general weakness and fatigue (61%), impaired memory and attention (54%), rapid fatigue in mental activity (48%).

Analysis of the results of neuropsychological scales showed an accurate decline of cognitive status in hypertensive patients, whereas in the group of almost healthy individuals, cognitive disorders were not recorded in any of the patients (Table 2).

Table 2. Assessment of cognitive functions in patients with arterial hypertension

Scales	1 group (n=89)			2 group (n=30)		
	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.
GPCOG	6,9*	7,0*	1,4	8,3	8,0	0,7
MMSE	26,5*	27,0*	1,8	28,9	29,0	1,0
Schulte test	52,3*	49,6*	10,7	33,4	32,7	4,2

Note: * - $p < 0,01$

At the same time, 2 patients (2.2%) according to MMSE scale had mild dementia (20-23 scores), moderate cognitive impairments (24-26 scores) were diagnosed in 34 patients

(38.2%), mild cognitive impairments (27-28 scores) - in 39 patients (43.8%) (Fig.1). The greatest difficulties for such patients were while performing the sections: Attention, Accountability, Memory, Copy.

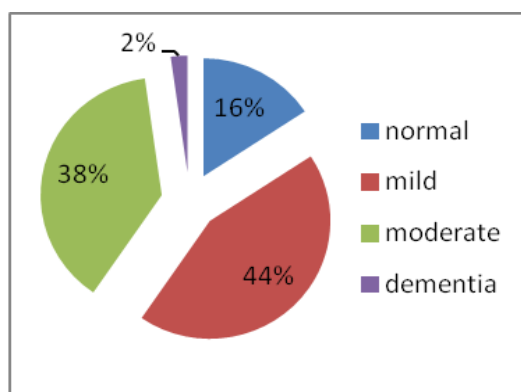


Figure 1. Frequency of detection of cognitive impairment of different severities in hypertensive patients according to MMSE scale

Hypertensive patients needed significantly more time to complete tasks according to the Schulte tables. Their median test index was 52.3 ± 10.7 seconds, while in the group of healthy individuals the time to complete tasks was 33.4 ± 4.2 seconds (Fig. 2). Hypertensive patients missed figures, complained of inability to focus, rapid fatigue. It should be noted that the detected changes were more manifested in male patients, although the difference was statistically insignificant ($p > 0.01$). In particular, in female hypertensive patients the median index according to MMSE scale was 27.3 ± 1.7 , while in male ones it was 26.5 ± 1.8 . Worse indices of the tasks fulfilment rate according to the Schulte tables were also observed in males (54.1 ± 10.7 and 49.1 ± 10.8 , respectively).

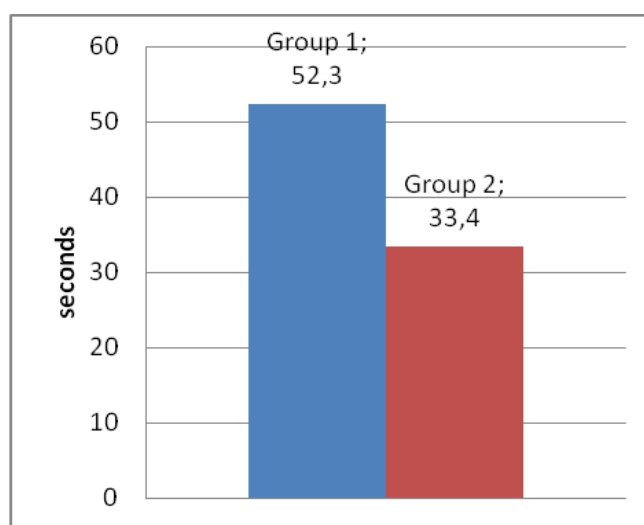


Figure 2. Comparison of indices of rate of tasks fulfilment according to Schulte tables

The study also evaluated factors that, in addition to high blood pressure, may affect the development of cognitive impairment in hypertensive patients. All hypertensive patients were divided into subgroups: patients with increased BMI and with normal BMI; patients with elevated level of LDL-C and with normal level of LDL-C; smokers, ex-smokers and non-smokers. Thus, it is important to notice the negative effect of elevated level of LDL-C on cognitive function in hypertensive patients. The results of the neuropsychological scales of such patients were significantly lower than in hypertensive patients and normal level of LDL-C - MMSE - 26.1 ± 1.8 and 27.5 ± 1.4 , respectively; GPCOG - 6.4 ± 1.3 and 7.9 ± 1.1 , respectively). It took 12.1 ± 1.5 seconds more for these patients to complete the tasks according to the Schulte Tables.

Table 3. Characteristics of the hypertensive patients with elevated level of LDL-C and hypertensive patients with normal level of LDL-C

Index	Patients with elevated level of LDL-C (n=58)	Patients with normal level of LDL-C (n=31)
Age	$50,8 \pm 9,6$	$49,1 \pm 8,2$
Males, %	50,8	45,2
Females, %	48,2	54,8
LDL-C, mmol/L	$6,0 \pm 1,2^*$	$2,6 \pm 0,6$
GPCOG, scores	$6,4 \pm 1,3^*$	$7,9 \pm 1,1$
MMSE, scores	$26,1 \pm 1,8^*$	$27,5 \pm 1,4$
Schulte tables, sec	$56,5 \pm 9,8^*$	$44,9 \pm 8,2$

Note: * - $p < 0,01$

At the same time, cognitive impairment were found to be more marked in hypertensive patients and increased BMI. The average index of these patients according to MMSE scale was significantly lower than the average index of patients with normal BMI (26.4 ± 1.4 and 28.0 ± 1.2 , respectively). The speed of completion of tasks according to the Schulte tables was not significantly different in patients with normal and high BMI and in both groups exceeded the norms (48.8 ± 11.2 and 48.3 ± 11.6 , respectively). 17% (n=9) of hypertensive patients had first-degree obesity and 83% (n=44) hypertensive patients had overweight. But the degree of obesity was not significantly associated with worse MMSE test results and was 26.4 ± 1.5 in overweight patients and 26.4 ± 1.2 in patients with first-degree obesity ($p > 0.01$).

Table 4. Characteristics of the hypertensive patients with increased BMI and hypertensive patients with normal BMI

Index	Patients with increased BMI (n=53)	Patients with normal BMI IMT (n=36)
Age	50,5 ± 9,3	48,5 ± 8,7
Males, %	52,8	55,6
Females, %	47,2	44,4
BMI, kg/m ²	28,0 ± 2,6*	23,2 ± 1,4
GPCOG, scores	6,6 ± 1,4*	7,4 ± 1,5
MMSE, scores	26,4 ± 1,4*	28,0 ± 1,2
Schulte tables, sec	48,8 ± 11,2	48,3 ± 11,6

Note: * - $p < 0,01$

Smoking is another important risk factor that adversely affects cognitive function, such as attention and sensomotor reactions rate. This is evidenced by the median indices of the Schulte test completion - 56.9 ± 11.0 seconds in hypertensive patients who smoke compared to 47.7 ± 8.5 seconds in hypertensive patients who do not smoke. The total sum of scores according to MMSE scale in smokers was also slightly lower than that of non-smokers, although no significant difference was found (26.3 ± 1.5 and 26.8 ± 2.0 , respectively, $p > 0.01$). Also it is important to notice that slightly worse results were also found in individuals of the control group who smoked.

Table 5. Characteristics of the hypertensive patients who smoke and hypertensive patients who don't smoke or have smoked formerly

Index	Smokers (n=34)	Ex-smokers (n=24)	Non-smokers (n=31)
Age	48,9 ± 9,1	51,7 ± 10,8	48,9 ± 8,9
Males, %	79,4	87,5	41,9
Females, %	20,6	12,5	58,1
GPCOG, scores	6,5 ± 1,3	6,7 ± 1,5	6,7 ± 1,2
MMSE, scores	26,3 ± 1,5	26,7 ± 1,4	26,8 ± 2,0
Schulte tables, sec	56,9 ± 11,0*	48,1 ± 9,8	47,7 ± 8,5

Note: * - $p < 0,01$

Discussion. The obtained results to a certain extent coincide with clinical and epidemiological studies, which convincingly demonstrated that high systolic pressure in midlife directly correlates with the risk of cognitive decline and development of dementia in the elderly [4]. Increase in systolic pressure for every 10 mm Hg raises the risk of moderate cognitive impairment by 7%, severe - by 9% [5]. Also, according to the data of the analysis of

12 clinical trials, where the effect of different classes of antihypertensive drugs on the development and progression of dementia was compared, it was found that the risk of cognitive impairment was 9% lower in individuals taking antihypertensive therapy, regardless of the class of drugs [6].

The effect of elevated cholesterol on the occurrence of cognitive impairment is not clear enough and there is currently no consensus on this issue. Some studies have demonstrated that even moderately elevated level of total cholesterol increases the risk of dementia [7], but there are studies where connection between cholesterol and cognitive function [8] has not found. Also, taking of lipid lowering drugs, in particular statins, has proved to be ineffective for the prevention of cognitive impairment and dementia [9].

There is also controversial information about the effect of obesity on cognitive function. Data presented in literature suggests, however, that the connection between obesity and cognitive function is not a direct one; it means that obesity affects cognitive sphere of different people, especially depending on their age group. In particular, according to some studies, a lower BMI is associated with an increase in the occurrence of dementia, especially in the elderly [10]. However, in middle-aged people, the results of the studies were opposite - increased BMI was associated with worse cognitive indices, especially memory and executive functions, and increased the risk of dementia [11]. The negative effect of smoking on cognitive function was also proven. The results of neuropsychological tests among smokers were 4-8% lower than non-smokers and former smokers, especially reflected in the processes of remembering and information processing speed [12]. The study, conducted among the participants aged 43 to 53 years, found that smoking more than 20 cigarettes a day was associated with a more detected memory decline [13].

Conclusions

1. Hypertension is a significant independent risk factor for developing new cases of cognitive impairment. In particular, patients with stage 2 hypertension according to the MMSE scale reported mild cognitive impairment in 43.8% of cases, moderate cognitive impairment in 38.2%, and mild dementia in 2.2%.

2. Factors that definitely affect the development of cognitive impairment in hypertensive patients are increased BMI, hypercholesterolemia, and smoking.

3. Timely diagnosis of cognitive impairment, as well as early detection and correction of risk factors is very important and will improve cognitive status and prevent dementia.

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