

Original research**COGNITIVE DISORDERS IN PATIENTS WITH HYPERTENSION: ARE THERE GENDER DIFFERENCES?**Viktoriiia Krotova^{1*}, Oleksandra Rosytska¹, Tetyana Khomazyuk¹**Author information:** ¹Dnipro State Medical University, 9, V. Vernadsky str, Dnipro, Ukraine.

Received: 07-14-2023; Accepted: 08-20-2023; Published: 09-07-2023.

Abstract. Background: Given the profound differences between women and men, there is a need to study gender as a vital variable and factor in blood pressure regulation, control, and treatment. The level of anxiety and depression, which significantly affect the psychological characteristics and patients' quality of life, and the status of the autonomic nervous system represent a rather significant layer of hypertension problems due to its specificity, accumulating its medical, social, gender, and humanitarian aspects, which are related to sexual characteristics.

Material and Methods: The study results are based on the data of a comprehensive examination of 185 working patients with controlled hypertension (H) stage II. According to the neuro-psychological testing on MMSE, MoCA and Life Quality scales, 157 people with various severity cognitive disorders (CD) were found. There were 87 (55.4 %) women and 70 (44.6 %) men among them, and the average age [M(SD)] was 52.3 (8.2) years; the average duration of H was 10 (8-12) years. The comparison and control groups were adequate for the purpose. The standard methods of parametric and non-parametric statistics processed the obtained data.

Results: As a result of the study, significant differences were found in patients with hypertension and CD of both sexes compared with healthy individuals and patients with hypertension without cognitive impairment in relation to the daily blood pressure profile (VAR SBP, VAR DBP) both during the day and at night. The females, even middle-aged, with controlled hypertension but high systolic blood pressure variability have a substantial risk of developing CD. Male patients with hypertension, even in the absence of CD, are more prone to depression, according to the HADS scale. In the presence of hypertension with CD, they are characterized by significantly worse personal-role physical and emotional functioning compared to female patients on the life quality scale. The often-irresponsible attitude of men to the doctor's advice and regular antihypertensive treatment probably plays a significant role in the formation of gender differences in the quality of life of patients with hypertension and CD.

Conclusion: It is necessary to ensure early diagnosis and monitoring of CD as a marker of brain damage due to hypertension and determine the level of anxiety and depression, which significantly affect the psychological characteristics and quality of life even of patients with controlled hypertension, regardless of gender. However, middle-aged women, even with controlled hypertension but high SBP variability, have a priority risk of CD development.

Keywords: Hypertension, Cognitive disorders, Neuropsychological tests, Quality of life, Gender characteristics, Autonomic (vegetative) index, Blood pressure

INTRODUCTION. The association between blood pressure (BP) and cognitive function is an actual complex problem of mental health all over the World. It has been suggested

that hypertension (H) may predict cognitive disorders (CD) in later years, and it seems that the debut timing of H is a crucial variable. High BP in midlife is a risk factor for stroke and dementia arising from Alzheimer's Disease and cerebrovascular disorders, suggesting that high BP in midlife harms the brain, resulting in CD. It is noted that hypertension is a crucial risk factor for stroke, myocardial

Corresponding Author: Viktoriiia Krotova, MD, PhD
Dnipro State Medical University, 9, V. Vernadsky str, Dnipro,
Ukraine. Email: vika_krotova@ukr.net

infarction, and heart failure. It is also a precursor of vascular dementia and early forms of vascular CD [1-3]. The evidence generally suggests that high BP is associated with reduced cognitive function and a greater risk of dementia [4-8]. In addition, it is estimated that by 2040, the number of Americans with some form of CD, including dementia, will be 8.3 million women and 3.3 million men, possibly linked to cardiovascular disease (CVD) and a risk factor associated with CVD [9-11]. In this regard, studies show that a more pronounced risk associated with H is conferred by younger age, lower level of education, the presence of APOE e4 alleles, and in combination with other CV risk factors [12, 13]. Randomized trials of antihypertensive agents for the prevention of CD or dementia suggest that risk reduction can be achieved with some drug classes, and ongoing studies and meta-analyses have been conducted, discussing the potential mechanisms of action of drugs affecting the central nervous system. Although several studies suggest gender differences, results are mixed regarding the relative vulnerability of women versus men [14]. The difference in the course of cardiovascular diseases in women and men suggests that the interaction of gender and age is essential for CD [15, 16].

It is important to note that sex and gender are separate, though related, concepts. Sex refers to the biological differences that arise from sex chromosome expression (e.g., XX and XY) [17, 18].

Gender is a separate construct defined by sociocultural expectations and attitudes that shape behaviors, lifestyle choices, and experiences [19]. Therefore, "gender" refers to individuals belonging to a social group. We use the descriptive term "gender" in this paper as we cannot distinguish between these terms. Despite evidence of gender differences in CD presentation and progression, studies infrequently focus on gender as a modifying variable.

Some studies may help explain the increased prevalence of CD and dementia in women, including studies related to stroke, microvascular disease (disease of the small blood vessels), and gender-related issues in CVD differences [20, 21-23, 24, 25]. The relationship between H and menopausal status showed that cognitive performance was worse in hypertensive women compared with normotensive postmenopausal women. Notably, this finding was not present in premenopausal women, suggesting the importance of investigating hormonal and other influences that may operate in different samples of women. Men have a higher prevalence of H than women

up to age 64, but after this age, the prevalence of H is higher in women than in men. The higher prevalence of CD and dementia in women may be partially explained by sex-related differences in CV factors, CVD and outcomes, or lack of treatment of CVD [26-28]. Importantly, for both women and men, preventing CD and dementia should be seen as a lifelong process. Therefore, to help support optimal brain health, we support the recommendations of national organizations such as the American Heart Association and others to promote CV health as a means of supporting brain health.

THE AIM OF THE STUDY: To determine the presence of gender characteristics and the structure of cognitive disorders in patients with hypertension of both genders.

MATERIAL AND METHODS. The study design was defined as an open, prospective, monocentric clinical trial in parallel groups of patients. The study results are based on the data of a comprehensive examination of 185 working patients with controlled H of the II stages, aged from 30 to 70 years [average age - 52.5 (8.4) years]. The H duration in the examined patients ranged from 5 to 23 years; the median was 10 (9-12) years. According to the data of neuropsychological testing (using the MMSE and MoCA methods) [29], 157 people with CD of various degrees of severity were found among patients with controlled H (the main group). According to the results of the study of cognitive functions in 157 patients (97 - according to the MMSE method, 60 - according to the MoCA method), cognitive disorders of various degrees of severity were found. Thus, according to the MMSE method, mild CD (27-26 points) was found in 39 (40.2 %) patients and moderate CD (25-24 points) in 58 (59.8 %). When analyzing the results of testing patients using the MoCA method, 22 (36.7 %) patients received 25 points, and 38 (63.3 %) received 24 points. There were 87 (55.4 %) women in the physiological menopausal period (subgroup 1.1) and 70 (44.6 %) men (subgroup 1.2) among patients with H with CD, the average age was 52.3 (8.2) years, the average duration of H was 10 (8-12) years. Most of the examined were in the age group from 50 to 59 years - 66 (42.0 %), from 40 to 49 years - 44 (28.0 %), from 60 to 70 years - 40 (25.5 %), and from 34 to 39 years old - 7 (4.5 %). The comparison group consisted of 28 patients with controlled H of the II stage without CD, aged from 34 to 68 years [on average - 54.2 (7.5) years] and duration of the disease - 10 (9-11.5) years. By gender, there were 15 (53.6 %) women (subgroup 2.1) and 13 (46.4 %) men (subgroup 2.2).

The practically healthy group consisted of 28 people, who, in terms of age [average - 54.0 (7.0) years] and gender

(women - 46.4 %, men - 53.6 %), corresponded to the cohorts of the studied patients with H ($p>0.05$). All research groups were also statistically compared by the level of education of patients ($p>0.05$): most patients – 69.5 % had higher education, 26.3 % had secondary special education, and only 4.2 % had secondary professional education.

All the examinees underwent general clinical, instrumental, and laboratory diagnostics to verify the H diagnosis and identify concomitant pathology. A general clinical examination and instrumental and laboratory diagnostic methods were performed according to standard protocols for cardiac patients. Additional research methods were also performed: daily blood pressure (BP) monitoring, home and office ambulatory blood pressure monitoring (ABPM), electrocardiography, and main arteries of the head and neck sonography. The neuropsychological examination included an integrated assessment of cognitive functions on the MMSE, MoCA scale, and HADS anxiety and depression survey. Wayne's test determined the presence of autonomic disorders and quality of life - by the SF-36 Health Status Survey scale and general CV risk - by the SCORE scale. Regional Committees for Medical and Health Research Ethics reviewed and approved the studies involving human participants. The patients/participants provided written informed consent to participate in this study. The obtained data were processed by the methods of parametric and non-parametric statistics with the presentation of statistical

values were performed using the non-parametric Kruskal-Wallis's test (H) with a posteriori pairwise comparison using Dunn's test (Q), relative values using the Pearson agreement test (χ^2). The relationship between indicators was evaluated based on the results of correlation analysis with the calculation of Spearman's rank correlation coefficient (r). The results of the statistical analysis were considered reliable at $p\leq 0.05$.

RESULTS. The analysis of the obtained data showed that patients with H, both with the presence of CD and without CD, had high indicators of the autonomic index (58.78 ± 0.66 and 54.16 ± 2.30 points), which indicated the presence of vegetative disorders, mostly moderate (35.1 %) and severe (58.9 %). We found weak but reliable associations of the autonomic (vegetative) index with the level of SBP ($r_s=+0.21$; $p<0.01$), with the variability of SBP and DBP at night ($r_s=+0.26$; $p<0.001$ and $r_s=+0.27$; $p<0.001$), as well as with the presence of CI in patients with H ($r_s=+0.15$; $p<0.05$). It was established that the high vegetative index, according to Wayne, was directly correlated with all the investigated indicators of anxiety: for anxiety levels according to HADS – $r_s=+0.26$; $p<0.001$; for personal and reactive anxiety – $r_s=+0.28$; $p<0.001$ and $r_s=+0.31$; $p<0.001$. A high degree of personal anxiety hurt the increase in the time for completing tasks according to the Schulte tables ($r_s=+0.24$; $p<0.05$), the general indicator of work efficiency ($r_s=+0.16$; $p<0.05$) and mental stability ($r_s=-0.21$; $p<0.05$), Figure 1.

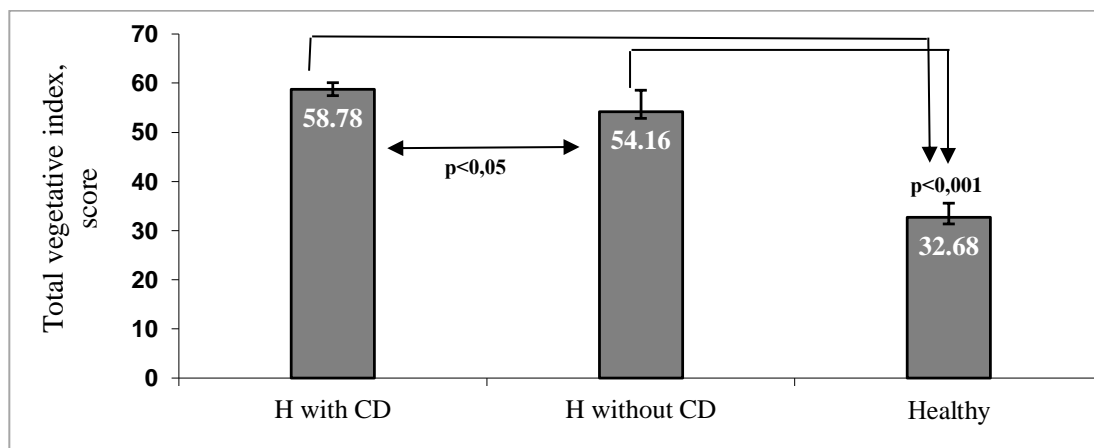


Figure 1. Average indicators (M, 95 % CD) of the state of the autonomic nervous system in the study groups when testing according to Wayne.

characteristics in the form of the arithmetic mean (M), standard deviation (SD), or median (Me) with an interquartile range (25 %-75 %). Given the small size of individual study samples, multiple comparisons of mean

Most often, signs of vegetative deficiency manifest in poor tolerance to cold and heat and worsening well-being when weather conditions change. The examinees noted the

presence of increased anxiety, irritability, restlessness, and sudden mood changes. Increased sweating, hyperventilation syndrome, and gastrointestinal tract disorders without existing organic pathology were recorded less frequently.

There were weak but significant associative associations of

the autonomic (vegetative) index with equal SBP ($r_s=+0.21$; $p<0.01$), with the variability of SBP and DBP at night ($r_s=+0.26$; $p<0.001$ and $r_s=+0.27$; $p<0.001$), as well as the presence of CD in patients with H ($r_s=+0.15$; $p<0.05$). The complex clinical and anamnestic characteristics of female and male patients in the selected research groups are shown in Tables 1 and 2.

Indicator	Main group (H and CD), n=87	Comparison group (H without CD), n=15	Control Group (Practically healthy), n=13	Differences between groups (p)
Age, years, M (SD)	53.5 (8.2)	54.3 (8.5)	52.5 (6.2)	$p_H=0.649$
BMI, kg / m ² , M (SD)	30.7 (4.7)*	29.0 (3.7)	27.7 (3.1)	$p_H=0.043$
Increased body weight, n (%)	28 (32.2 %)	7 (46.7 %)	7 (53.8 %)	$p_{\chi^2}=0.217$
Obesity I-III st., n (%)	50 (57.5 %)*	7 (46.7 %)	3 (23.1 %)	$p_{\chi^2}=0.062$
Duration of hypertension, years, Me (25 %-75 %)	10 (8-12)	10 (8-12)	–	$p_H=1.00$
Systolic blood pressure, mm Hg, M (SD)	135.2 (4.1)**	135.7 (3.8)**	123.5 (5.3)	$p_H<0.001$
Diastolic blood pressure, mm Hg, M (SD)	81.0 (5.6)**	77.7 (5.0)	76.8 (2.1)	$p_H<0.001$
Heartrate, beats/min, M (SD)	77.7 (11.7)	78.7 (11.8)	76.6 (10.8)	$p_H=0.876$
Microalbuminuria, n (%)	7 (8.0 %)	2 (13.3 %)	0 (0 %)	$p_{\chi^2}=0.419$
Cholesterol, mmol / l, M (SD)	5.44 (1.23)*	5.33 (0.88)*	4.53 (0.83)	$p_H=0.036$
Intima-media complex, mm, M (SD)	1.06 (0.77)	0.99 (0.15)	0.95 (0.15)	$p_H=0.762$
Thickening of the intima-media complex, n (%)	47 (54.0 %)	10 (66.7 %)	5 (38.5 %)	$p_{\chi^2}=0.328$
VAR SBP, mm Hg, daytime, Me (25 %-75 %)	16 (15-19)*###	11 (11-12)**	9 (9-10)	$p_H<0.001$
VAR SBP, mm Hg, at night, Me (25 %-75 %)	13 (12-17)*###	7 (7-10)	9 (7-9)	$p_H<0.001$
VAR DBP, mm Hg, daytime, Me (25 %-75 %)	13 (10-15)**	10 (9-13)	10 (10-10)	$p_H<0.001$
VAR DBP, mm Hg, at night, Me (25 %-75 %)	10 (9-13)**	9 (7-9)	9 (7-10)	$p_H=0.002$
Heavy heredity for hypertension, n (%)	69 (79.3 %)*	11 (73.3 %)	7 (53.8 %)	$p_{\chi^2}=0.232$
High risk on the SCORE scale (≥ 5 %), n (%)	15 (17.2 %)	5 (33.3 %)*	0 (0 %)	$p_{\chi^2}=0.068$

Notes: 1. p_H (p_{χ^2}) – the level of significance of the differences in indicators between groups as a whole according to the Kruskal-Wallis test (χ^2);

2. * – $p<0.05$; ** – $p<0.001$ compared to subgroup 3.2;

3. # – $p<0.05$; ### – $p<0.001$ compared to subgroup 2.2.

Table 1. Complex characteristics of female study participants (n=102).

Indicator	Main group (H and CD), n=87	Comparison group (H without CD), n=15	Control Group (Practically healthy), n=13	Differences between groups (p)
Age, years, M (SD)	50.8 (8.8)	54.1 (6.7)	55.2 (7.7)	$p_H=0.137$
BMI, kg / m ² , M (SD)	30.2 (5.6)*	30.9 (4.4)*	26.5 (2.1)	$p_H=0.011$
Increased body weight, n (%)	26 (37.1 %)*	6 (46.2 %)	12 (80.0 %)	$p_{\chi^2}=0.010$
Obesity I-III st., n (%)	38 (54.3 %)**	7 (53.8 %)*	1 (6.7 %)	$p_{\chi^2}=0.003$
Duration of hypertension, years, Me (25 %-75 %)	10 (9-12)	10 (10-11)	–	$p_H=1.00$
Systolic blood pressure, mm Hg, M (SD)	134.8 (4.6)	133.8 (3.5)	130.5 (9.7)	$p_H=0.247$
Diastolic blood pressure, mm Hg, M (SD)	80.4 (5.1)	77.3 (5.4)	80.6 (6.8)	$p_H=0.148$
Heartrate, beats/min, M (SD)	80.1 (12.2)*	80.0 (10.4)	71.9 (9.1)	$p_H=0.050$
Microalbuminuria, n (%)	6 (8.6 %)	2 (15.4 %)	0 (0 %)	$p_{\chi^2}=0.324$
Cholesterol, mmol / l, M (SD)	5.68 (1.08)*	5.90 (1.24)*	5.01 (0.54)	$p_H=0.047$
Intima-media complex, mm, M (SD)	1.09 (0.85)**	0.98 (0.11)*	0.84 (0.07)	$p_H=0.002$
Thickening of the intima-media complex, n (%)	35 (50.0 %)**	9 (69.2 %)**	0 (0 %)	$p_{\chi^2}<0.001$
VAR SBP, mm Hg, daytime, Me (25 %-75 %)	15 (14-16)**###	11 (11-11)*	10 (9-11)	$p_H<0.001$
VAR SBP, mm Hg, at night, Me (25 %-75 %)	13 (11-14.5)**###	8 (7-9)	7 (7-9)	$p_H<0.001$
VAR DBP, mm Hg, daytime, Me (25 %-75 %)	13 (10-14.5)**###	9 (9-10)	10 (7-10)	$p_H<0.001$
VAR DBP, mm Hg, at night, Me (25 %-75 %)	10 (9-13)**###	7 (6-9)	7 (6-8)	$p_H=0.001$
Heavy heredity for hypertension, n (%)	57 (81.4 %)	10 (76,9 %)	9 (60.0 %)	$p_{\chi^2}=0.196$
High risk on the SCORE scale (≥ 5 %), n (%)	15 (21.4 %)*	0 (0 %)	0 (0 %)	$p_{\chi^2}=0.029$

Notes: 1. p_H (p_{χ^2}) – the level of significance of the differences in indicators between groups as a whole according to the Kruskal-Wallis test (χ^2);

2. * – $p<0.05$; ** – $p<0.001$ compared to subgroup 3.2;

3. # – $p<0.05$; ### – $p<0.001$ compared to subgroup 2.2.

Table 2. Complex characteristics of male study participants (n=83).

Probable differences between hypertensive patients and practically healthy individuals, especially in the presence of CD, were noted in the levels of BMI, total cholesterol, the size of the intima-media complex, the risk of fatal CV events according to the SCORE (Systemic Coronary Risk Estimation - 1988) scale.

In the formed study groups, BP indicators did not reliably differ, so in patients with H, on the background of antihypertensive therapy, the level of BP was controlled by both SBP and DBP data. The analysis of the obtained data showed that patients with H of both sexes, both with the presence of CD and without CD, had high indicators of the vegetative index. However, significant differences were noted in patients with H and CD of both genders compared

to healthy individuals and H patients without CD regarding the daily profile of BP (VAR SBP, VAR DBP), both during the day and at night.

The psychological characteristics and assessment of the quality of life of female and male participants in the selected research groups are shown in Tables 3 and 4.

According to the data of the correlation analysis, a direct correlation of average strength was established between the day and night variability of SBP and DBP and the development of CD in patients with H, regardless of the gender of the patients: with VAR SBP during the day - $r=0.573$ ($p<0.001$), with VAR SBP at night - $r=0.614$

Indicator		1.1 Main group (H and CD), n=87	2.1 Comparison group (H without CD), n=15	3.1 Control group (Practically healthy), n=13	Differences between groups (p)
Vegetative index, score, M (SD)		52.6 (12.8)**	54.5 (13.2)**	31.2 (8.8 %)	$p_H<0.001$
HADS, anxiety scale	score, M (SD)	9.55 (3.37)*	8.60 (2.29)	7.38 (1.45)	$p_H=0.003$
	8-10 score, n (%)	42 (48.3 %)	6 (40.0 %)	3 (23.1 %)	$p_{\chi^2}=0.219$
	11 and more score, n (%)	30 (34.5 %)*	2 (13.3 %)	1 (7.7 %)	$p_{\chi^2}=0.051$
HADS, depression scale, score, M (SD)		4.38 (1.84)	3.80 (1.61)	3.62 (2.10)	$p_H=0.253$
CD, according to the MoCA scale, score, M (SD)		24.5 (0.5)##	26.4 (0.8)	-	$p_H<0.001$
CD, according to the MMSE scale, score, M (SD)		25.5 (1.2)**	-	27.5 (0.9)	$p_H<0.001$
Quality of life, score, Me (25 % - 75 %):					
General Health (GH)		50 (40-55)**##	80 (72-82)	72 (55-90)	$p_H<0.001$
Physical functioning (PF)		60 (55-75)**	50 (30-55)**	100 (75-100)	$p_H<0.001$
Role-playing physical functioning (RP)		50 (25-100)*	50 (25-50)*	75 (60-100)	$p_H<0.004$
Role emotional functioning (RE)		38 (25-67)	50 (38-63)	67 (34-100)	$p_H=0.113$
Social functioning (SF)		38 (30-50)**##	50 (50-75)	67 (50-75)	$p_H<0.001$
BodilyPain (BP)		51 (41-71)**	72 (41-74)	75 (64-100)	$p_H<0.002$
Vitality (VT)		55 (40-70)**##	70 (60-75)	85 (70-100)	$p_H<0.001$
Mental health (MH)		56 (44-68)**##	88 (78-90)	95 (88-95)	$p_H<0.001$

Notes: 1. p_H (p_{χ^2}) – the level of significance of the differences in indicators between groups as a whole according to the Kruskal-Wallis test (χ^2);

2. * – $p<0.05$; ** – $p<0.001$ compared to subgroup 3.2;

3. # – $p<0.05$; ## – $p<0.001$ compared to subgroup 2.2.

Table 3. Psychological characteristics and quality of life of female study participants (n=102).

Indicator		1.2 Main group (H and CD), n=87	2.1 Comparison group (H without CD), n=15	3.1 Control group (Practically healthy), n=13	Differences between groups (p)
Vegetative index, score, M (SD)		50.1 (12.4)**	53.8 (12.6)**	33.9 (6.6)	$p_H < 0.001$
HADS, anxiety scale	score, M (SD)	9.04 (2.65)*	9.38 (2.02)*	7.60 (1.72)	$p_H = 0.050$
	8-10 score, n (%)	27 (38.6 %)	6 (46.2 %)	8 (53.3 %)	$p_{\chi^2} = 0.543$
	11 and more score, n (%)	25 (35.7 %)*	4 (30.8 %)*	0 (0.0 %)	$p_{\chi^2} = 0.023$
HADS, depression scale, score, M (SD)		4.29 (1.96)	4.92 (1.19)	5.53 (1.41)	$p_H = 0.056$
CD, according to the MMSE scale, scores M (SD)		25.0 (1.1)**	-	27.9 (1.3)	$p_H < 0.001$
CD, according to the MoCA scale, score, M (SD)		24.2 (0.4)##	27.3 (1.5)	-	$p_H < 0.001$
Quality of life, score, Me (25 % - 75 %):					
General Health (GH)		50 (35-60)**##	75 (72-87)	90 (75-90)	$p_H < 0.001$
Physical functioning (PF)		55 (50-75)**	30 (25-75)**	100 (75-100)	$p_H < 0.001$
Role-playing physical functioning (RP)		25 (0-75)*	25 (25-50)*	75 (50-100)	$p_H < 0.004$
Role emotional functioning (RE)		34 (0-50)**##	38 (38-50)*	100 (50-100)	$p_H = 0.001$
Social functioning (SF)		50 (38-50)**##	75 (63-75)	75 (50-100)	$p_H < 0.001$
Bodily Pain (BP)		51 (32-70)**	62 (42-72)*	100 (71-100)	$p_H < 0.001$
Vitality (VT)		50 (35-65)**##	75 (60-75)*	90 (75-100)	$p_H < 0.001$
Mental health (MH)		56 (50-64)**##	90 (88-90)	95 (80-95)	$p_H < 0.001$

Notes: 1. p_H (p_{χ^2}) – the level of significance of the differences in indicators between groups as a whole according to the Kruskal-Wallis test (χ^2);

- 2. * – $p < 0.05$; ** – $p < 0.001$ compared to subgroup 3.2;
- 3. # – $p < 0.05$; ## – $p < 0.001$ compared to subgroup 2.2.

Table 4. Psychological characteristics and quality of life of male study participants (n=83).

($p < 0.001$), with VAR DAT during the day - $r = 0.426$ ($p < 0.001$), with VAR DAT at night - $r = 0.453$ ($p < 0.001$).

Cognitive disorders in patients with H hurt patients' quality of life (QL), significantly worsening indicators of self-assessment of general ($r = -0.541$; $p < 0.001$) and mental ($r = -0.562$; $p < 0.001$) health, social functioning ($r = -0.412$; $p < 0.001$) and viability ($r = -0.347$; $p < 0.001$). The obtained data (Table 5) show that women with H and CD are more likely to have SBP variability, a QL profile with worse social functioning, and a more frequently determined risk of CV complications, according to SCORE (≥ 5 %). At the same time, men with H, even in the absence of CD, are more

prone to depression according to the HADS scale. In the presence of H with CD, they are characterized by significantly worse role-based physical and emotional functioning. Men's attitude to doctor's advice and regular antihypertensive treatment probably plays a significant role in forming gender differences in patients' quality of life with H and CD.

DISCUSSION. While mild CD is an established risk factor for dementia. It is well-known that not all patients with mild CD progress to dementia, and many revert to normal cognition [30, 31]. It is the same important for both gender H patients. Our study is another attempt at a systematic

Indicator	Group H	Women (n=102)	Men (n=83)	p
VAR SAT, daytime	CD	16 (15-19)	15 (14-16)	$p=0.034$
SCORE (≥ 5 %)	Without CD	5 (33.3 %)	0 (0.0 %)	$p=0.022$
HADS, depression scale	Without CD	3.80 (1.61)	4.92 (1.19)	$p=0.050$
Role-playing physical functioning (RP)	CD	50 (25-100)	25 (0-75)	$p=0.048$
Role Emotional Functioning (RE)	CD	38 (25-67)	34 (0-50)	$p=0.003$
Social functioning (SF)	CD	38 (30-50)	50 (38-50)	$p=0.050$
Irregularity of treatment	CD	20 / 53 (37.7 %)	27 / 44 (61.4 %)	$p=0.020$

Table 5. Probable differences between the characteristics of patients with hypertension of different genders.

assessment of gender aspects in the CD in patients with arterial H; it is necessary to develop personalized treatment regimens, improving the QL and social adaptation of both women and men. The higher prevalence of CD and dementia in patients with H may be explained by damage to the vascular wall as a target organ and "small vessel disease," also noted partly by gender-related differences in CVD risk factors caused by the hormonal background and not only. Men's attitude to doctor's advice and regular antihypertensive treatment probably play a significant role in gender differences in the level of patients' QL of H with CD. We have obtained the characteristics of the gender profile of CD concerning QL in middle-aged patients with controlled Hand and a low risk of CV events, which should favor further investigating gender-specific issues. We understand the limitations of this study associated with a small number of participants in the study groups, as well as the formation of special gender groups by age, physiological characteristics, and treatment outcomes. However, the results allowed us to focus on the importance of mental health, timely diagnosis, and personalization of the CD treatment along with adequate antihypertensive therapy.

CONCLUSION. It is necessary to ensure early diagnosis and monitoring of CD as a marker of brain damage due to hypertension, and determine the level of anxiety and depression, which significantly affect the psychological characteristics and quality of life even of patients with controlled hypertension, regardless of gender. However middle-aged women, even with controlled hypertension

but high SBP variability, have a priority risk of CD development.

Conflict of Interest: The authors have no conflict of interest with the publishing journal.

Funding: The study was not funded by any source.

Originality: The authors state that the current study is original and has not been submitted anywhere else.

Data Availability Statement: Data associated with this paper can be presented on demand.

REFERENCES:

- Holmen J, Holmen TL, Tverdal A, Holmen OL, Sund ER, Midthjell K. Blood pressure changes during 22-year of follow-up in large general population - the HUNT Study, Norway. *BMC Cardiovasc. Disord.* 2016, 16:94. doi: 10.1186/s12872-016-0257-8
- Kjeldsen SE, Narkiewicz K, Burnier M, Oparil S. Intensive blood pressure lowering prevents mild cognitive impairment and possible dementia and slows the development of white matter lesions in the brain: the SPRINT Memory and Cognition IN Decreased Hypertension (SPRINT MIND) study. *Blood Press.* 2018;27:247
- Lisko I, Kulmala J, Annetorp M, Ngandu T, Mangialasche F, Kivipelto M. How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med.* 2021;289:807–30. <https://doi.org/10.1111/joim.13227>
- Gabin, JM, Tambs K, Saltvedt, I., Sund, E., and Holmen, J. Association between blood pressure and Alzheimer disease measured up to 27 years prior to diagnosis: the

- HUNT Study. *Alzheimers Res. Ther.* 2017, 9:37. doi: 10.1186/s13195-017-0262-x
5. Hestad K, Engedal K, Schirmer H and Strand BH. The Effect of Blood Pressure on Cognitive Performance. An 8-Year Follow-Up of the Tromsø Study, Comprising People Aged 45–74 Years. *Front. Psychol.* 2020, 11:607. doi 10.3389/fpsy.2020.00607
 6. Satizabal CL, Seshadri S. Role of improved vascular health in the declining incidence of dementia. *Stroke.* 2017;48:2013–20. <https://doi.org/10.1161/STROKEAHA.117.013369>.
 7. Selmer R, Iglund J, Ariansen I, Tverdal A, Njolstad I, Furu K, *et al.* NORRISK 2: a Norwegian risk model for acute cerebral stroke and myocardial; 2017.
 8. Sindi S, Kåreholt I, Ngandu T, Rosenberg A, Kulmala J, Johansson L, *et al.* Sex differences in dementia and response to a lifestyle intervention: Evidence from Nordic population-based studies and a prevention trial. *Alzheimers Dement.* 2021;17:1166–78. doi:10.1002/alz.12279
 9. Gorelick PB, Furie KL, Iadecola C, Smith EE, Waddy SP, Lloyd-Jones DM, Bae HJ, Bauman MA, Dichgans M, Duncan PW, Girgus M, Howard VJ, Lazar RM, Seshadri S, Testai FD, van Gaal S, Yaffe K, Wasiaik H, Zerna C. Defining optimal brain health in adults: a presidential advisory from the American Heart Association/ American Stroke Association. *Stroke.* 2017;48:e284–e303
 10. Sachdev PS, Lipnicki DM, Crawford J, Reppermund S, Kochan NA, Trollor JN, *et al.* Risk profiles for mild cognitive impairment vary by age and sex: the Sydney Memory and Ageing study. *The American Journal of geriatric psychiatry.* 2012;20:854–65. <https://doi.org/10.1097/JGP.0b013e31825461b0>
 11. Williamson JD, Pajewski NM, Auchus AP, Bryan RN, Chelune G, Cheung, AK, *et al.* Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA.* 2019, 321, 553–561. doi: 10.1001/jama.2018.21442
 12. Hay M, Barnes C, Huentelman M, Brinton B, Lee R. Hypertension and Age-Related Cognitive Impairment: Common Risk Factors and a Role for Precision Aging. *Current Hypertension Reports.* 2020, 22: 80 <https://doi.org/10.1007/s11906-020-01090-w>
 13. Rouch L, Cestac P, Hanon O, Cool C, Helmer C, Bouhanick B, Chamontin B, Dartigues JF, Vellas B, Andrieu S. Antihypertensive drugs, prevention of cognitive decline and dementia: a systematic review of observational studies, randomized controlled trials and meta-analyses, with discussion of potential mechanisms. *CNS Drugs.* 2015, 29:113–130
 14. Hopstock LA, Bona KH, Eggen AE, Grimsgaard S, Jacobsen BK, Lochen ML, *et al.* Longitudinal and secular trends in blood pressure among women and men in birth cohorts born between 1905 and 1977: the Tromsø study 1979 to 2008. *Hypertension.* 2015, 66, 496–501. doi: 10.1161/hypertensionaha.115.05925
 15. Gilsanz P, Mayeda ER, Glymour MM, Quesenberry CP, Mungas DM, DeCarli C, *et al.* Female sex, early-onset hypertension, and risk of dementia. *Neurology.* 2017, 89:1886–93. doi:10.1212/WNL.0000000000004602.
 16. Leening MJG, Ferket BS, Steyerberg EW, Kavousi M, Deckers JW, Nieboer D, Heeringa J, Portegies MLP, Hofman A, Ikram MA, Hunink MGM, Franco OH, Stricker BH, Witteman JCM, Roos-Hesselink JW. Sex differences in lifetime risk and first manifestation of cardiovascular disease: prospective population based cohort study. *BMJ,* 2014, 349, g5992.
 17. American Psychological Association Publication manual of the American Psychological Association : the official guide to APA style.
 18. Scott J, Marshall G A Dictionary of Sociology, OUP Oxford; 2009.
 19. Clayton JA, Tannenbaum C. Reporting sex, gender, or both in clinical research? *JAMA – J Am Med Assoc.* 2016, 316, 1863–1864
 20. Abell JG, Kivimaki M, Dugravot A, Tabak AG, Fayosse A, Shipley M, *et al.* Association between systolic blood pressure and dementia in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension. *Eur. Heart J.* 2018, 39, 3119–3125. doi: 10.1093/eurheartj/ehy288
 21. Blanken AE, Nation DA. Does gender influence the relationship between high blood pressure and dementia? Highlight in areas for further investigation. *J Alzheimers Dis.* 2020, 78(1): 23–48. doi:10.3233/JAD-200245
 22. Anstey KJ, Peters R, Mortby ME, Kiely KM, Eramudugolla R, Cherbuin N, *et al.* Association of sex differences in dementia risk factors with sex differences in memory decline in a population-based cohort spanning 20–76 years. *Sci Rep.* 2021, 11:7710. doi:10.1038/s41598-021-86397-7
 23. Blanken AE, Nation DA. Does Gender Influence the Relationship Between High Blood Pressure and Dementia? Highlighting Areas for Further Investigation. *J Alzheimers Dis.* 2020, 78:23–48. doi:10.3233/JAD-200245
 24. Song JJ, Ma Z, Wang J, Chen LX, Zhong JC. Gender differences in hypertension. *J. Cardiovasc. Transl. Res.* 2019, 27, 176–181. doi: 10.1007/s12265-019-09888-z

25. Zutphen EM, Rijnhart JJM, Rhebergen D, Muller M, Huisman M, Beekman A, et al. Do Cardiovascular Risk Factors and Cardiovascular Disease Explain Sex Differences in Cognitive Functioning in Old Age? *J Alzheimers Dis.* 2021, 80:1643–55. doi:10.3233/JAD-201173
26. Kim S, Kim MJ, Kim S, Kang HS, Lim SW, Myung W, et al. Gender differences in risk factors for transition from mild cognitive impairment to Alzheimer's disease: A CREDOS study. *Comprehensive Psychiatry.* 2015, 62:114–22. <https://doi.org/10.1016/j.comppsy.2015.07.002>
27. Nespolo AM, Marcon SR, Lima NVP, Dias TL, Espinosa, MM. Health Condition and Memory Performance: a study with older adult women. *Rev. Bras Enferm.* 2017, 70, 640–646. doi: 10.1590/0034-7167-2016-0529
28. Pankratz VS, Roberts RO, Mielke MM, Knopman DS, Jack CR, Geda YE, et al. Predicting the risk of mild cognitive impairment in the Mayo Clinic Study of Aging. *Neurology.* 2015, 84:1433–42. <https://doi.org/10.1212/WNL.0000000000001437>
29. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 1975, 12, 189–198
30. Koepsell TD, Monsell SE. Reversion from mild cognitive impairment to normal or near Normal cognition; Risk factors and prognosis. *Neurology.* 2012, 79, 1591–1598.
31. Visser PJ, Kester A, Jolles J, Verhey F. Ten-year risk of dementia in subjects with mild cognitive impairment. *Neurology.* 2006, 67, 1201–1207.