Cognition and comorbidity in postmenopausal women

Artem Popov1, Nadezhda Izmozherova2, Tatiana Oboskalova3, Yelena Gavrilova2, and Yelena Safianik2

1Urals State Medical University, Hospital Therapy and Urgent Medical Care Service Department, 620028, Repin Str., 3, Ekaterinburg, Russian Federation
2Urals State Medical University, Pharmacology and clinical Pharmacology Department, 620028, Repin Str., 3, Ekaterinburg, Russian Federation
3Urals State Medical University, Obstetrics and Gynecology Department, 620028, Repin Str., 3, Ekaterinburg, Russian Federation

Abstract. Objective: to assess frequency and clinical significance of cognitive function impairment in postmenopausal woman.
Methods: A cross-sectional study included 462 women under the age of 65. Arterial hypertension, carbohydrate metabolism impairment, chronic heart failure, coronary heart disease frequency were registered. Mini Mental State Examination was used to assess cognitive function.
Results: mild cognitive function impairment was found in 223 (48%) postmenopausal women, 28 cases (6%) of dementia were registered. Mild cognitive impairment was associated with arterial hypertension (OR 1.74; 95% CI 1.16 – 2.64), chronic heart failure (OR 1.70; 1.16 – 2.49), dementia was associated with coronary heart disease (3.49; 1.54÷7.89).
Conclusion: cognitive impairment is frequent in postmenopausal women and associated with arterial hypertension, chronic heart failure and coronary heart disease.

1 Introduction

The World Health Organisation (WHO) reports global population to be rapidly ageing [1]. This demographic transition affects almost all aspects of society. It remains still unclear whether the acquired additional life years are a good quality of life period. A good health and social relations, feeling of independence and being in demand contribute to the conception of healthy and active ageing, declared by the WHO [2]. Population ageing determines the increase of cognitive functions impairment frequency [2]. Clinical spectrum and severity of cognitive deficiency varies from mild cognitive impairment to senile dementia [3].

Dementia is a syndrome caused by a chronic progressive brain disease, which includes multiple disturbance of memory, thinking, orientation, comprehension, calculation, learning
capacity, language and judgement as higher cortical functions while the consciousness is not clouded [4]. Dementia prevalence being estimated as 6 to 7% general European population, mild cognitive impairment (MCI) is appreciably more frequent in aged population strata [3,5]. Intellectual decrease in subjects with MCI is accompanied by complaints of slight forgetfulness, short-tome memory and other cognitive issues not causing dependence [3,4]. Preterm MCI onset may be related to elderly people multimorbidity [6]. On the other hand, cognitive dysfunction may significantly decrease patients’ compliance to the assigned treatment and prophylactic measures [7].

The aim of the study was to assess frequency and clinical impact of MCI in postmenopausal women.

2 Methods

A cross-sectional study included 462 postmenopausal women aged 44 to 65 who applied to physician due to menopausal symptoms [8]. Inclusion criteria were signed informed consent, spontaneous amenorrhea for 12 months or more, non-institutional independent living. Median postmenopausal period was 8.9 y (25% - 75% :5.0 ÷ 12.5).

Standardized medical history registration, anthropometry, general physician physical examination were performed. Mini Mental State Examination (MMSE) was used to screen for cognitive impairment [9]. MMSE scale values 28 to 30 points were assessed as normal range, MCI values 27 to 25 were estimated as MCI, 24 points and less were estimated as severe cognitive impairment requiring specialist consultation.

Arterial hypertension (AH) was diagnosed according to European 2013 Clinical Guidelines [10]. Stable angina pectoris was verified according to Russian 2008 Guidelines [11]. Chronic heart failure was registered according to National 2013 Guidelines [12]. Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) and type 2 diabetes were diagnosed according to Standards of specialized diabetes care [13].

Free “WinPEPI” software was used to calculate χ², and odds ratios. The study was approved by the Local Ethics Committee, the Municipal Central City Hospital 6, Ekaterinburg.

3 Results

In this outpatient sampling less than a half (211 persons) had normal cognition, there were also 223 cases (48%) of MCI and 28 cases (6%) of severe cognitive impairment (see fig. 1).

![Fig.1. Cognitive function in postmenopausal women](image-url)
Cognition decrease was associated with statistically significant odds of hypertension and chronic heart failure. Demention was also associated with coronary heart disease. (see. Tables 1, 2).

**Table 1. Cardiovascular Disease and Cognitive Function in Postmenopausal Women**

| Conditions                          | Normal (n=221) | MCI (n=223) | Demention (n=28) | χ² | P  |
|------------------------------------|----------------|-------------|------------------|----|----|
| CHD                                | 42 (19.9%)     | 58 (26.0%)  | 13 (46.4%)       | 9.973 | 0.007 |
| Glucose metabolism impairment      | 48 (22.7%)     | 63 (28.3%)  | 10 (35.7%)       | 2.226 | 0.322 |
| AH                                 | 133 (63.0%)    | 167 (74.8%) | 23 (82.1%)       | 9.363 | 0.009 |
| Cerebrovascular events and/or myocardial infarction | 10 (4.7%) | 16 (7.2%) | 2 (7.1%) | 1.191 | 0.551 |
| CHF                                | 83 (39.3%)     | 117 (52.5%) | 13 (46.4%)       | 7.523 | 0.023 |

**Table 2. Odds of MCI and Dementia in Cardiovascular Disease (OR, 95%CI)**

| Conditions                          | MCI n=223 | Dementia (n=28) |
|------------------------------------|-----------|-----------------|
| CHD                                | 1.41 (0.90÷2.22) | 3.49 (1.54÷7.89) |
| Glucose metabolism impairment      | 1.09 (0.52÷2.27) | 2.41 (0.72÷8.06) |
| AH                                 | 1.74 (1.16÷2.64) | 2.70 (0.99÷7.38) |
| Cerebrovascular events and/or myocardial infarction | 1.75 (0.79÷3.88) | 1.55 (0.32÷7.45) |
| CHF                                | 1.70 (1.16÷2.49) | 1.34 (0.61÷2.95) |

In this sampling, no significant relation of cognitive dysfunction with glucose metabolism disorders, history of cerebrovascular ischemic events and myocardial infarction was found.

### 4 Discussion

Cognitive functions refer to memory, gnosis, speech, praxis, intelligence which provide the process of rational knowledge of the environment and comfortable existence in it [4]. Focal or diffuse brain damage may impair cognitive functions [14,15]. Reduced memory and thinking speed lead to impaired social adaptation by limiting self-service and communication capabilities [3,5,16].

Hypertension is the most important cerebral blood flow limitation factor. Impaired cerebral microcirculation is reported to be detected not only in patients with cerebral disorders, but also in subjects without neurological symptoms [7, 16, 17]. In hypertensive subjects, in spite of high systemic blood pressure (BP), cerebral hypo-perfusion foci can expand and deepen during inadequate antihypertensive therapy. These processes are caused by a shift in the upper and lower limits of cerebral blood circulation autoregulation towards higher BP levels. So even minimal high BP decrease in conditions of impaired regulation, causes hypoperfusion and an increase in neurological symptoms. Hypoperfusion is even more pronounced in conditions of cerebral vascular stenosis [14, 15, 18]. In our study,
cognitive impairment was also associated with an increase in the frequency of hypertension and CHF in the absence of anamnestic data on cerebrovascular diseases. A 10 mmHg blood pressure increase causes 40% cardiovascular accidents additional risk. [19]. The morphological basis of these events is small-focal and diffuse changes in deep parts of the brain, which may not be manifested or associated with anamnestic data on cerebral catastrophes, i.e., be asymptomatic. At the same time, the presence of multiple small-focal changes in the brain substance may precede the development of vascular (multiinfarction) dementia [14]. The predominant localization of lacunar infarcts in the frontal lobes of the brain determines violations of intellectual and mnestic functions in such patients. There is a direct link between AH at 50 and cognitive function at 70: the lower BP registered at the age of 50, the better the cognitive function is found at the age of 70. Thus, hypertension is now considered the major risk factor for dementia of any origin [10, 18, 20, 21].

Cognitive impairment can be caused not only by ischemic brain damage. Another morphological substrate for cognitive disorders in hypertension may be diffuse white matter lesion, cortical atrophy, and cerebral hypoperfusion due to peculiar structural changes in small intracerebral arterioles [4, 5]. Brain hemispheres cortical (granular) atrophy is a result brain cortex neurons death and leads to the functional disorders observed. In the case of multiple small-focal lesions of the deep parts of the brain, white matter spongiosis, violations of higher mental functions are caused by disconnection of brain structures, in particular, damage to the connections of the frontal parts with the temporal, parietal, and limbic-reticular complex structures [5, 15].

In perimenopause, when the level of estrogens is reduced by 90% from the reproductive period, complaints of memory and attention loss are reported by 60% women [22]. During reproductive years, improving verbal skills and memory in women is associated with periods of high estrogen levels in the menstrual cycle [23]. Taking into account data on the neuroprotective effect of estrogens, it could be expected that after menopause, cognitive function in women will decrease faster than in men. However, out of 8 studies of the effect of gender on the rate of cognitive decline, 4 showed a faster deterioration in women, and 4 showed no difference [22, 23]. Several meta-analyses of studies evaluating the effect of estrogen intake on postmenopausal cognitive function have been published. But the majority of women who took estrogens in these studies had higher socioeconomic status and education than women in the control groups, and had fewer risk factors for cardiovascular disease and initially better cognitive function [22, 23].

It is suggested that a slight cognition decrease after age of 50 may be estimated as normal [4]. According to the "Canadian Study of Health in Aging", cognitive impairment that goes beyond the age limit, but does not reach the severity of dementia, was diagnosed in 16.8% elderly and old people [24]. A lower incidence of MCI (10.7%) was found in the "Italian study of Aging", but MCI was a predictor of dementia, senile asthenia, depression, falls, and premature death in this trial [21]. According to the results of the all-Russian epidemiological study, the prevalence of cognitive disorders is up to 25% in elderly outpatients of neurologists [25]. Memory disorders and reduced learning ability in old age are caused by impaired function of the D1 and D2 receptors in the caudate nucleus, shell, and hippocampus. The dopaminergic system of the prefrontal cortex is involved in providing short-term memory. As age increases, the activity of the mesocortical dopaminergic system decreases [4]. Data on neuromorphological changes in MCI are very sparse. About half of the patients had Alzheimer's type changes in the brain: neurofibrillar glomeruli and senile plaques in the medial parts of the temporal lobes and significant diffuse amyloid deposition in the neocortex. Magnetic resonance brain imaging reveals temporal lobes atrophy [14, 15, 16].
The causative relationship between the MCI and its progression to dementia with a history of previous ischemic strokes is quite obvious: the dementia was registered in 25% subjects within the first 6 months after the index event [16, 17, 18]. The identified risk factors also included age, female gender, low education level, diabetes mellitus, smoking, and white matter lesions detected by comprehensive imaging methods [16, 17, 18].

Cognitive function directly correlates with the motor activity of the subjects. Physical activity decrease determines the risk of premature death from all causes, including the progression of cardiovascular diseases, while mild cognitive impairment may be at least partially reversible in cases of successful re-habilitation and everyday activity increase [19, 20, 21].

Thus, the identification of cognitive disorders necessitates a more thorough search for cardiovascular diseases in postmenopausal women. On the other hand, detection and effective management of cardiovascular conditions in postmenopausal patients requires mandatory assessment of cognitive function as a predictor of low treatment adherence and premature death [2].

5 Conclusion

Thus, cognitive impairment is frequent in postmenopausal women and associated with arterial hypertension, chromic heart failure and coronary heart disease.

Place the figure as close as possible after the point where it is first referenced in the text. If there is a large number of figures and tables it might be necessary to place some before their text citation.

References

1. World report on ageing and health. WHO (2015)
2. J.R. Beard, I. Araujo de Carvalho, Y. Sumi, A. Officer, J.A. Thiyagarajan, Bull. World. Health. Organ., 95, 730–730A (2017)
3. World Alzheimer Report 2015 The Global Impact of Dementia An analysis of prevalence, incidence, cost & trends. Alzheimer’s Disease International (ADI), London (2015)
4. N.N. Yakhno, V.V. Zakharov, A.B. Lokshin, N.N. Koberisky, E.A. Mkhitaryan Dementia: a guide for physicians 3rd ed. (M.: Medpress-inform, 2011)
5. O.S. Levin, Handbook of outpatient physician, 2, 57 (2012)
6. National Guideline Centre (UK). Multimorbidity: Assessment, Prioritisation and Management of Care for People with Commonly Occurring Multimorbidity (London: National Institute for Health and Care Excellence (UK), 2016)
7. X. Gonda, M. Pompeii, G. Serafini, G. et al., Ann Gen Psychiatry, 14, 27 (2015)
8. ACOG Practice Bulletin N 141: management of menopausal symptoms. Obstet. Gynecol., 123, 202 (2012)
9. M.F. Folstein, S.E. Folstein, P.R. McHugh, Journal of psychiatric research, 12(3), 189 (1975)
10. 2013 ESH/ESC guidelines for the management of arterial hypertension, J. Hypertens., 31(7), 1281 (2013)
11. 2013 ESC guidelines on the management of stable coronary artery disease: The Task Force on the management of stable coronary artery disease of the European Society of Cardiology, Russ. J. Cardiol., 7(111), 7 (2014)
12. National recommendations PRAS cardiology and internal medicine on the diagnosis and treatment of chronic heart failure (fourth revision), J. Heart Failure, 14, 7(81), 380 (2013)
13. I.I. Dedov, M.V. Shestakova, A.A. Aleksandrov, G.R. Galstyan, O.R. Grigoryan, R.M. Esayan, et al., Diabetes mellitus, 16(1S) (2013)
14. S.G. Bugrova, Clin. Gerontol., 10-11, 22 (2009)
15. I.V. Damulin, Pharmateca, 19-20 (2011)
16. M.J. González-Moneo, G. Sánchez-Benavides, J.M. Verdu-Rotellar, et al., BMC Cardiovascular Disorders, 16, 163 (2016)
17. G.A. Hawker, R. Croxford, A.S. Bierman, P.J. Harvey, B. Ravi, et al., PLoS ONE, 9(3), e91286 (2014)
18. B. McGuinness, S. Todd, A.P. Passmore et al., J. Neurol. Neurosurg. Psychiatry, 79, 4 (2009)
19. S. Capewell, E.S. Ford, J.B. Croft, J.A. Critchley, K.J. Greenlund, D.R. Labarthe, Bulletin of the World Health Organization, 88, 120 (2010)
20. M. Montero-Odasso, L. Bherer, S. Studenski, et al., Can Geriatr J., 18(3), 159 (2015)
21. V. Solfrazzi, E. Scafato, D. Seripa, et al., J. Am. Med. Dir. Assoc., 18(1), 89.e1 (2017)
22. G.A. Greendale, M-H. Huang, R.G. Wight, et al., Neurology, 26, 72(21), 1850 (2009)
23. E. Barrett-Connor, A.L. Gail, Semin. Reprod. Med., 27(3), 275–282 (2009)
24. The Canadian Study of Health and Aging: risk factors for Alzheimer's disease in Canada, Neurrol., 44(11), 2073 (1994)
25. E.I. Chukanova, Consilium medicum, 2, 58 (2011)