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## ABSTRACT

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## PECULIARITIES OF THE COURSE, DIAGNOSIS, AND TREATMENT OF MULTIPLE SCLEROSIS

**Introduction.** Multiple sclerosis (MS) is a chronic progressive disease of the central nervous system, which is characterized by demyelination and degeneration of nerve fibers and has a polymorphic clinical picture and a tendency to an unfavourable course [1]. The disease usually affects young and working-age people, leading to early disability and poor quality of life, which makes it a socially significant problem of our time [2].

The main **objective** was to increase the efficiency of diagnosis and treatment of patients with multiple sclerosis based on a comprehensive analysis of clinical-neurological, psychodiagnostic, and neuroimaging features of the onset and course of the disease.

**Materials and Methods:** Clinical and neurological examination of patients using the Functional System Score (FSS) and Expanded Disability Status Scale (EDSS); cognitive functions examination using the Mini-Mental State Examination (MMSE), the clock-drawing test, the five-word test; brain magnetic resonance imaging; the 36-Item Short Form Health Survey (SF-36).

According to statistics, there are about 3 million patients with multiple sclerosis worldwide. In Ukraine, about 20,000 people have multiple sclerosis. Currently, a hypothesis has been made about multiple sclerosis as a multifactorial disease that is, to a great extent, attributable to genetic predisposition (i. e., features of the immune reaction) and the influence of external factors [1].

Multiple sclerosis mainly affects young and mature people – 12 to 55 years old. Although multiple sclerosis can sometimes make its debut in puberty, however, the frequency of the disease gradually increases with age up to the middle of the third decade of life, with a subsequent decrease up to the age of 50–60 [3]. Recently, a trend toward the rejuvenation of multiple sclerosis has been observed. About 3% of all patients with multiple sclerosis are children under 16. Multiple sclerosis debuting at a later age is not sufficiently studied and is rarely diagnosed, although in about 20% of patients, the first signs of this pathology appear after age 40 [4, 11].

**Keywords:** multiple sclerosis, age-related features, quality of life, disability degree, cognitive impairments, treatment efficacy.

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## ОСОБЛИВОСТІ ПЕРЕБІГУ, ДІАГНОСТИКИ ТА ЛІКУВАННЯ РОЗСІЯНОГО СКЛЕРОЗУ

**Актуальність.** Розсіяний склероз (РС) – це хронічне прогресуюче захворювання центральної нервової системи, яке характеризується демієлінізацією та дегенерацією нервових волокон, має поліморфну клінічну картину та схильність до несприятливого перебігу [1]. Хвороба зазвичай уражає людей молодого та працездатного віку, призводячи до ранньої інвалідизації, зміни якості життя, що дозволяє вважати її соціально значущою проблемою сучасності [2].

**Основною метою і завданням** було підвищення ефективності діагностики та лікування хворих на розсіяний склероз на підставі комплексного аналізу клініко-неврологічних, психодіагностичних, нейровізуалізаційних особливостей дебюту та перебігу захворювання.

**Матеріали та методи.** Клініко-неврологічне обстеження хворих з використанням клінічних неврологічних шкал функціональних систем (FS) та EDSS; дослідження когнітивних функцій з використанням шкал MMSE, тесту малювання годинника, тесту запам'ятовування 5 слів; магнітно-резонансна томографія головного мозку; опитувальник оцінки якості життя SF-36.

За статистикою у світі налічується близько 3 млн. хворих на розсіяний склероз. В Україні розсіяним склерозом страждають біля 20000 людей. Наразі сформовано гіпотезу про розсіяний склероз як мультифакторне захворювання, у виникненні якого значна роль належить генетичній схильності (особливості імунної реакції) та впливу зовнішніх факторів [1].

Розсіяним склерозом хворіють переважно люди молодого та зрілого віку – від 12 до 55 років. Хоча інколи розсіяний склероз може дебютувати у пубертатному віці, з віком частота захворюваності поступово збільшується до середини третього десятиріччя життя, з наступним зниженням до 50-60-и річного віку [3]. Останнім часом визначається тенденція до “омолодження” розсіяного склерозу. Близько 3% усіх хворих на розсіяний склероз складають діти, які не досягли 16-річного віку. Розсіяний склероз, що починається в більш пізньому віці, вивчений недостатньо, рідко діагностується, хоча близько у 20% пацієнтів перші ознаки даної патології з'являються після 40 років [4,11].

**Ключові слова:** розсіяний склероз, вікові особливості, якість життя, ступінь інвалідизації, когнітивні порушення, ефективність лікування.

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## INTRODUCTION / ВСТУП

Multiple sclerosis (MS) is a chronic, multifactorial, progressive disease of the central nervous system with a relapsing-remitting course. MS is characterized by periods of remission and exacerbations accompanied by a variety of neurological symptoms. MS occurs mainly in people with a genetic predisposition (with a peculiar immune response) as a result of provoking factors, for example, viral and bacterial infections, lack of sunlight, or hyperinsolation [5]. There is no consensus as to whether MS is exclusively an autoimmune, genetically determined disease since the specific triggers of the immune attack have not yet been identified. Therefore, MS is considered an immune-mediated disease of the central nervous system (CNS) and belongs to the group of demyelinating diseases, with the main pathological manifestation being the destruction or degradation of myelin. Recently, there has been enough evidence disproving that MS is exclusively a disease due to demyelination [6, 12]. Myelin sheath decomposition, even in the early stages of the disease, can be accompanied by damage to axons, although axon loss is particularly significant during the exacerbation and progression stages of the disease. In recent years, data have been obtained on the MS-related damage to both the white and gray matter of the CNS, which causes irreversible neurological deficits and is accountable for the slowly growing brain atrophy throughout the disease [7, 10].

The course of MS debuting at an older age differs from the course of the disease with a typical onset. The first signs in patients with late-onset MS are usually movement disorders with predominating lower-limb paraparesis (in more than 50% of patients), often with a significant increase in muscle tone. Some publications indicate a higher frequency of the primary-progressive course in the case of a late debut [8, 9].

Methods of study: a clinical and neurological examination of patients using the Functional System Score (FSS) and Expanded Disability Status Scale (EDSS); cognitive functions examination using the Mini-Mental State Examination (MMSE), the clock-drawing test, the five-word test; brain

magnetic resonance imaging (MRI); the 36-Item Short Form Health Survey (SF-36).

**Materials and Methods.** The paper presents the results of the examination of 120 patients with a confirmed diagnosis of MS. The diagnosis was established according to the McDonald criteria (2017) based on clinical data, the course of the disease, and the MRI data. The patients aged 20 to 65 years had a relapsing or progressive MS course. They were divided into groups according to the age of onset. There were two groups: Group I (young age) – with a debut at the age of 22–35 for men, 21–35 for women; Group II (older age) – with a debut at the age of 36–60 years for men, 36–55 for women. Group I consisted of 60 patients (20–35 years old) with the onset of the disease at the age of  $24.2 \pm 3.6$ . Group II consisted of 60 patients (35–60 years old) with the onset of the disease at the age of  $43.0 \pm 5.6$ .

According to the FSS and EDSS scores, cases were divided into three grades: mild (score 1 to 3.0 points), moderate (3.5 to 5.5), and severe ( $> 6.0$ ).

The quality of life (QoL) was assessed using the SF-36 Health Survey Questionnaire developed at the US Center for Medical Outcomes Study (1992).

The Mini-Mental State Examination (MMSE) score, the clock-drawing test, and the five-word test were used to study the level of intellectual productivity in patients with MS.

MRI of the brain was performed using tomographs with a magnetic field strength of at least 1.5 T. T1- and T2-weighted images were evaluated, including the number, size, and localization of lesions; changes over time; and degree of brain atrophy (if any).

Statistical processing of the obtained data was carried out using Statistica 8.0, Stata 11 (StatSoft Inc., USA), and Microsoft® Excel 2020 (Microsoft Corporation, USA) software.

## Results and Discussion

It was established that women were predominating among the patients of Groups I and II (58.3% and 55.0%, respectively), the men-to-women ratio was 1.4:1 and 1.2:1, respectively.

The relapsing course of MS was significantly more often observed in the group of young patients, while the progressive MS course was more common in the group of older patients. 59 patients

of Group I were diagnosed with relapsing MS, and 1 patient – with secondary progressive MS. Among the patients of Group II, 42 subjects presented with relapsing MS course, 11 subjects – with secondary progressive MS, and 7 subjects – with primary progressive MS.

Analyzing the possible risk factors that could trigger MS onset, it was found that most often, patients reported emotional stress (ES) and acute respiratory viral infections (ARVI) – 47 (39.2%) and 19 (15.8%) cases, respectively. A correlation with a craniocerebral injury was established in 5 (4.1%) patients, with hypothermia – in 1 (1.7%) patient. 14 (11.6%) subjects considered physical overexertion a probable risk factor for the development of MS; 3 of 68 (4.4%) women pointed to pregnancy and childbirth. 31 (25.8%) patients with MS failed to indicate any factor that preceded the onset of the disease. Thus, we revealed a significant predominance of patients who pointed to ES and ARVI, whereas the number of patients with ES was significantly higher ( $p = 0.004$ ). A comparison of possible provoking factors in patients of different age groups showed that the correlation between ARVI and the onset of the disease was observed in 14 (23.3%) patients in Group I, which was significantly higher than in Group II (5; 8.3%) ( $p = 0.045$ ). Patients of Group II pointed to a psychotrauma as a provoking factor (29; 48.3%) more often as compared to patients of Group I (18; 30.0%) ( $p = 0.04$ ). Regarding other risk factors for MS onset, no significant difference between the groups was found. Patients of Group I failed to associate the onset of the disease with any of the specified factors more often than patients of Group II, but these values were not statistically significant: 17 (28.3%) and 14 (23.3%) subjects, respectively. In the entire cohort of patients, the time interval (TI) between the risk factor exposure and the onset of the disease averaged  $17.6 \pm 5.6$  days for ARVI vs.  $72.0 \pm 44.9$  days for ES (a statistically significant difference,  $p = 0.001$ ). A comparison of TI in subjects showed that the interval between ARVI and the manifestation of the first symptoms was identical in patients of both groups. Thus, in Group I, it equaled  $17.8 \pm 6.5$  days, and in Group II, it was  $17.2 \pm 3.1$  days. In our opinion, this fact is of particular interest, as it may indicate the period of immunopathological (autoimmune) process activation in patients of both age groups. The first MS symptoms after ES occurred at different time intervals in patients of Groups I and II. Thus, in Group I, the disease

debuted almost twice as soon as in Group II: in  $46.0 \pm 27.1$  and  $87.2 \pm 46.6$  days after ES, respectively (a statistically significant difference,  $p = 0.0018$ ). Probably, the stress factor causing an immune reaction and increasing the permeability of the blood-brain barrier determines a longer immunopathological process in older patients. According to our data, most subjects were born in spring and summer (76 out of 120; 63.3%). In this regard, statistically significant differences were obtained for March, May, and June. In the group of older MS patients, March, June, and December were most frequently reported as the months of birth, but statistical significance was obtained only for the individuals born in March (26.6%) ( $p = 0.003$ ).

Analysis of the clinical picture of multiple sclerosis revealed that the onset of the disease was represented as mono- and polysymptomatic manifestations in both groups. Monosymptomatic onset (MO) in the young age group was observed in 51 (85.0%) patients, while polysymptomatic onset (PO) – was in 9 (15.0%) patients ( $p = 0.001$ ). In the older age group, MO was observed in 52 (86.6%) patients, PO – in 8 (13.3%) patients ( $p = 0.0012$ ). Thus, in patients of Groups I and II, MO significantly prevailed over PO, but there was no statistically significant difference between the groups. With regard to neurological symptoms in MO of MS, vision disorders, i.e., optic neuritis with a significant decrease in visual acuity (usually unilateral) and, as a rule, favourable subsequent recovery (14; 27.4%), were in the first place in terms of frequency in the group of young patients. The second most frequent symptom of the debut was movement disorder (12; 23.5%). Sensitivity disorders, as the first manifestations of MS, were noted in 11 (21.5%) patients and were characterized by a feeling of numbness of various localization and paresthesias. In 10 people (19.6%), the disease started with brainstem symptoms: diplopia, vestibular disorders (vertigo, instability, nausea, vomiting); in fewer subjects, MS manifested with other cranial nerve lesions. MO in young MS patients was characterized by a dominant lesion of the visual analyzer and corticospinal tract. In patients of Group II, MO started with movement disorders in 23 (44.2%) subjects, coordination disorders – in 11 (21.1%) subjects, brainstem disorders – in 7 (13.4%) subjects, sensory disorders – in 5 (9.8%) subjects, and retrobulbar neuritis – in 6 (11.5%) subjects. We established that in MO patients, corticospinal disorders significantly prevailed in Group II over Group I ( $p = 0.013$ ),

while Group I presented with a statistically significant predomination of retrobulbar neuritis at the onset of the disease ( $p = 0.04$ ).

According to the duration of MS onset, all cases were classified into short-term (up to 1 month), medium-term (up to 2 months), long-term (up to 3–4 months), and of indefinite duration. Analysis of the onset duration revealed that in patients of Group I, short-term onsets occurred in 48 cases (80.0%), medium-term onsets were observed in 5 cases (8.9%), and long-term onsets – in 7 cases (11.7%). In Group II, the number of patients with a short-term onset equaled 32 (53.3%), with a medium-term onset – 16 (26.6%), with a long-term onset – 5 (8.3%), with indefinite duration – 7 (11.6%). In the young age group, short-term onsets significantly prevailed over long-term onsets ( $p = 0.02$ ), while in the older age group, a reverse pattern was observed: medium-term and indefinite-duration onsets were more frequent than short-term cases ( $p = 0.009$  and  $p = 0.03$ ).

When evaluating the first remission after the disease onset, it was found that in the young age group, complete recovery of neurological deficit was observed in 57 (95.0%) patients and incomplete recovery – in 3 (5.0%) patients. In the older age group, complete remission was established in 35 (58.3%) cases, incomplete remission – in 18 (30.0%) cases, no clinical remission – in 7 (11.7%) cases. Thus, Group I of patients was distinguished by a significantly higher frequency of complete remission ( $p = 0.0001$ ), while in Group II, there was a statistically significant prevalence of patients with incomplete recovery of neurological functions ( $p = 0.002$ ) or no clinical remission ( $p = 0.006$ ).

The interval between the first and second exacerbations (first remission) was classified into short-term (up to 1 year), medium-term (1 to 5 years), and long-term (over five years). In Group I, 21 (35%) patients had a short-term remission, 30 (50%) patients had a medium-term remission, and 9 (15.0%) patients had a long-term remission. In Group II, 11 (14%) patients had short-term remission, 25 (41.6%) patients had a medium-term remission, and 18 (30.0%) patients had long-term remission. No clinical remission was observed in 6 (10%) patients with primary-progressive MS on account of the rapid further progression of the disease. Short-term remissions were significantly more frequent in Group I ( $p = 0.038$ ), while Group II was characterized by a significantly higher number of long-term remissions ( $p = 0.02$ ) or no

remission ( $p = 0.01$ ). No statistically significant difference was found between groups for medium-term remission.

The analysis of EDSS scores revealed that the patients of Group I were distinguished by a significant prevalence of mild-degree disability, while the patients of Group II were characterized by moderate and severe degrees of disability.

In Group I, the average EDSS score in patients with MS duration of 1 to 5 years was  $2.4 \pm 0.7$ ; with MS duration of 6 to 10 years, it was  $2.9 \pm 0.9$ . In Group II, the average EDSS score in patients with MS duration of 1 to 5 years was  $3.5 \pm 1.2$ ; with MS duration of 6 to 10 years, it was  $3.7 \pm 1.1$  ( $p = 0.001$ ;  $p = 0.025$ ).

In patients with MS duration 11 to 15 years, no statistically significant difference was found between the groups with regard to the degree of disability. Thus, it was concluded that in the first years of the disease, younger patients were distinguished by a mild degree of disability, while older patients reached moderate and severe degrees of disability more quickly, which was associated with the predominance of a more aggressive MS course in Group II.

At the time of the examination, the clinical picture of the disease was characterized by motor disorders, coordination disorders, sensory disorders, cranial nerve function disorders, and pelvic organ function disorders. In the structure of the leading clinical syndromes, corticospinal tract disorders and cerebellar lesions predominated in the older age group vs. the younger age group, while the frequency of sensory disorders and cranial nerve lesions did not differ significantly. Disorders of motor functions, statics, walking, and coordination, as well as pelvic disorders in patients of the older age group, led to more significant disability.

The results of the neuropsychological examination confirmed that impaired cognitive function is a significant component of the clinical picture of MS. Screening of cognitive functions using the MMSE scale in all subjects revealed four variants of outcomes of cognitive functions assessment: normal (65.8%) cognitive function, mild (20.8%) cognitive impairment, moderate (11.6%) cognitive impairment, mild dementia (1.6%). No moderate or severe dementias were diagnosed in the studied patients. In general, mild impairment predominated in the structure of cognitive disorders in young and older patients (18.3% and 23.3% of cases, respectively). However, moderate impairment was more often

observed in patients of the older age group (18.3% vs. 3.3% in Group I;  $p < 0.05$ ). Thus, older patients with MS were characterized by a greater degree of cognitive impairment than younger patients. The average MMSE score in young patients with cognitive impairment amounted to  $26.8 \pm 1.1$ ; in older patients, it was significantly lower –  $25.5 \pm 1.1$  ( $p < 0.005$ ).

A comparison of the MMSE subtest results showed that almost all subjects presented with adequate retention of language, reading, writing, and copying skills, perception, and visual-spatial functions without statistically significant deviations from the norm. Disorientation and long-term memory impairment were the dominant symptoms of cognitive disorders in MS patients. At the same time, statistically significant differences were registered in the group of older patients.

The study of mnemonic activity using the five-word test revealed disorders of the immediate and delayed recall of words. Repeated demonstration of the sheets with words to some patients increased the number of recalled words; however, 28.3% of patients in Group I and 48.0% of patients in Group II failed to remember more than two words after the fifth attempt. In Group I patients with cognitive impairment (CI), the average number of immediately recalled words after five attempts equaled 3.6 words; for the delayed word recall, this number amounted to 3.4 words; in Group II, these values were 2.9 and 2.8 words, respectively ( $p < 0.005$ ). At the same time, more significant violations were observed in all five attempts in patients of Group II vs. Group I.

According to the five-word test, mild cognitive impairment prevailed in both groups of patients (20.0% of young patients and 33.3% of older patients). However, these disorders were diagnosed significantly more often in patients of the older age group vs. young patients. Moderate disorders were presented less often: in 8.3% of patients in Group I and 10.0% of patients in Group II, with no statistically significant difference between them. Severe disorders were detected only in older patients (5.0%).

The study of visuospatial disorders revealed by the clock-drawing test found a significant difference between the study groups. Twenty-four patients of Group I presented with some deviations from the norm (the clock-drawing test score  $< 10$ ); the average score amounted to  $7.7 \pm 1.5$ . In Group II, poor results of the clock-drawing test were reported in 33 subjects, with the average score

being  $6.3 \pm 1.4$  ( $p = 0.014$ ). Cognitive disorders were observed in 47.5% of young and older patients. However, their severity was more marked in the group of older patients.

The MRI data analysis of MS patients confirmed that the most characteristic location of demyelinating lesions was the periventricular area (92.5%). The lesions were also located in the brain stem, cerebellum, and corpus callosum. In patients of Group I, brain stem location of lesions and optic nerve damage were more common. In the older age group, cerebellar lesions prevailed statistically significantly. In patients of both Groups I and II, small- and medium-size foci were predominantly observed (3–4 mm to 2 cm in diameter). In addition, older patients had a significantly greater number of confluent lesions (14.5%) than young patients (6.7%). Apart from the signs of multifocal lesions, MRI revealed diffuse changes. Leukoaraiosis was diagnosed in 8.3% of patients in Group II. Atrophic processes of the brain were detected in 6 (10%) patients of Group I and 17 (28.3%) patients of Group II ( $p = 0.011$ ).

Thus, a comparison of MRI data in Groups I and II revealed common features regarding localization and frequency of demyelinating lesion development; however, a detailed analysis showed that, despite the similarity of quantitative and qualitative changes, some indicators differed between the groups. Therefore, in older patients, demyelinating lesions were more often located in the cerebellum, had confluent nature, and were accompanied by leukoaraiosis and diffuse cerebral atrophy (DCA), which might be indicative of more significant brain damage.

A comparison of brain MRI data and the results of the neuropsychological examination showed a statistically significant correlation observed in Group I between the cognitive impairment degree (as defined by the MMSE scale) and the localization of lesions in the brain stem or cerebellum and the presence of DCA. In Group II, a statistically significant correlation was established between the cognitive impairment degree and the localization of lesions in the brain stem or corpus callosum; multiple lesions; leukoaraiosis; and DCA. In addition, the patients of Group II demonstrated a statistically significant correlation between the cognitive impairment degree as defined by the five-word test and the lesions of confluent nature (5/11; 45.4%); leukoaraiosis (5/5; 100%); and DCA (8/17; 47.0%); while the cognitive impairment degree as defined by the clock-drawing test correlated with the cerebellar

location of lesions (20/29; 68.9%) ( $p = 0.03$ ). Accordingly, the analysis of the correlation between cognitive impairment as defined by a neuropsychological examination and MRI data demonstrated a statistically significant association with the location of lesions in the brain stem or cerebellum and the presence of DCA and leukoaraiosis, which might indicate the more significant damage to these structures in the cognitive impairment formation in MS patients. On the other hand, this association was not significant in the young age group.

A decrease in quality of life in MS patients was observed as soon as in the first years of the disease. To a greater extent, it was related to the physical aspect and various functioning parameters (physical, social, emotional), indicating the limitation of patients' daily activities. The most remarkable changes in quality of life were noted in older patients compared to young patients. For all subjects with a disease duration of up to 10 years, general trends toward changes in the quality of life were observed, which were more significant in older patients. Subsequently, as the neurological deficit grew and the duration of the disease exceeded 11 years, the functioning parameters continued to decrease progressively, with no significant differences between the groups. These data characterized not only the increasing neurological deficits but also the psychological problems experienced by patients.

Analysis of the association between QoL and the disease duration demonstrated an inversely proportional correlation, i.e., QoL decreased with increasing disease duration. In the young age group, the integral assessment score of the QoL based on 8 parameters of the SF-36 scale depended on the duration of the disease by as much as 27.4% ( $r = -0.524$ ;  $p < 0.05$ ). At the same time, such parameters as physical functioning (18.5%), vitality (7.7%), and role-physical functioning (5.2%) ( $p < 0.03$ ) occurred to be most susceptible to the duration of the disease. Some parameters in young people had no statistically significant correlation with the disease duration: pain (0.1%), general health (0.7%), and mental health (0.1%) ( $p > 0.05$ ). In patients of the older age group, in general, a gradual decrease was observed in QoL parameters with the increase in the duration of the disease ( $r = -0.379$ ). The given

general characteristics of QoL indicated a decrease in the susceptibility of QoL parameters to the duration of the disease in older age. At a young age, due to the short duration of MS, there were no significant changes in quality of life; only after eight years of the disease, a dramatic decline in QoL was observed. In older people, the negative changes associated with increasing disease duration were less apparent due to the uniform decrease in the parameters from the first years of the disease.

All patients in the exacerbation stage were prescribed pulse therapy with methylprednisolone (1000 mg daily for five days). The analysis of the treatment efficacy in Group I revealed a positive effect in 51 patients, minor improvement – in 6 patients, no effect – in 3 patients. In patients of Group II, a positive effect of treatment was observed in 39 subjects, minor improvement – in 12 subjects, while in 9 subjects, the pulse therapy with corticosteroids was ineffective. Accordingly, the effectiveness of pulse therapy was demonstrated in patients of both groups, but it was significantly higher in the young age group ( $p = 0.017$ ). In the older age group, the percentage of patients with the insufficient outcome or no effect after the pulse therapy was significantly higher than in the young age group.

Nineteen subjects of Group I were treated with disease-modifying drugs (DMDs), and the other 41 subjects received symptomatic therapy. In Group II, eight patients were treated with DMDs, and 52 patients received symptomatic therapy. The difference in the frequency of prescribing preventive therapy for patients of different ages was statistically significant ( $p < 0.05$ ).

Thus, patients who had been receiving DMDs for two years, both young and older, had a lesser degree of disability vs. patients of comparable age and similar disease duration receiving symptomatic treatment only. At the same time, older patients receiving DMDs achieved a greater degree of disability in 2 years vs. young patients receiving the same therapy.

In this manner, in contrast to the traditional ideas suggesting that the late onset of MS is more favourable, our study has proved the unfavorable course of MS in patients with the onset at an older age.

patients) and acute respiratory viral infections (15.8%). In young patients, the disease was more often preceded by acute respiratory viral infections, while in older patients, emotional stress prevailed

## CONCLUSIONS / ВИСНОВКИ

The most frequent possible risk factors for MS in all ages were emotional stress (39.2% of

as a risk factor. The time interval between an acute respiratory viral infection development and the onset of the disease was shorter and had no statistically significant difference between the age groups ( $17.6 \pm 5.6$  days). After emotional stress, this interval was longer, especially in older patients ( $87.2 \pm 46.6$  days vs.  $46.0 \pm 27.1$  days in young patients;  $p = 0.0018$ ). In the case of a late onset ( $43.0 \pm 5.6$  years), the first symptoms of MS were mainly motor disorders, while with early onset ( $24.2 \pm 3.6$  years), the symptoms were more often related to visual disorders. In patients with an onset at an older age, MS had primary-progressive and secondary-progressive character significantly more often. Older patients had a more significant neurological deficit according to the EDSS scale as compared to younger patients with the same duration of the disease –  $4.3 \pm 1.1$  and  $3.1 \pm 1.0$ , respectively ( $p < 0.05$ ).

Cognitive impairments were determined in 47.5% of patients with MS and were characterized mainly by disorientation, difficulties with calculation, disorders of short-term and long-term memory, as well as visuospatial disorders, and were more pronounced in older patients. Mild and moderate cognitive impairments were observed in 18.3% and 5.0% of young patients and 23.3% and 18.3% of older patients, respectively; mild dementia was reported in only 3.3% of older patients.

Brain MRI changes were typical for MS patients of all ages. At the same time, older patients were more often diagnosed with demyelinating lesions in the cerebellum and confluent lesions, and diffuse cerebral atrophy ( $p < 0.05$ ), which might indicate the prevalence of the neurodegenerative process. We established a correlation between the diffuse atrophic process in the brain as defined by MRI data and

cognitive disorders in patients of both age groups. Apart from that, a correlation was observed between demyelinating lesions in the cerebellum and confluent lesions and cognitive disorders in older patients.

Quality of life parameters in older MS patients were significantly lower than in young patients. If the disease duration was up to 10 years, the physical component and one of the psychological components – role-emotional functioning – were mainly affected. A downward trend was confirmed for quality of life in patients of both age groups with a disease duration of more than 11 years, with no significant difference between the groups.

In older patients, the pulse therapy with methylprednisolone performed in case of exacerbation was less effective than in young patients. DMDs were twice as often prescribed to young patients, while older patients were treated mainly for their symptoms with limited effectiveness. The DMDs significantly reduced the number of exacerbations and were the most optimal treatment method for patients of any age.

Given the insufficient effectiveness of pulse therapy in older patients, it is necessary to recommend preventive therapy for such patients, which should be regulated by the relevant standards of treatment.

The data we received is consistent with the results of published works by Anna JE Combes, Estelle Seyman, R Bunganic, and Nida Aslam, but partially contradicts the conclusions of the publications by Anna Pokryszko-Dragan, Yavor Yalachkov, and Berardino Barile, which did not significantly affect the content and structure of the paper, but suggested the subject of further research.

#### PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

Thus, different data on the role of patients' age in MS development and course indicate the need for further study of this problem. An in-depth study of MS initial manifestations in different ages will allow to expand the understanding of its clinical and diagnostic features and contribute to developing therapeutic strategies to treat this serious disease

#### CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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#### AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

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