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DISCRIMINANT MODELS OF THE LIKELIHOOD AND CHARACTERISTICS OF MULTIPLE SCLEROSIS PROGRESSION IN UKRAINIAN MEN DEPENDING ON BODY SIZE PARAMETERS

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In young Ukrainian men, based on the characteristics of body size, reliable discriminant models were built, which allow with high probability (correctness of the classification matrix 100 % of cases, Wilks' Lambda statistics=0.051, p<0.0001) to attribute the studied subjects to "typical" for practically healthy people or the general group of patients with multiple sclerosis. Based on the characteristics of body size between multiple sclerosis men with mild (EDSS 1.5–2.0) and moderate (EDSS 3.5–4.5) disorders, a reliable interpretation of the obtained classification indicators is also possible with medium probability (correctness of the classification matrix 96.8 % of cases, Wilks' Lambda statistics=0.342, p<0.0001).

Key words: nervous diseases, multiple sclerosis, anthropometric indicators, discriminant models, practically healthy and sick men.

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ДИСКРИМІНАНТНІ МОДЕЛІ МОЖЛИВОСТІ ВИНИКНЕННЯ ТА ОСОБЛИВОСТЕЙ ПЕРЕБІГУ МНОЖИННОГО СКЛЕРОЗУ В УКРАЇНСЬКИХ ЧОЛОВІКІВ У ЗАЛЕЖНОСТІ ВІД ОСОБЛИВОСТЕЙ РОЗМІРІВ ТІЛА

В українських чоловіків молодого віку на основі особливостей розмірів тіла побудовані достовірні дискримінантні моделі, які дозволяють з високою ймовірністю (коректність класифікаційної матриці 100 % випадків, статистика Wilks' Lambda=0,051, p<0,0001) віднести досліджуваних до «типових» для практично здорових або загальної групи хворих на множинний склероз. На основі особливостей розмірів тіла між хворими на множинний склероз чоловіками з легкими (EDSS 1,5–2,0) та помірними (EDSS 3,5–4,5) порушеннями також можлива достовірна інтерпретація отриманих показників класифікації з середньою ймовірністю (коректність класифікаційної матриці 96,8 % випадків, статистика Wilks' Lambda=0,342, p<0,0001).

Ключові слова: нервові захворювання, множинний склероз, антропометричні показники, дискримінантні моделі, практично здорові та хворі чоловіки.

The study is a fragment of the research project "Constitutional features of body structure in people with multiple sclerosis and its impact on the course of the disease", state registration No. 0121U114309.

Multiple sclerosis is a chronic immune-mediated disease of the central nervous system characterized by inflammation, demyelination, and neurodegeneration. It predominantly affects the brain, spinal cord, and optic nerves, leading to a variety of symptoms, including muscle weakness, sensory disturbances, visual impairment, and cognitive dysfunction. Clinically, multiple sclerosis is classified into subtypes, with the most common being relapsing-remitting, secondary progressive, and primary progressive variants [5].

Multiple sclerosis is one of the most prevalent neurological diseases among young adults globally. The average worldwide prevalence is approximately 33 per 100,000 people, but this varies significantly by geographic region. In high-latitude regions, such as Northern Europe, prevalence can reach 100–200 per 100,000, while in tropical regions, it is significantly lower, ranging from 5–20 per 100,000. Women are predominantly affected, with the female-to-male ratio having increased over recent decades, reaching as high as 3:1 in certain areas. The highest risk of developing the disease occurs between the ages of 20 and 40, coinciding with the most active period of life. Overall, the disease poses a substantial burden on healthcare systems, especially in countries with high prevalence rates [10].

The disease significantly impacts physical activity levels, which are associated with disability progression in patients. According to a systematic review by Charron S. et al. [3], individuals with multiple sclerosis exhibit markedly reduced levels of physical activity compared to healthy populations, even in the early stages of the disease. Reduced physical activity is linked to fatigue, impaired gait, and balance disturbances.

Quality of life is also substantially compromised in this patient population. Studies consistently report significantly lower quality-of-life scores in people with multiple sclerosis compared to the general population. For instance, research utilizing the EQ-5D scale shows mean quality-of-life scores ranging from 0.6 to 0.7, indicating moderate impairment. Additionally, the psychological well-being of patients is greatly affected, with many reporting increased levels of anxiety and depression [9].

It is crucial to note that multiple sclerosis has a complex genetic etiology, with genetic factors interacting with environmental influences to contribute to disease development. Studies highlight the HLA gene, particularly HLA-DRB1 variants, as a significant genetic risk factor. Although genetic predisposition varies across populations, genetic factors are estimated to account for approximately 30 % of disease risk. However, multiple sclerosis is a multifactorial disease, with environmental factors such as infections, low vitamin D levels, and smoking complementing genetic susceptibility [13]. In this context, anthropometric parameters of the patient's body may serve as potential predictors of disease onset or progression characteristics.

The purpose of the study was to construct and analyze the discriminant models of the possibility of occurrence and features of the course of multiple sclerosis in young Ukrainian men depending on body size.

Materials and methods. On the basis of the Department of Nervous Diseases of the National Pirogov Memorial Medical University, Vinnytsya and the Medical Center "Salyutem" (Vinnytsya), a clinical, laboratory and anthropo-somatotypological (according to the schemes of Bunak V.V. (1941) modified by Shaparenko P.P. (2000), Carter J. and Heath B. (1990), Matiegka J. (1921) and the American Institute of Nutrition (Shephard R.J., Shephard R.F., 1991) [1]) examination of 35 young men (25–44 years old according to the WHO age periodization, 2015) patients with multiple sclerosis was conducted. Committee on Bioethics of National Pirogov Memorial Medical University, Vinnytsya (protocol No.10 from 10.12.2021) found that the studies do not contradict the basic bioethical standards of the Declaration of Helsinki, the Council of Europe Convention on Human Rights and Biomedicine (1977), the relevant WHO regulations and laws of Ukraine.

The diagnosis of multiple sclerosis was established based on the 2017 McDonald criteria. To evaluate the degree of disability, the Expanded Disability Status Scale (EDSS) was utilized. The group of patients with mild impairments (EDSS 2.0–3.0) included 24 men; with moderate impairments (EDSS 3.5–4.5) – 7 men; with moderately severe impairments (EDSS 5.0–6.5) – only 4 men. Therefore, for further modeling of the features of the course of multiple sclerosis depending on body size, we used only patients with mild and moderate impairments.

As a control group, the primary anthropo-somatotypological indices of 82 practically healthy Ukrainian men of a similar age group were taken from the data bank of the National Pirogov Memorial Medical University, Vinnytsya Research Center.

Discriminant models of the possibility of occurrence and features of the course of multiple sclerosis depending on body size were built in the "Statistica 6.0" license package.

Results of the study and their discussion. When classifying practically healthy Ukrainian men and those with multiple sclerosis (general group) based on anthropo-somatotypological parameters, the classification matrix achieves 100 % accuracy. The discriminant variables distinguishing between practically healthy men and those with multiple sclerosis include the intercrest distance of the pelvis (CRIS), the intertrochanteric distance of the pelvis (TROCH), the widths of the distal epiphyses of the forearm (EPRP) and thigh (EPB), the transverse lower thoracic diameter of the torso (PNG), the maximum width of the head (B_SH_GL), the upper forearm circumference (OBPR1), and the chest circumference during exhalation (OBGK2). Among these variables, the intercrest distance of the pelvis contributes most significantly to discrimination. Overall, the set of all anthropometric variables demonstrates highly pronounced discrimination (Wilks' Lambda statistic=0.051; $p<0.001$) between practically healthy individuals and the general group of Ukrainian men with multiple sclerosis.

The determined classification indices (Df) allow us to attribute the obtained anthropometric indices to "typical" ones for practically healthy or the general group of Ukrainian men with multiple sclerosis. Below, in the form of equations, the definition of the Df index is given, where the attribution to practically healthy men is possible with a Df value close to 291.7; to men with multiple sclerosis – with a Df value close to 269.1:

– Df (for healthy men)= CRIS×2.000 + TROCH×1.068 + EPRP×9.065 + EPB×29.32 - PNG×1.471 + B_SH_GL×13.67 - OBPR1×0.140 + OBGK2×0.042 - 291.7;

– Df (for the general group of men with multiple sclerosis)= -CRIS×2.268 + TROCH×3.643 + EPRP×20.78 + EPB×19.37 + PNG×0.281 + B_SH_GL×11.29 - OBPR1×2.494 + OBGK2×0.597 - 269.1;

where (here and in the following), transverse dimensions of the trunk and pelvis – in cm; width of the distal epiphyses of the long tubular bones of the limbs – in cm; head dimensions – in cm; girth dimensions of the body – in cm.

The calculated χ^2 criterion with the removal of consecutive roots confirms the statistical significance of both discriminant functions (Table 1).

Table 1

Stepwise analysis report incorporating the χ^2 criterion for all canonical roots of practically healthy and multiple sclerosis-affected Ukrainian men, considering body size parameters

	Eigen-Value	Canonicl R	Wilks'Lambda	Chi-Sqr.	df	p-level
0	18.74	0.974	0.051	331.1	8	0.0000

Notes: here and in subsequent similar tables Eigenvalue – root values for each discriminant function; Canonicl R – canonical value R for different roots; Wilks' Lambda – Wilks' Lambda statistic; Chi-Sqr. – standard χ^2 test of consecutive roots; Df – number of degrees of freedom; p-level – p-level is associated with the corresponding χ^2.

When dividing Ukrainian men only into patients with multiple sclerosis with mild (EDSS 2.0–3.0) and moderate (EDSS 3.5–4.5) impairments, taking into account anthroposomatotypological indicators, the classification matrix covers 96.8 % of cases. Among patients with multiple sclerosis with mild and moderate impairments, the discriminant variables are the upper forearm circumference (OBPR1), the height of the anthropometric trochanteric point (ATV), the skinfold thickness on the thigh (GBD) and on the posterior surface of the shoulder (GZPL), and the width of the face (SH_LICA). Among these indices, the greatest contribution to discrimination is made by the value of the upper forearm circumference. In general, the set of all anthropometric variables has an average (Wilks' Lambda statistic=0.342; $p<0.001$) discrimination between Ukrainian men with multiple sclerosis with mild and moderate impairments.

The definition of the Df indicator is given in the form of equations below, where the assignment to men with multiple sclerosis with mild impairments is possible at a Df value close to 221.1; to men with multiple sclerosis with moderate impairments – at a Df value close to 213.5:

– Df (for men with multiple sclerosis with mild impairments)= OBPR1×1.966 + ATV×2.627 - GBD×0.998 + GZPL×1.775 + SH_LICA11.72 - 222.1;

– Df (for men with multiple sclerosis with moderate impairments)= OBPR1×0.231 + ATV×3.250 - GBD×0.431 + GZPL×0.905 + SH_LICA×9.882 - 213.5;

where, the longitudinal dimensions of the body are in cm; the skinfold thickness is in mm.

The calculated χ^2 criterion with the removal of consecutive roots confirms the statistical significance of both discriminant functions (Table 2).

Table 2

Stepwise analysis report with inclusion of χ^2 criterion for all canonical roots of multiple sclerosis patients with mild and moderate impairments of Ukrainian men taking into account body size

	Eigen-Value	Canonicl R	Wilks'Lambda	Chi-Sqr.	df	p-level
0	1.923	0.811	0.342	28.43	5	0.0000

Thus, both in the classification of Ukrainian men into practically healthy and those with multiple sclerosis (general group) and in the classification of men with multiple sclerosis into those with mild and moderate impairments, the analysis of the derived discriminant equations reveals that a reliable interpretation of the classification parameters is possible ($p<0.001$ in both cases). Specifically, for the differentiation between healthy individuals and patients, Wilks' Lambda=0.051; and for those with mild versus moderate impairments, Wilks' Lambda=0.342. The discriminant models distinguishing practically healthy men from the general group of men with multiple sclerosis include transverse pelvic dimensions, the widths of distal epiphyses of the long tubular bones of the limbs, circumferential body measurements (accounting for 25.0 %), as well as the transverse lower thoracic diameter of the torso and the maximum head width (accounting for 12.5 %). The discriminant models distinguishing men with mild versus moderate impairments of multiple sclerosis include skinfold thickness (40.0 %), upper forearm circumference, the height of the trochanteric anthropometric point, and facial width (accounting for 20.0 % each). The intercrest pelvic distance contributes most significantly to the discrimination between practically healthy men and the general group of men with multiple sclerosis, while upper forearm circumference is the most significant variable in distinguishing men with mild versus moderate impairments of multiple sclerosis. A substantially higher percentage of inclusion of transverse body dimensions and head sizes, which are highly genetically determined indices [1], in the discriminant models between healthy men and those with multiple sclerosis indicates a predominant genetic predisposition to this multifactorial disease. Conversely, the predominance of skinfold thickness and circumferential body measurements, which are less genetically determined indices [1], in the discriminant models distinguishing men with mild and moderate impairments points to a significant influence of external factors on the progression of this condition.

The relationship between anthropometric parameters and the risk and progression of multiple sclerosis (MS) has been established in numerous studies by international researchers [12, 15].

One of the key aspects of such research is the role of adiposity. M.M. Almramhi et al. [2], utilizing Mendelian randomization, investigated the impact of body fat on MS susceptibility and severity. Their

findings demonstrated that a high level of body fat increases the risk of MS development and correlates with more severe disease forms. Specifically, increased fat deposits were associated with disease severity ($p<0.001$), underscoring fat as a significant anthropometric factor in the pathogenesis of MS.

Another critical anthropometric factor is body mass index (BMI). A meta-analysis revealed that elevated BMI in MS patients is associated with faster disease progression. The authors reported that patients with higher BMI values face a greater likelihood of disability progression compared to those with normal BMI levels ($p<0.05$). Additionally, obesity was identified as a contributor to accelerated neurodegeneration and exacerbation of MS symptoms [4].

Abdominal obesity also plays a significant role in MS severity. Elevated measures of abdominal fat, particularly waist circumference, showed a statistically significant association with more severe disease courses. Patients with greater waist circumference exhibited higher disability levels ($p<0.01$) [7]. Furthermore, Drehmer E. et al. [6] found that increased abdominal fat correlated with elevated levels of inflammatory markers, such as IL-6, which contribute to neuroinflammation and disease progression in MS.

Other studies also emphasize the importance of managing anthropometric parameters in MS patients. A systematic review and meta-analysis demonstrated that high BMI and increased waist circumference are significant predictors of disability progression in MS. These anthropometric parameters could serve as critical indicators for assessing the risk of disease development and its severity [8].

I. Lutfullin et al. [11] reinforced these findings, reporting that obesity in MS patients is associated with a higher likelihood of disability progression. They highlighted weight management as a crucial strategy to reduce the risk of worsening clinical outcomes in MS.

It is essential to note that, beyond the direct influence of fat deposits on MS risk and progression, genetic factors play a considerable role. For instance, Wesnes et al. demonstrated that anthropometric parameters, including high BMI and waist circumference, exerted a more pronounced effect on MS risk in regions with increased genetic susceptibility, such as Norway and Italy. This study emphasized that the interplay between genetic predisposition and anthropometric factors is critical for understanding MS risk [14].

However, it is worth mentioning that most of the reviewed studies predominantly focus on weight-related parameters, while other anthropometric indices are scarcely addressed. Further exploration of diverse anthropometric measures could broaden the understanding of their role in MS pathogenesis and progression.

Conclusions

1. The developed discriminant models based on anthropometric parameters enable highly accurate prediction of the likelihood of multiple sclerosis onset in Ukrainian men (classification matrix covers 100 % of cases, Wilks' Lambda statistic=0.051; $p<0.001$) and moderate accuracy in predicting the specific characteristics of disease progression (classification matrix covers 96.8 % of cases, Wilks' Lambda statistic=0.342; $p<0.001$).

2. The constructed models distinguishing practically healthy men from those with multiple sclerosis most frequently include transverse pelvic dimensions, widths of the distal epiphyses of the long tubular bones of the limbs, and circumferential body measurements (each accounting for 25.0 %). For men with multiple sclerosis differentiated by mild and moderate impairments, the models primarily include skinfold thickness (40.0 %).

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BIOMECHANICAL ASPECTS OF INTRACRANIAL INJURIES CAUSED BY FALLS FROM THE HEIGHT OF "OWN HEIGHT" ONTO THE SURFACE

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The main purpose of the study was to analyze the biomechanical conditions of intracranial injuries caused by a fall from "own height". The study was based on the analysis of forensic medical examination materials, examination data, and a preliminary investigation of 190 people falling to the surface from their "own height". The victims were divided into 6 age groups (<20, 20–29, 30–29, 40–49, 50–59, and ≥60). Intracranial trauma was identified in 97 individuals (51.1 %). It was found that both isolated and combined intracranial trauma was registered predominantly in the age group ≥60. The analysis of the obtained results shows that in all falls onto the surface, the brain, its membranes, and blood vessels are damaged. Thus, the study of biomechanical conditions leading to damage to intracranial structures will significantly increase the objectivity of forensic experts' conclusions about the mechanisms and circumstances of craniocerebral injuries resulting from falls "own height".

Key words: fall from height, cranial fracture, intracranial injury, mortality.

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БІОМЕХАНІЧНІ АСПЕКТИ ВНУТРІШНЬОЧЕРЕПНИХ ПОШКОДЖЕНЬ, ВИКЛИКАНИХ ПАДІННЯМ З ВИСОТИ «ВЛАСНОГО ЗРОСТУ» НА ПОВЕРХНЮ

Основною метою дослідження був аналіз біомеханічних умов внутрішньочерепних ушкоджень, спричинених падінням з висоти «власного зросту». Дослідження проводилося на підставі аналізу матеріалів судово-медичної експертизи, даних огляду та попереднього розслідування 190 осіб, які впали на поверхню з висоти «власного зросту». Постраждалі були розділені на 6 вікових груп (<20, 20–29, 30–29, 40–49, 50–59 і ≥60). Внутрішньочерепну травму виявлено у 97 осіб (51,1 %). Встановлено, що як ізольована, так і поєднана внутрішньочерепна травма реєструвалася переважно у віковій групі ≥60 років. Аналіз отриманих результатів показує, що при всіх падіннях на поверхню ушкоджується головний мозок, його оболонки та судини. Таким чином, вивчення біомеханічних умов, що призводять до пошкодження внутрішньочерепних структур, дозволить суттєво підвищити об'єктивність висновків судово-медичних експертів щодо механізмів та обставин черепно-мозкових травм, отриманих внаслідок падінь з висоти «власного зросту».

Ключові слова: падіння з висоти, перелом черепа, внутрішньочерепна травма, летальність.

Craniocerebral injuries are a critical public health issue and a socio-economic problem worldwide [6, 10]. These injuries are one of the most important aspects of forensic medical examination, as they occupy the leading place among mechanical injuries.

In recent decades, there has been a steady increase in natural disasters, technological accidents, transportation incidents, and military conflicts worldwide, which are accompanied by mass traumatic injuries, particularly to the brain. Skull and brain injuries account for more than a third of all injuries, and according to WHO data, they increase by at least 2 % annually [3].

Since the occurrence of craniocerebral trauma can be a consequence of especially dangerous crimes against human life and health, the high social significance of determining the mechanism and origin of identified craniocerebral injuries is undeniable. This is especially important in craniocerebral injuries caused by "spontaneous" falls, as well as in cases where the victim is pushed to the surface as a result of