Research Article

The prevalence and phenotypic characteristics of the syndrome of premature aging in women in peri- and post-menopausal period

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ABSTRACT

Aim: This paper presents the results of our own study of the prevalence and phenotypic characteristics of the syndrome of premature aging in women in peri- and post-menopausal period. **Materials and Method:** It presents data on that against the background of menopausal changes since the age of 50 years, premature aging syndrome develops in women, which manifests itself in accelerated aging by 1.3–1.6 times. Neurohumoral mechanisms described in premature aging in postmenopausal period and associated with a cytokine tension increase in the level of serum pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukins 1 and 6. **Results and Discussion:** Results of phenotypic characteristics of premature aging in women in peri- and post-menopausal period are given: A significant decrease in the strength index with a simultaneous significant increase in the body mass index, the proportion of fat, and the area of the subcutaneous and visceral fat.

KEY WORDS: Peri- and post-menopausal period, Phenotype, Premature aging, Sarcopenic obesity, Women

INTRODUCTION

In recent years, the premature aging syndrome has been widely discussed in the literature.[1-4] In this regard, timely detection and correction of the syndrome of premature aging, which is the main and most common form of aging of over 40–50s, gains its importance.[5,6] It should be noted that there are certain gender differences in the nature of the course of the disease. In men, the syndrome of premature aging begins earlier is associated with lifestyle and bad habits. Onset in women usually coincides with climacteric changes that are characterized not only by clinical symptoms but also by the addition of a number of diseases due to decrease of estrogen protection.[7-9] While the climacteric syndrome has clear clinical manifestations, which makes its diagnosis relatively simple, it is extremely early to speak of the successes of its timely detection and, accordingly, adequate therapy. For example, until now, many specialists are extremely cautious about the prescription of hormone replacement therapy, lack of knowledge of their indications, and contraindications. In addition, existing measures to prevent premature aging are often focused on the elimination of its clinical manifestations without taking into account the need to correct its biological manifestations. Therefore, it is important to study the relationship between the phenotypic manifestations of premature aging in peri- and post-menopausal period, its genetic and molecular characteristics.

Objective of the Research

The objective of this study was to study the phenotypic characteristics of the syndrome of premature aging in women in peri- and post-menopausal period.

MATERIALS AND METHODS

To comprehensively study the parameters of the biological age of women in peri- and post-menopausal periods and identify whether they have premature aging syndrome, 175 women aged 45–64 years, were examined, mean age was 54.5 ± 2.5 years old. In this

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case, to assess the dynamics of the premature aging, the patients were divided by age based on a 5-year interval: 45–49 years, 50–54 years, 55–59 years, and 60–64 years.

Inclusion criteria were the passage of a planned routine inspection, the appearance of the complaints, characteristic for the perimenopausal period, and the absence of hormone replacement therapy for menopausal symptoms; exclusion criteria were the presence of severe or exacerbated/decompensated somatic and neuropsychiatric diseases, and the patient's refusal of informed consent for her in-depth examination.

To identify the status characterizing the processes of premature aging, we conducted the following anthropometric examination within the framework of an in-depth prophylactic study: Measurement of body weight (in kg), measurement of blood pressure and calculation of pulse pressure (in mmHg), timed inspiratory and expiratory capacity - Stange and Genchi's tests (in seconds), determination of the vital capacity of the lungs (spirography, in liters), a static balancing test according to the standard method (in seconds), patient questioning for identifying self-rated health index (on a 10-point visual analog scale, in points), and measurement of handgrip (torque, in kg). These indicators provided an opportunity to calculate the actual and proper biological age according to the method by V.P. Voitenko[10] and the aging factor indicating the presence of the syndrome of premature aging. The formula for women was used:

$$ABA = 1.46 + 0.42 \times PP + 0.25 \times W + 0.7 \times SRH - 0.14 \times SB,$$

Where
ABA - actual biological age,
PP - pulse pressure,
W - body weight
SRH - self-rating health
SB - static balancing.

To identify the factors that accelerate the aging process in women in peri- and post-menopausal periods, we performed the following studies: 1) Instrumental examination - screening densitometry of the bones of the hands (the force index *F* was used, expressed in %: *F* = hand strength (daN) × 0.98/body weight (kg) × 100); 2) laboratory tests - determination of HOMA IR score, levels of serum proinflammatory cytokines (tumor necrosis factor α [TNF-α], interleukins 1 [IL-1] and interleukins 6 [IL-6] [in pg/ml]), and lipid metabolism - triglyceride, total cholesterol, low-density lipoprotein, and high-density lipoprotein in the blood serum (mmol/l).

An additional anthropometric examination was performed to determine body composition. For this purpose, we calculated the following parameters: Fat mass according to the Mateika formula (2009) (in kg), fat fraction (in %), lean mass (in kg), and subcutaneous and visceral fat (in cm^2).

To calculate these indicators, we used the following formulas:

- Fat mass = total fat (kg) × average value of subcutaneous fat (in millimeters) × body surface area (in square centimeters) × 0.13;
- Average value of subcutaneous fat = total thickness of skin-fat folds (in millimeters) on the shoulder in front and behind, forearm, back, abdomen, thigh, lower leg, and chest/14;
- Percentage of fat = total fat (kg) × 100/body weight (kg);
- Muscle mass = height (in centimeters) × mean value of the shoulder, forearms, thighs, and drumsticks radii (without the subcutaneous tissue and skin) (in centimeters) × 6.5, wherein the mean value of the radii defined by the following formula: Sum of the four circumferences/25.12 - sum of five fat folds/100.

Calculation of the above-described anthropometric indicators allowed us to diagnose sarcopenic obesity as a factor of the syndrome of accelerated aging. To identify factors that determine the acceleration of the aging process in women in peri- and post-menopausal periods, we studied in selected groups the prevalence of cardiovascular and metabolic diseases, as well as the severity of the main manifestations of the climacteric syndrome (fever sensation, sweating, headache, blood pressure variation, vasomotor rhinitis, dryness of the mucous membranes of the genital tract, and anxiety-depressive syndrome) on a 10-point visual analog scale.

RESULTS AND DISCUSSION

An in-depth anthropometric study used to calculate the biological age by Voitenko's method found that most of the calculated parameters, with the exception of body weight, which tended to increase, statistically significantly worsened as age increased. The summary characteristic of the obtained anthropometric data, necessary for calculating the biological age, is presented in Table 1.

Using these indicators, we found that the dynamics of the index of the actual biological age/proper biological age (aging factor) in the studied age groups was as follows: 45–49 years - 1.0±0.02, 50–54 years - 1.3±0.01, 55–59 years old - 1.4±0.01, and 60 years and over - 1.6±0.02; $P < 0.05$. That is, at a normal mean biological age in the age group of 45–49 years, starting from the age of 50, the biological age advanced the passport age, that is, the syndrome of premature aging developed.

Its actual prevalence in the studied groups was as follows: 45–49 years - 5 patients (12.2%), 50–54 years - 32 patients (71.1%), 55–59 years - 38 patients (86.4%), and 60 years and older - 41 patients, which was 91.1% [Table 2].

The study of the factors associated with the process of premature aging in women in perimenopausal period resulted in the following data.

The patients in the age group of 60 years and older had a subclinical development of osteopenia at normal indicator of bone mineral density (T-score); in the younger age groups: 45–49 years - −0.9 ± 0.08, 50–54 years - −0.9±0.03, 55–59 years - −0.8 ± 0.07, and 60 years and older - −1.5 ± 0.09 (strong positive correlation with premature aging syndrome, r=+0.90; $P < 0.05$).

The study revealed that the average age of the onset of menopause was 48.7 ± 1.5 years (47–51 years), with the first menopausal disorders occurring the age of 46.5 ± 1.2 years (45–47 years). The comparison of clinical and laboratory data with biological markers of the processes of premature aging showed that against the background of menopausal disorders there was an age-dependent deterioration of the lipid profile (a strong positive correlation with the syndrome of premature aging, r = +0.92; $P < 0.05$), the formation of chronic immune inflammation (a strong positive correlation with the syndrome of premature aging, r = +0.88; $P < 0.05$), and an increase in the insulin resistance index (a strong positive correlation with the syndrome of premature aging, r = +0.93; $P < 0.05$). At the age of 50–54 years, worsening of pathological processes occurred and continued exacerbating at the age of 55–59 years, with their stabilization at the age of 60 years and older [Table 3].

The correlation analysis showed that the HOMA score in the over 50s significantly exceeded the normal values and significantly increased during the aging process - 50–54 years - 1.9 ± 0.2, 55–59 years - 2.1 ± 0.1, and 60 years and older - 2.4 ± 0.2, which indicates a strong positive correlation with premature aging syndrome, r = +0.9; $P < 0.05$. Triglyceride values did not exceed their normal range, but statistically significantly increased with age, the total cholesterol level exceeded the normal values at the age of 60 years and older - 6.2 ± 1.0 mmol/l, which had a strong positive correlation with the syndrome of premature aging, r=+0.9; $P < 0.05$.

We found that as the age increased, after the onset of menopause, there were statistically significant changes and anthropometric markers characterizing the processes of premature aging. Thus, there was a progressive significant decrease in the force index F from 56.8 ± 1.2% in women aged 45–49 years to 51.3 ± 0.9% at the age of 50–54 years, 46.2 ± 1.0% at the age of 55–59 years, and 42.1 ± 1.1% at the age of 60 years and older ($P < 0.05$ compared with the related age groups). A decrease in muscle strength was accompanied by a significant ($P < 0.05$) increase in the body mass index, the proportion of fat, and the area of subcutaneous and visceral fat, indicating the development of sarcopenic obesity [Table 4].

The correlation analysis showed a strong positive correlation of sarcopenic obesity with a syndrome of premature aging (r = +0.86, $P < 0.05$).

Table 1: Dynamics of calculated indicators of biological age by V.P. Voitenko in patients in peri- and post-menopausal period and their chronicity

Data required for the calculation of biological age	Age group (years)			
	45–49 (*n*=41)	50–54 (*n*=45)	55–59 (*n*=44)	60 and over (*n*=45)
Body weight (kg)	71.4±3.4	73.1±2.8	75.4±2.9	79.5±4.1
Systolic blood pressure, mmHg	139.4±5.7	141.5±4.1	159.1±3.2*	165.4±3.1*
Diastolic blood pressure, mmHg	89.3±1.2	91,7±1.1	94.3±2.1*	97.1±2.4*
Pulse pressure, mmHg	50.1±1.5	49.8±1.4	64.8±2.1*	68.3±2.0*
Stange's test (s)	43.4±1.2	42.8±1.1	40.1±0.9*	37.5±0.8*
Genchi's test (s)	38.3±1.1	37.0±0.8	36.1±0.7	35.0±0.5*
Vital capacity (L)	2.6±0.1	2.5±0.2*	2.4±0.1*	2.3±0.1*
Static balancing (s)	51.3±1.1	50.4±1.0	48.3±0.8*	45.2±0.9*
Self-rating health	8.1±0.2	8.0±0.1	7.4±0.3*	7.0±0.4*

*$P<0.05$ compared with the previous age group

Table 2: Age-specific features of the prevalence of the syndrome of premature aging in women in peri- and post-menopausal period (by Voitenko's method)

Indicator	Age group (years)			
	45–49 (*n*=41)	50–54 (*n*=45)	55–59 (*n*=44)	60 and over (*n*=45)
	abs. (%)	abs. (%)	abs. (%)	abs. (%)
Prevalence	5 (12.2)	32 (71.1)	38 (86.4)	41 (91.1)
Average aging factor (normally equal to 1.0)	1.0±0.02	1.3±0.01*	1.4±0.01*	1.6±0.02*

* $P<0.05$ compared with the previous age group. Abs: Absorbance

Table 3: Dynamics of clinical and laboratory indicators in patients in peri- and post-menopausal period

Indicator	Age group (years)			
	45–49 (*n*=41)	50–54 (*n*=45)	55–59 (*n*=44)	60 and over (*n*=45)
HOMA score	1.7±0.4	1.9±0.02*	2.1±0.01*	2.4±0.02*
TNF-α, pg/ml	5.1±0.02	5.5±0.03*	5.9±0.01*	6.7±0.04*
IL-1, pg/ml	2.1±0.01	2.4±0.02*	2.7±0.01*	3.1±0.02*
IL-6, pg/ml	2.7±0.02	3.1±0.01*	3.5±0.02*	3.9±0.01*
Triglycerides, mol/l	1.2±0.01	1.4±0.02*	1.5±0.1	1.7±0.02*
Total cholesterol, mol/l	4.7±0.12	5.2±0.13*	5.7±0.14*	6.2±0.04*
LDL	1.01±0.02	1.04±0.01*	1.06±0.02*	1.07±0.01
HDL	1.27±0.06	1.26±0.01	1.0±0.01*	0.84±0.02*

*P<0.05 compared with the previous age group, TNF-α: Tumor necrosis factor, IL-6: Interleukin 6, IL-1: Interleukin 1

Table 4: Dynamics of in-depth anthropometric data on body composition in women in perimenopausal period

Indicator	Age group (years)			
	45–49 (*n*=41)	50–54 (*n*=45)	55–59 (*n*=44)	60 and over (*n*=45)
Fat mass (kg)	18.7±0.9	22.1±0.5*	24.8±0.5*	27.1±0.7*
Fat proportion (%)	30.5±0.02	32.1±0.03*	33.9±0.04*	35.8±0.03*
Subcutaneous fat (cm^2)	212.2±5.1	228.4±1.3*	249.3±2.5*	261.1±2.2*
Visceral fat (cm^2)	45.1±0.4	51.5±1.3*	57.8±2.1*	65.9±2.9*
Body mass index	23.1±1.2	27.4±0.8*	29.1±0.5*	33.1±0.7*

*P<0.05 compared with the previous age group

Summary

The development of the syndrome of premature aging is observed in women in peri- and post-menopausal periods since the age of 50 years, and its prevalence increases with age - at 50–54 years it is reported in 71.1% of the observed patients, at the age of 55–59 years - in 86.4%, and at the age of 60–64 years - in 91.1% of women. Against the menopausal changes, starting at the age of 50 years, women develop a syndrome of premature aging, which is manifested by acceleration of the aging rate at the age of 50–54 years by 1.3, at the age of 55–59 years by - 1.4, and at the age of 60 and older - by 1.6 times.

Neurohumoral mechanisms described in premature aging in post-menopausal period and associated with a cytokine tension increase in the level of serum pro-inflammatory cytokines such as TNF-a and interleukins 1 and 6.

Premature aging in peri- and post-menopausal period is accompanied by a significant decrease in the force index from 56.8% in women aged 45–49 to 51.3% at the age of 50–54, 46.2% at the age of 55–59 years, and 42.1% at the age of 60 years and older ($P < 0.05$), with a simultaneously observed significant increase in the body mass index, the proportion of fat and the area of subcutaneous and visceral fat, indicating the formation of sarcopenic obesity.

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