POSTION STATEMENT

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about a dissertation
for the award of an educational and scientific degree "doctor" on the topic " BODY COMPOSITION, BIOCHEMICAL INDICATORS, GRIP STRENGTH AND WALKING SPEED IN WOMEN WITH HYPERTHYROIDISM "
of Dr. Gergana Tosheva Mrinova
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I. Structure of the dissertation

The presented dissertation work covers 151 standard typewritten pages and is structured as follows:

1. Literature review – 47 pages
2. Aims and objectives – 1 page
3. Materials and methods – 8 pages
4. Results – 45 pages
5. Discussion – 6 pages
6. Conclusions – 2 pages
6. References to contributions – 1 page
7. Bibliography – 25 pages; covers 325 literary sources (13 - in Cyrillic, 312 - in Latin).

The content is presented correctly and in detail. The most frequently used abbreviations are listed. The individual chapters and sub-chapters are properly formatted, which provides clarity and overview of the dissertation work. The material is illustrated with 38 tables and 53 figures.

The structure of the dissertation work and the independent participation of the dissertation candidate in its preparation comply with the requirements according to the

regulations on the conditions and procedure for acquiring scientific degrees and occupying academic positions at MU-Varna.

II. Actuality, significance and practical focus of the topic

Hyperthyroidism is a common condition characterized by increased circulating thyroid hormones, which in turn induce a catabolic state characterized by increased energy expenditure, increased basal metabolic rate, increased lipolysis, bone matrix breakdown, and increased protein metabolism.

One of the main effects of hyperthyroidism is rapid weight loss without any change in the individual's diet or exercise regimen. This is due to the increased basal metabolic rate, which causes the body to expend more energy even at rest. In addition, excess thyroid hormones have a catabolic effect on muscle tissue, stimulating the breakdown of muscle proteins for energy. This can lead to a decrease in muscle mass and strength, with patients often reporting muscle weakness, especially in the proximal muscles of the extremities, such as the hips and shoulders.

Muscle loss is a component of sarcopenia, a disease associated with poor quality of life, immobility, increased hospital stay, as well as cognitive impairment and increased early mortality among those affected. On the other hand, accelerated bone metabolism can lead to increased bone breakdown, increasing the risk of osteoporosis. This is due to an imbalance between bone resorption and formation, in which bone loss predominates.

The high incidence of hyperthyroidism, especially in women, and the pronounced effects it causes on the body composition of those affected, with a significant increase in the risk of sarcopenia and osteoporosis, makes the topic of the dissertation particularly relevant. On the other hand, although the relationship between thyrotoxicosis and osteoporosis is very well studied, there is scant data in the literature assessing the involvement of muscles in hyperthyroidism, through simultaneous assessment of changes in body composition, grip strength and walking speed, and the results are contradictory. This highlights the need for more in-depth research on the relationship between changes in body composition, quantitative and qualitative indicators of sarcopenia, and the state of hyperthyroidism.

III. Components of the dissertation

The literature review is purposefully constructed, with emphasis placed on the

relevant aspects of the main topic. The influence of thyroid hormones on body composition in normal and pathological conditions, their role in the proper development and function of muscle tissue, their effect on skeletal muscle in conditions of hyperthyroidism, including some rarer pathologies such as thyrotoxic myopathy and thyrotoxic periodic paralysis and the possibility of worsening of existing myopathies in conditions of hyperthyroidism, are discussed in detail.

At the next stage, the various methods for studying body composition are described and analyzed - anthropometric and instrumental (nuclear magnetic resonance, computed tomography, dual-energy absorptiometry, bioelectrical impedance), as well as the individual components of body composition in normal and hyperthyroid conditions and its effects on body water, fat tissue, muscle tissue and bone mass. The relationship between some biochemical indicators (vitamin D, creatinine, CPK and albumin) and body composition is also examined.

Particular attention in the literature review is paid to sarcopenia as a generalized disease of the skeletal muscles, which is associated with an increased likelihood of adverse consequences such as an increased risk of falls, fractures, disability and immobilization, impaired quality of life, cardiovascular risk and mortality. The recommendations for research and diagnostic criteria for sarcopenia are reviewed, the pathogenetic mechanisms of its development, the possibilities for prevention and treatment, as well as the relationship between hyperthyroidism and sarcopenia are presented in detail.

In summary, the aspects of changes in body composition in hyperthyroidism and their relationship with sarcopenia covered in the literature review represent an adequate justification of the goal and objectives and logically justify the motivation for developing the dissertation topic.

The formulation of the **goal and tasks** is clear and precise and concerns the assessment of the relationship between hyperthyroidism in women and body composition, grip strength and walking speed (diagnostic components for sarcopenia), as well as with some biochemical indicators (vitamin D, creatinine, creatine phosphokinase, albumin). The tasks are eight in number and adequately reflect the goal set.

The **"Material and Methods"** section provides a detailed description of: the study design; the method of patient recruitment with inclusion and exclusion criteria; the indicators studied. The strict selection of the included contingent according to

standardized criteria guarantees the reliability of the results obtained. The methods of the individual clinical and laboratory indicators, as well as the definitions used, are precisely described.

The **"Results"** section contains the individual aspects of the dissertation work and are presented following the logic of the tasks set to achieve the goal. Task 1 reflects the results of the comparison of anthropometric and biochemical parameters between women with hyperthyroidism and healthy controls, with no significant differences between the two groups in terms of anthropometric indicators, while hormonal studies, expressed in a significantly reduced value of serum TSH and increased levels of FT3 and FT4, characterize the hyperthyroid state of patients with thyrotoxicosis and, as expected, show a statistically significant difference compared to the control group. The average values of the immunological indicators - TPO Ab and TRAb are also significantly higher in hyperthyroid individuals. Of the biochemical indicators studied, two stand out with a significant difference in values between the two groups - creatine phosphokinase and vitamin D, with the values of both being lower among hyperthyroid patients compared to euthyroid controls. Respectively, the frequency of vitamin D insufficiency and deficiency is significantly higher in the presence of hyperthyroidism.

The results of task 2 present the comparison of body composition indicators between hyperthyroid women and controls. It is established that bone mass among women in a hyperthyroid state is statistically significantly lower than that of healthy controls. The differences in terms of visceral and subcutaneous adipose tissue in both groups are insignificant. However, significant differences are established in terms of muscle mass in all four studied limbs, as the amount of muscle tissue in each of the limbs of patients in a hyperthyroid state is less compared to euthyroid controls with preserved lateralization - regardless of the thyroid status of the women, the amount of muscle is greater in the right half compared to the left.

The results of task 3 compare grip strength, limb muscle mass index (ASM/m^2) and walking speed (diagnostic components of sarcopenia) between women with hyperthyroidism and healthy controls. It was found that the decrease in the amount of muscle tissue in the upper limbs in hyperthyroid women is also associated with significantly lower muscle strength, more pronounced muscle weakness, lower amount of muscle tissue in the limbs, expressed as ASMI and lower walking speed compared to healthy women. Based on the results of the diagnostic indicators for

sarcopenia, a very high percentage of women with thyrotoxicosis was registered - 35.56%, compared to only one case in the control group.

The results of task 4 analyze the relationships between anthropometric indicators and body composition, as well as between anthropometric indicators and diagnostic criteria for sarcopenia - ASMI, grip strength and walking speed. It is interesting to note that, unlike healthy controls, in whom no correlations were found between age and the amount of muscle tissue, in women with hyperthyroidism, increasing age is associated with a decrease in the amount of skeletal muscle in each area of the body. On the other hand, with increasing age, the ASMI index decreases, and this relationship is observed only in hyperthyroid individuals.

The results of task 5 assess the relationship between hormonal and biochemical indicators and body composition, as well as between hormonal and biochemical indicators and the diagnostic components of sarcopenia - grip strength, skeletal muscle mass of the limbs/m^2 and walking speed. It was found that the decrease in TSH from euthyroid to hyperthyroid state is accompanied by a decrease in muscle mass in each of the limbs, as well as a decrease in bone mass, while peripheral thyroid hormones (FT3 and FT4) do not show a relationship with any of the parameters of body composition. Furthermore, the decrease in serum TSH is accompanied by a decrease in ASMI, grip strength and a slowdown in walking speed. On the other hand, none of the target biochemical indicators (25(OH)D, creatinine, CPK and albumin) showed significant correlations with the distribution of body composition.

The results of task 6 consider the risk of developing secondary sarcopenia and the threshold age above which the probability of secondary sarcopenia increases. The analysis conducted for this purpose demonstrates that the age above which screening for the presence of secondary sarcopenia should be carried out among women with newly diagnosed hyperthyroidism is 54 years, i.e. 11 years earlier than the age threshold for primary sarcopenia. These results are particularly valuable from a clinical point of view.

The results of task 7 look for correlations between anthropometric, hormonal and biochemical indicators, on the one hand, and the diagnostic components for sarcopenia - ASMI, grip strength and walking speed - on the other hand, among individuals affected by sarcopenia, and no significant relationships were found

between some of the studied hormonal and biochemical parameters and ASMI, grip strength or walking speed.

The results of task 8 compare the studied parameters among women with hyperthyroidism, compared to those with hyperthyroidism and established sarcopenia. No differences were found in the anthropometric and hormonal indicators between the two studied groups, while in terms of biochemical indicators, lower levels of creatine phosphokinase and higher levels of creatinine, total protein, albumin and liver enzymes were found in women with thyrotoxicosis and sarcopenia compared to those without. Contrary to expectations, however, individuals with thyrotoxicosis but without sarcopenia had lower vitamin D values. Furthermore, bone mass was lowest among women suffering from both thyrotoxicosis and sarcopenia, followed by the subgroup with thyrotoxicosis only and highest among the control group.

The discussion *is logically structured and examines the results in the context of the literature available to date on the subject. The text shows good knowledge of the problem and insight into the hypotheses set out in the scientific work*

The conclusions *are presented separately for the different tasks and specifically and accurately and reflect in a summary the results related to the main and most important aspects of the work.*

The contributions *are divided into those of national and international importance. Most of the contributions are original and contribute to the enrichment of the overall knowledge in the field of the relationship between thyrotoxicosis and changes in body composition and in particular sarcopenia.*

The bibliography *covers 325 literary sources and meets the requirements while being sufficiently comprehensive and up-to-date.*

The PhD candidate has 4 publications related to the dissertation, 1 participation in a national scientific forum and 3 participations in international congresses and symposia.

CONCLUSION: The dissertation work of Dr. Gergana Tosheva Marinova "BODY COMPOSITION, BIOCHEMICAL INDICATORS, GRIP STRENGTH AND WALKING SPEED IN WOMEN WITH HYPERTHYROIDISM" is up-to-date and properly structured. The design of the individual studies and the overall structure of the work

correspond to the set goals and objectives. The dissertation meets all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its Implementation and the Regulations for the Conditions and Procedure for Acquiring Scientific Degrees and Holding Academic Positions at MU-Varna for Acquiring the Educational and Scientific Degree "Doctor" in the Doctoral Program "Endocrinology".

I give a positive review and I strongly recommend that the members of the esteemed scientific jury vote positively for awarding the educational and scientific degree "Doctor" to Dr. Gergana Tosheva Marinova.

Заличено на основание чл. 5, §1, б. „В“ от Регламент (ЕС) 2016/679

24.02.2025 Signature :

Sofia /ass. prof. A. Gateva/