

STATEMENT

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UMHAT "KASPELA"- Plovdiv;
Member of the scientific jury for the award of educational
and scientific degree - "PhD"

Professional field: Medicine

PhD program: Endocrinology

Author of the dissertation: Dr. Radina Stoyanova Dimitrova

Form of PhD studies: Full-time

Department: Second Department of Internal Medicine, Unit of Endocrinology, Medical University of Varna.

Topic: COMPARATIVE CHARACTERISTICS OF METABOLIC MARKERS IN THE ASSESSMENT OF BONE HEALTH IN POSTMENOPAUSEAL AGE

Scientific adviser: Prof. Dr. Kiril Hristov Hristozov, PhD, MU-Varna.

1. General presentation of the procedure and the PhD student

The presented dissertation and the accompanying documents are in accordance with the procedure for obtaining the educational and scientific degree "PhD" according to the Act on career development of the academic staff in the republic of Bulgaria and the Regulations for the development of the academic staff in Medical University - Varna (ed. 15.09.2020) and its appendices. The provided set includes the following documents: Dissertation; executive summary of dissertation; Application to the Rector for disclosure of defense procedure; completed higher education, qualification degree "Master"; Order for enrollment; protocol of the PhD minimum exam; protocol of the department council with a positive decision on readiness for defense; Order for completion with the right to defense; Declaration of originality; list of publications related to the topic of the dissertation; Declaration of authenticity of the submitted documents; Declaration registration of profiles in scientific databases.

2. Biographical data of the candidate:

Dr. Radina Dimitrova was born in 1985. in the town of Shumen. She graduated with honors from the High School of Natural Sciences and Mathematics in 2004. She obtained master's degree in medicine at MU-Varna in 2010. Until 2013, Dr. Dimitrova worked in the Emergency Department for Adults of the University Hospital "St. Marina" - Varna, and since 2014 is part of the team of the Clinic of Endocrinology and Metabolic Diseases. In 2016 she was appointed assistant at MU-Varna at the Department of Internal Medicine, unit of Endocrinology. In 2018 Dr. Dimitrova acquired a degree in endocrinology and metabolic diseases. She is a PhD student at the Second Department of Internal

Medicine, Endocrinology, MU-Varna since 2018. Dr. Dimitrova is certified in the methods of neck ultrasound, fine-needle aspiration biopsy of the thyroid gland, parathyroid lesions and cervical lymph nodes. She is the first author and co-author of numerous full-text publications and participations in national and international scientific forums in the field of thyroidology, bone health and diabetes. She is a co-author of a textbook on Internal Medicine for healthcare professionals.

3. General characteristics of the dissertation

The dissertation contains 174 standard pages and is illustrated with 22 tables and 84 figures. The bibliography contains 411 titles, of which 3 in Cyrillic and 408 in Latin. The dissertation was discussed and referred for public defense at a meeting of the Department Council at the Second Department of Internal Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

3.1. Assessment of relevance of the topic of the PhD thesis

Metabolic syndrome (MS) and osteoporosis are conditions associated with increased morbidity and long-term health risks for the affected subjects. The components of MS - visceral obesity, hyperglycemia, hypertension and dyslipidemia have different effects on bone tissue. The net result of these effects is difficult to predict, especially in the context of key determinants of bone health such as age and duration of menopause. The growing prevalence of MS and osteoporosis, the significant morbidity associated with them, as well as the ambiguous and often contradictory findings about the relationship between the two conditions define the topic as relevant and interesting and motivate the implementation of current scientific research.

3.2. Literature review and knowledge of the problem

The literature review is comprehensive, contains detailed information on the problem, citing modern literature sources. At the beginning of the review, the author presents current data on the importance, prevalence and risk factors for the development of the two pathological entities - osteoporosis and MS. The main part analytically presents the publications concerning the relationship between the individual components of MS, bone health and fracture risk, outlining the guidelines for future research.

3.3. Research Methodology

The goal of the study is clearly defined. The six tasks are correctly formulated for the fulfillment of the goal. The section "material and methods" is described in 4 pages - includes a detailed presentation of the selection criteria, along with the clinical, laboratory, instrumental and statistical methods used. The research methodology is up-to-date and includes widely accepted and validated methods. Most of them are accessible for the daily endocrine practice, which increases the practical value of the results and

conclusions. The design of the study is well structured and allows the collection of sufficient scientific information for a detailed study of the problem.

3.4. Results, discussion, conclusions

The "Results and Discussion" section is presented on 79 pages. It describes and illustrates the results of the study. The analysis was performed competently using well-established statistical methods, the graphical analysis is well selected.

In general, the study confirms the positive relationship between body weight and bone-mineral density (BMD). A threshold values for body weight was determined for the sample, below which the risk of osteoporosis increases - 66.5 kg. Threshold values are calculated for the major risk factors - age and age of menopause. The results confirm the high prevalence of type D deficiency in our population, stating that the deficiency is more pronounced in people with higher body mass index. The author found that higher basal insulin levels and HOMA index were associated with better BMD parameters at the proximal femur. The study does not find a correlation between lipid fractions and bone health in the context conflicting literature on the problem. The analysis outlines blood pressure and hypertension as additional determinants of bone health in postmenopausal women. A significant correlation was observed between TNF-alfa values and decreased bone density. The presence MS is characterized by higher bone mass at the level of the proximal femur in women with postmenopausal osteoporosis, as well as a lower fracture risk. However, the individual assessment of the components of the MS provides divergent results. The author critically interprets the obtained dependencies and after analytical commentary on his own results and literature data does not accept that the visceral obesity associated with MS is a protective factor against the development of osteoporosis. The candidate comes to the conclusion that the fracture risk can be increased in women with MS according to the number, combination and degree of manifestation of its individual components.

The discussion is at a high professional level and summarizes the data obtained in the context of current views on the problem. The conclusions are 10 and correctly summarize the results of the study.

4. General evaluation of the dissertation

The presented dissertation of Dr. Radina Dimitrova is a completed modern scientific study of the relationship between the components of MS and changes in bone health in postmenopausal women. The dissertation work shows that the PhD student has acquired in-depth theoretical knowledge and practical experience, demonstrating skills to conduct an independent research.

5. Contributions and significance of the PhD thesis

The study provides valuable data on the relationship of a number of metabolic markers with bone characteristics in postmenopausal women in our population. This determines the essential scientific and scientific-applied contributions of the dissertation. In addition to the confirmatory results underlying the leading importance of age, duration of menopause and body weight, original contribution for the country are the estimated relationships between bone parameters and changes in blood pressure and the use of some antihypertensive drugs. The proposed diagnostic and therapeutic algorithm for prevention and treatment of osteoporosis in accordance with the risk profile for bone health in postmenopausal age is also interesting.

6. Publication activity related the topic of the dissertation

The candidate applies 5 full-text publications on the topic of the dissertation - 4 with literature reviews and 1 with original results of the study. Dr. Dimitrova is the first author of all attached articles.

7. Personal contribution of the PhD student

The acquaintance with the materials on the defense creates a persuasion that each phase of the study is conducted independently or with the active participation of the PhD student.

8. Executive summary

The executive summary abstract is prepared on 89 pages and reflects in summary form the design of the study, the main results, discussion and conclusions.

9. Critical remarks and recommendations

The number of observation units in the control group is small, which makes it difficult to interpret and achieve statistical significance in some comparative analyzes. It would be appropriate to combine the control group and the osteopenia group into one when comparing some variables.

The reported significant difference in the mean age of the study and control groups made it difficult to assess the significance of metabolic changes for reduced bone density in the study sample. However, it is good to note that during the data processing the PhD student made efforts to minimize the influence of the age by using appropriate statistical methods.

It is recommended to expand the publishing activity by presenting the original results of the research in national and international peer-reviewed publications.

It is important to note that the listed critical remarks do not reduce the scientific value of the PhD thesis, as well as the significance of the results obtained.

10. General assessment and conclusion

The dissertation contains clinically significant scientific, scientific-applied and applied results, some of which represent an original contribution to science and meet the requirements of the the Act on career development of the academic staff in the republic of Bulgaria and the Regulations for the development of the academic staff in Medical University – Varna. The dissertation presented for an opinion statement shows that the PhD student Dr. Radina Dimitrova has acquired in-depth theoretical knowledge and professional skills in the scientific specialty of endocrinology and has the qualities and skills for conducting an independent research.

In connection with the above, I give my positive assessment of the research and I propose to the esteemed scientific jury to award the educational and scientific degree "PhD" of Dr. Radina Stoyanova Dimitrova in a PhD program in Endocrinology.

Assoc. Prof. Dr. Boyan Nonchev, Ph.D.



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и ендокринология