TO

THE CHAIRPERSON OF THE SCIENTIFIC JURY,

APPOINTED BY ORDER No. RD-15-05-99/09.10.2023

OF THE EXECUTIVE DIRECTOR AND THE PROCURATOR

AT "ACIBADEM CITY CLINIC UMHAT TOKUDA"

# REVIEW


## By Prof. Dr. Kiril Karamfiloff Karamfiloff, PhD.

## Head of Cardiology Clinic at Aleksandrovska UMHAT,

## MU-Sofia


Concenrning dissertation thesis for obtaining the educational and scientific degree "**PhD**"
in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine, PhD program "Angiology".
**Author**: Dr. Polya Todorova Antova
**Form of doctoral studies**: Independent preparation
**Scientific unit**: Clinic of angiology,
**Topic**: "Peripheral arterial disease of the lower extremities in women - risk profile, clinical presentation, outcome of the disease"
**Research supervisor**: Prof. Dr. Milena Staneva Staneva, PhD.

**1. General presentation of the procedure and the PhD student**

When writing the dissertation, requirements for the procedure in terms of dissertationability, choice of topic, internal defense and selection of a Scientific Jury were observed.

Dr. Polya Todorova Antova has been enrolled in the PhD student program of independent preparation by order No. 140 of 26.03.2019 of the Executive Director and Procurator of "Acibadem City Clinic UMHAT Tokuda". She completed the individual plan and successfully passed the PhD student minimum exam. On 30.05.2023 the completed dissertation thesis was presented and successfully defended before an expanded Scientific Collegium of the Angiology Clinic, after which, at a meeting of the Scientific Council (Protocol 47/01.06.2023), it was dismissed with the right of defense.

By order No. 15-05-99/09.10.2023 of the Executive Director and Procurator of the hospital, I am appointed as an external member of the Scientific Jury in connection with the dissertation thesis of Dr. Polya Antova. I am determined to prepare and submit a Review. The PhD student's dissertation thesis, the accompanying abstract and a set of documents and materials related to the official defense fully meet the legal requirements of the above-mentioned regulatory framework.

No plagiarism was detected from the submitted reference Metadata StrikePlagiarism.com.

I declare that I have no conflict of interest with the author of the dissertation.

Dr. Polya Todorova Antova was born on June 9, 1986 in Vratsa. She graduated the Science and Mathematics High School "Acad. Ivan Tsenov" Vratsa in 2005. 2011 graduated in medicine at the Medical University, Sofia. Since 2012 until 2016 is a specialist in angiology at the Clinic of Cardiology and Angiology, then at the Clinic of Vascular Surgery and Angiology of the MHAT Tokuda Hospital Sofia. Dr. Antova acquired a specialty in "Angiology" in June 2016. in MU Sofia, and in the same year she also acquired a certificate in "Ultrasound Vascular Diagnostics" from MU Sofia. Since 2017, she has been working in the Angiology Clinic at "Acibadem City Clinic UMHAT Tokuda" EAD.

Annually attends and participates in national and international scientific forums.

She is a member of the Bulgarian Society of Angiology, the Bulgarian Association of Neurosonology and Cerebral Hemodynamics, the Bulgarian Association of Ultrasound in Medicine, the Scientific Council of "Acibadem City Clinic UMHAT Tokuda" from September 2021 to June 2023.

**2. Relevance of the topic**

The topic of the dissertation is well chosen and relevant. Peripheral arterial disease of the extremities is the third most common atherosclerotic cardiovascular disease (CVD) after ischemic heart disease (CHD) and cerebrovascular disease (CHD). However, globally, compared to other CVDs, PAD continues to be underdiagnosed, treated and prevented, resulting in over 1 million limb amputations per year, or an average amputation every 30 seconds. In this context, women are particularly vulnerable. Despite literature data of a similar or higher prevalence of PAD in women and men, clinical recognition is often delayed in women. The search for women-specific risk factors and the presence of a number of peculiarities in the course and outcome of PAD in them, makes the current dissertation thesis extremely relevant.

**3. Knowing the problem**

The PhD student knows the state of the problem and creatively evaluates the literary material.

**4. Research methodology**

The chosen research methodology allows achieving the set goal and obtaining an adequate answer to the tasks solved in the dissertation work.

**5. Characterization and evaluation of the dissertation work and contributions**

Dr. Antova's dissertation is written in a volume of 146 pages, illustrated with 22 figures and 48 tables. It is structured correctly and includes 8 sections:

Abbreviations and symbols used - 2 pages;

1. Introduction – 2 pages;
2. Literature review – 26 pages;
3. Aim and tasks – 1 page;
4. Material and methods – 7 pages;
5. Own results – 62 pages;
6. Discussion and Conclusion – 23 pages;
7. Conclusions and recommendations – 3;
8. Bibliography - 18 pages; The bibliographic reference contains 218 literary sources, of which 5 are in Cyrillic and 213 are in Latin.

In **the introduction**, the problem is well formulated and the purpose of the dissertation is justified.

**The literature review** is competently written and shows a good knowledge of the problem under consideration in its various aspects. The role of demographic and social characteristics, as well as risk factcrs for PAD in the studied population, is very well examined.

***The aim*** of the dissertation thesis is fcrmulated in accordance with the topic of the dissertation and the presented literature review. Dr. Antova sets the goal of her research work to determine the risk profile, features of the course and outcome in patients with peripheral arterial disease of the limbs, WITH A REVIEW determining the influence of female gender and develop ng a personalized algorithm for diagnosis, treatment and follow up in the female sex.

In order to fulfill the objectives, the following tasks are set:

1. To determine and compare the demographic and social characteristics of PAD in both sexes to determine the risk group depending on gender.
2. To determine and compare the gender dependence of the frequency of risk factors and comorbidities in patients with PAD
3. To determine and compare the gender dependence of the clinical stage of disease at its initial diagnosis and the degree of involvement of the arterial system of the limbs.
4. To follow up patients of both sexes within 1 year and to evaluate their condition after treatment.
5. To track the outcome of the disease and determine the frequency of subsequent vascular interventions in both sexes.
6. Based on the obtained results, determine the importance of female gender as a risk factor for PAD.
7. To develop and approve an algorithm for the prevention, diagnosis and follow-up of PAD in the female sex, with an emphasis on recommendations for secondary prevention

In the "**Materials and methods**" section, 200 patients with PAD - 100 women and 100 men over the age of 18, who were examined by an angiologist for the period 2017 - 2022, are described in detail. The subjects were aged from 38 to 92 years, average age 68 years ±10. For the period 2018 - 2020, the study is retrospective, based on an electronic database, then in the period - 2020-2022, the collection of patient follow-up

data continues prospectively. The methodology describes in detail the risk factors, methods of research, therapy and follow-up in patients with PAD, comparing the features of the course in men and women.

The statistical processing of the data used appropriate methods and specialized statistical package SPSS (Statistical Package for the Social Sciences) version 16.0, which guarantees the reliability of the obtained results.

***Results:*** The results obtained by Dr. Antova are well illustrated and correspond to the set objectives of the study.

**The discussion** of results analyzes the data obtained and compares, where possible, with other publications on the topic.

**Conclusions and contributions**: Based on the obtained results, Dr. Antova logically draws 8 conclusions that correspond to the tasks set.

1. Regarding the demographic and social characteristics of women with PAD, with statistical significance, we found that:

- Women with PAD are older than men with PAD, p=0.05, with more than half of women, - 52% - being over 70 years of age, while only 38% of men fall into this group. In both sexes, the relative share of patients in the age group >70 years is the highest.
- Women with PAD are more often widowed - 32%, compared to only 4% of men, p=0.001.
- Women with PAD less often live in a village - 12% compared to 21% of men, p=0.03.

2. Regarding the frequency of risk factors and accompanying diseases in women with PAD, statistically significant differences between the two sexes are found in terms of:

- Women with PAD less often have a history of the disease, and we recorded this in 52% of them compared to 72% of men, p=0.009.
- Women with PAD are less likely to be smokers - 33% of women are smokers compared to 66% of men, p=0.001.
- Women with PAD more often have accompanying arthropathy - 19% compared to 7% of men, p=0.019.
- Women with PAD more often have accompanying neuropathy - 55% compared to 40% of men, p=0.047.
- Women with PAD more often have some degree of accompanying carotid atherosclerosis - 63% women versus 40% men, p=0.001.

3. Regarding the medications taken:

- Women with PAD less often receive anticoagulant therapy - 37% versus 52% of men, p=0.046.
- Women with PAD more often take analgesics - 33% of women versus 5% of men, p=0.001.

4. Regarding the clinical stage of the disease at its initial diagnosis, the following data are statistically significant:

- Women with PAD are more often in a more advanced stage of the disease at its initial diagnosis - 48% of women versus 27% of men with stage III and IV of PAD, p=0.002.

• Women with PAD more often have ABI < 0.3 - 23% women versus 12% men, p=0.024.

• Women with PAD more often had no prior vascular interventions, - 53% women versus 34% men, p=0.016

5. According to the degree of involvement of the arterial system of the limbs, the following gender-related significant differences were found:

• Women with PAD more often have multiple arterial lesions - 73% versus 58% of men have hemodynamically significant involvement of more than one artery, p=0.037

• Women with PAD more often have vessel thrombosis - 78% versus 50% men, p=0.001

6. In women with PAD, it is more common to affect the popliteal artery and distal arteries:

• Popliteal artery stenosis is detected with a higher frequency in women with PAD >70% - 15% women, compared to 3% men, p=0.007.

• Thrombosis of the posterior tibial artery is more common in women with PAD - 34% women versus 14% men, p=0.006.

• More often, women with PAD have thrombosis of peroneal artery - 18% women versus 7% men, p=0.018.

7. Regarding follow-up treatment, it is established that:

• In women with PAD, surgical treatment was performed less frequently, - 26% women versus 42% men, p=0.025.

• Hybrid treatment was performed less often in women with PAD, - 8% of women versus 22% of men, p=0.009.

8. The following statistically significant differences between the two sexes have been established in the data related to the follow-up of patients after treatment has been started or carried out:

• Women with PAD are less often followed up at the 6th month after therapy, - 40% of women compared to 57% of men had an examination in this period.

• Women with PAD are less frequently followed up even at the 12th month after diagnosis of the disease and started therapy, - 36% women versus 69% men, p=0.023 and p=0.001.

• Women with PAD more often did not return for examination, 47% women vs. 30% men, p=0.020

Scientific development expresses thoroughness and consistency. The contributions are 6 original - 1 of a theoretical and 5 of an applied nature.

Scientific-theoretical contributions:

1. The scientific development thoroughly evaluates the influence of risk factors in the studied patients with PAD. With these qualities, the work is the first in its nature and volume in Bulgaria.

Scientific-applied contributions:

1. The developed algorithm for behavior in women with PAD, which is based on the material and conclusions of the study, is distinguished by high practical value

2. Particularly expressive are the unsolved problems, which are the main motive for continuing the clinical study and developing options for improving patient care after discharge.
3. Due to the significant number of patients who do not show up for follow-up examinations, an innovative strategy should be considered to actively survey women who have undergone endovascular/vascular-surgical therapy and remind them by telephone for active follow-up through regular follow-up examinations, with the aim of post-procedural prophylaxis and monitoring
4. Based on the accumulated data and experience, an algorithm was developed and tested, which could serve as a basis for building a national program for active rehabilitation of patients with PAD, after treatment, as well as a proposal for maintaining strict control of risk factors, in order to improve the quality of life.
5. The study group is substantial in volume and can serve for clinical observation and publication in an international journal.
Based on the obtained results, their analyzes and conclusions, recommendations for women with PAD are made in the dissertation. The most significant result of this research work is the derived recommendations, which are of high practical value and, reaching a larger number of both general practitioners and various specialists, could serve as the basis of a program of prevention, timely diagnosis, treatment and follow-up of women with PAD.

**6. The abstract** is written on 69 pages, meets the requirements and fully reflects the results presented in the dissertation work. In an overview and clear way, in a summarized form, it gives an idea of the overall design of the work, the methods, the results and the main conclusions.

**7. Assessment of the publications and personal contribution of the doctoral student**

The PhD student has submitted 2 publications in national journals and 2 scientific communications at national scientific forums, one of which has been published in a journal with IF. In 1 publication, Dr. Antova is first author and independent author in 1 publication and 2 communications. This scientific activity is sufficient to show that the doctoral student is consistent in his scientific activity and exceeds the national minimum requirements for the educational and scientific degree "PhD".

## CONCLUSION

The dissertation contains scientific-theoretical and scientific-applied results that represent an original contribution to science, expanding our knowledge in the field of multifocal atherosclerosis and angiology. It is written in a strictly scientific style. It meets all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of LDASRB and the Regulations of "Acibadem City Clinic UMHAT Tokuda". The presented materials and dissertation results fully correspond to the specific requirements adopted in connection with the Regulations of "Acibadem City Clinic UMHAT Tokuda" for the application of LDASRB.

Dr. Polya Todorova Antova is a specialist in angiology with 11 years of work experience. Actively participates in research work. The PhD student shows qualities and skills for independent conduct of scientific research.

**Due to the above, I give my positive assessment and strongly recommend to the members of the Scientific Jury to positively assess the dissertation thesis "Peripheral artery disease of the lower extremities in women - risk profile, clinical presentation and outcome of the disease" and award Dr. Polya Todorova Antova the scientific and educational degree "PhD" in the field of Higher Education 7. Health care and sports, professional direction 7.1. Medicine, PhD program "Angiology".**

05.11.2023
Sofia

Prepared the review:
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