

**To the Chairman of the Scientific Jury  
appointed by order of the Executive  
Director of NHH No 111/01.03.2023**

## **OPINION**

By prof. Borislav Georgiev Georgiev, MD, PhD,  
Head of the Cardiology Clinic at the National Heart Hospital  
Member of the scientific jury for awarding the scientific and educational degree "Philosophy Doctor",  
determined by an order of the Executive Director of National Heart Hospital  
№-111/01.03.2023

**Subject:** Thesis of Dr. Boyka Ilieva Stoyanova, PhD student of independent training in "vascular surgery"  
on the topic

*"Comparative analysis of treatment methods in chronic total occlusions of superficial femoral artery*

**Scientific tutor** - Prof. Mario Stankev, MD, PhD

For the competition, Dr. Boyka Ilieva Stoyanova has presented all the necessary documents - thesis, abstract, and additional documents are in accordance with the requirements of the regulation for acquisition educational and scientific degree "PhD" and rules of National Heart Hospital for its implementation.

I find no gaps in the documentation presented.

I declare that I have no conflict of interest with the candidate.

All presented materials are precisely arranged and described.

There is no evidence of plagiarism.

### **Importance of the topic**

Atherosclerosis is a multifocal process - a systemic disease with manifestations in multiple vascular pools and has a much worse prognosis when two or three vascular beds are affected compared to one affected vascular region. Chronic arterial occlusions of the lower extremities constitute the major proportion among the diseases included in the PAD group. The most common localization of stenotic-occlusive changes in the arteries of the lower extremities is the superficial femoral artery (*a. femoralis superficialis, AFS*).

From the moment of the first descriptions to the present day, the concepts of the etiopathogenesis of vascular pathology have been refined, the surgical techniques of treatment have been improved, and thanks to the rapid technological progress, new methods have been introduced – endovascular and hybrid interventions. One of the biggest challenges facing modern vascular medicine, however, may remain the systematization and optimization of the algorithms of behavior in different types of pathology, subject to good medical practice and supported by evidence.

The **topic** of the PhD thesis is contemporary and avant-garde, in the course of recruiting the group of patients, both the recommendations for treatment and the techniques of behavior are changed. In the course of collecting the material for the dissertation, the new modern techniques of treatment are built and the benefits and challenges are outlined.

## **Structure of the PhD thesis**

The PhD thesis of Dr. Boyka Stoyanova is formed on 233 pages according to the requirements and contains an introduction, a literary review, objectives and tasks, materials and methods, results, discussion, and health, contributions, conclusion, annexes and bibliography. The dissertation is illustrated with 111 tables and 55 figures.

**The literature** review, presented in 46 pages. From a historical analysis of the topic, through the clinic and diagnostics to possible conservative and surgical approaches and their complications, the review shows the author's very good awareness of the issues. On the basis of it, Dr. Boyka Stoyanova defines unresolved problems that trace the future development of vascular surgery.

The bibliography contains 276 cited articles, of which 5 in Cyrillic and 271 in English. The writing of the cited publications is not uniform, and when writing Bulgarian books or textbooks, some attributes of the writing are missing.

Dr. Boyka Stoyanova **aims** to conduct a comparative analysis of the methods of treatment in chronic total occlusions of *a. femoralis superficialis*.

To achieve this goal, the author sets himself the following **tasks**:

1. To determine the primary, primary assisted and secondary patency in each of the methods of treatment, both in the whole group and in the subgroups of patients with diabetes and CLTI
2. To establish the influence of risk factors on patency in the three methods of treatment
3. To establish the influence of the previously performed reconstructions (overstanding, the same and the adjacent segment) on the patency of the current reconstruction
4. To establish the influence of prior antiplatelet/anticoagulation therapy on the patency of reconstruction
5. To determine the MFA patient group among those with PAD
6. To build an algorithm for treatment in patients with AFS CTO

## **Methodical approach**

A retrospective analysis of patients with AFS CTO treated in the Vascular Surgery Clinic at the National Heart Hospital was conducted in the period May 2012 – April 2017 inclusive – for a total of 5 years. The analysis includes three groups of patients, divided according to the type of treatment: 1) patients who have undergone surgical treatment (open surgery) – 151; 2) patients undergoing endovascular treatment – 198; 3) patients who have undergone hybrid treatment (hybrid surgery) – 100 patients.

A careful review of the data impresses the uneven distribution of patients over calendar years in the specified five-year period.

Dr. Boyka Stoyanova clearly and accurately describes the treatment algorithms (surgical, endovascular and hybrid). The description of the presented techniques for surgical, endovascular and hybrid treatment can be used as a good methodological guide for clarifying the approaches in temporary vascular surgery. It defines the indications for the three healing approaches.

Statistical analysis includes various analyses that are consistent with the hypothesis and the goals set. The collected data were processed using SPSS 20.0 statistical package. Descriptive statistics, Kolmogorov-Smirnov test in one sample, Chi-square test, Nonparametric Wilcoxon test, Variance analysis (ANOVA test), Non-parametric Kruskal-Wallis test, Kaplan-Mayer analysis, Log Rank test were used.

## Results

Results are presented on 57 pages.

They are presented in groups according to the type of treatment performed.

The **discussion** of the results follows the results and is 81 pages away. It includes not only a good analysis of the data described in the results, but also a thorough knowledge of international publications and analyses, which makes it extremely valuable from a scientific point of view. The data from these three comparative analyses prove that over time, endovascular treatment is required as the first method of choice and mainly in the milder stages of PAD, and the operative – in the heavier ones. With regard to hybrid surgery, it is not the age and stage of the disease that determines but the comorbidity and characteristic of the affected arterial segments (concomitant, multilesions in the ilio-femoral, femoro-popliteal segment or combination of AFS CTOs with AFC stenosis).

I am very impressed by the knowledge of drug therapeutic prophylactic strategies, the role of statins and antithrombotic drugs.

After a careful assessment of the available information (provided mainly by meta-analyses comparing open and endovascular surgery), as well as the dissertation data, Dr. Boyka Stoyanova proposes an algorithm for treatment of AFS CTO and an algorithm for “one region” treatment in the femoral segment.

**Conclusions:** Dr. Boyka Stoyanova offers 9 conclusions according to the assigned tasks. They come from the conducted research.

**Task 1:** To determine the primary, primary assisted and secondary patency in each of the treatment methods, both in the whole group and in the subgroups of patients with diabetes and CLTI.

1. Endovascular and hybrid treatment are associated with better patency (primary, primary assisted and secondary) both in the overall group and in the subgroups of patients with diabetes and CLTI;
2. The greatest benefit from surgical treatment would be given to patients with a life expectancy of more than two years.

**Task 2:** To establish the influence of risk factors on patency in the three treatment methods

3. Among the known risk factors with the greatest severity were male sex and advanced age, female sex and young age, smoking, arterial hypertension, dyslipidemia. Diabetes mellitus and concomitant involvement of the other two vascular beds are reported as independent risk factors.
4. The administration of adequate antithrombosis and lipid-lowering therapy (statin) pre- and post-procedural leads to a significant reduction in cardiovascular risk and limb-related events (increase in claudication distance, reduction of patients reaching to CLTI as well as those requiring intervention, reduction of retrobolosis and frequency of reinterventions, reduction of amputations and mortality);

**Task 3:** To establish the influence of the previously performed reconstructions (overstanding, same and substandard segment) on the patency of the present reconstruction

5. In surgical treatment for AFS CTOs, only the previously performed reconstructions in the femoral segment are important, and in the hybrid – those in the superior aorto-iliac segment, and in both cases the patency is significantly better in the initial treatment.
6. In endovascular treatment for AFS CTO, the previously performed reconstructions in the aorto-iliac and femoral segments had no effect on patency.

**Task 4:** To establish the influence of prior antiplatelet/anticoagulant therapy on the patency of reconstruction

7. Prior antithrombotic therapy had no effect on patency in AFS surgical and endovascular treatment for CTO. In hybrid treatment, less patency was found with prior antiplatelet therapy.

**Task 5:** To determine the MFA patient group among those with PAD

**8.** In patients with AFS CTO, the concomitant MSD amounts to 45.2%, and it is most prevalent among those with hybrid treatment and mainly at the expense of asymptomatic carotid stenosis. Concomitant CHD is estimated at 20%, without significant difference in the different treatment groups. Simultaneous involvement of the three vascular pools was found in 11.14%.

**9.** Among patients receiving treatment for AFS CTO there was a lower incidence of CHD and simultaneous involvement of the three vascular pools compared to that of patients with carotid stenosis.

**Contributions:** The contributions are 9, divided into two groups - of an original (5) and of a confirmatory nature (4).

**Scientific-practical contributions:**

**1.** This is the first time in Bulgaria that such a large one-center clinical study comparing endovascular, operative and hibirid treatment in patients with AFS CTO is conducted;

**2.** For the first time, an AFS treatment algorithm for patients with CTOs is proposed that emphasizes treatment options after previously conducted reconstructions in the same femoral segment;

**3.** The endo first strategy with the administration of drug-coated devices is recommended, and open surgery should be maintained as a treatment option after a single-vascular, hybrid and surgical one;

**4.** It is always recommended to administer autovenous (usually ipsilateral GSV) before synthetic graft in bypass surgery. In the absence of a sufficient one, other alternatives should be considered venous grafts (contralateral GSV, SSV, veins by hand). If possible, anastomoses are constructed T-L;

**5.** If it is not possible to perform autovenous bypass, semi-closed endarterectomy and synthetic bypass are an acceptable alternative;

**Confirmatory contributions:**

**6.** It was confirmed that the construction of T-L anastomoses in bypass surgery in the femoro-popliteal segment leads to better patency and preservation of the limb;

**7.** The superiority of drug coated balloons against ordinary ones in terms of patency in endovascular treatment of AFS CTOs was confirmed;

**8.** It was found that the presence and number of implants did not affect patency in hiberide treatment of AFS CTO;

**9.** It was confirmed that endovascular treatment of AFS CTOs was associated with the highest percentage of limb storage, but at the expense of an increased frequency of reinterventions.

**Publications**

In connection with the dissertation, the author presents 3 full-text publications from among a large number of available publications in national and international journals, chapters of monorafias, etc. Dr. Boyka Stoyanova actively participates in many scientific forums, but for the needs of the competition she has presented 5 participations in national forums.

**The abstract** contains 166 pages and reflects what is written in the dissertation. It is durable according to the requirements.

### General remarks

I am very impressed by the in-depth knowledge of Dr. Boyka Stoyanova not only in the knowledge of surgical and invasive techniques, but also in the drug treatment of these patients. I could not make general remarks to such a well-established scientific work, but it would be good to unify the cited references.

### Recommendations to the PhD student:

To publish some of the results of the study in foreign scientific periodicals, possibly with an impact factor. To publish part of the dissertation in a Bulgarian journal aimed not only at vascular surgeons. Specifically from internal medicine need such knowledge.

According to the minimum requirements of NACID for awarding the NSA "Doctor" Dr. Boyka Stoyanova meets the requirements as follows:

Group of indicators	minimum number of points	Indicator	Points
But	50	1. Dissertation for awarding educational and scientific degree "Doctor"	50
	<i>"Comparative Analysis of Methods of Treatment in Chronic Total Occlusions of Artery Femoralis Superphysicalis"</i>		
Y	60/n or distributed in the ratio	7. Publications and reports published in scientific journals, referenced and indexed in world-famous databases of scientific information	27
	Kostova-Lefterova D., N. Nikolov, S. Stanev, <b>B. Stoyanova</b> , K. Genova. Study of the practice and dose of the patient in endovascular and hybrid revascularization of the lower extremities. <i>Radiology and Radiology</i> , 2019 LVIII; 32-36. ISSN: 0486-400X (print) – <b>12 pts.</b> Desislava D Kostova-Lefterova, PhD, Nadelin N Nikolov, MD, PhD, Stefan S Stanev, MD, <b>Boyka B Stoyanova</b> , MD. Patient doses in endovascular and hybrid revascularization of the lower extremities. <i>Br J Radiol</i> 2018; 91: 20180176. Published online 2018 Aug 12. doi: <a href="https://doi.org/10.1259/bjr.20180176">10.1259/bjr.20180176</a> – <b>15 pts.</b>		
	30/n or distributed in the ratio	8. Publications and reports published in non-refereed journals with scientific review or published in edited collective volumes	10
	Nikolov N., D. Lukanova, <b>B. Stoyanova</b> . Vascular surgical aspect of the diabetic foot. <i>Science Endocrinology</i> , 2017;4. ISSN/ISBN: 1313-0897 (print) – <b>10 pts.</b>		
Total:			<b>87.00</b>

**Conclusion:** I appreciate the PhD thesis of Dr. Boyka Ilieva Stoyanova on "*Comparative analysis of methods of treatment in chronic total occlusions of superficial femoral artery*" as scientifically interesting and important for clinical practice. I believe that this thesis meets the requirements for awarding the educational and scientific degree "Philosophy Doctor" enshrined in the Law on the Development of Academic Staff in the Republic of Bulgaria and the Rules for the Development of the Academic Staff of the National heart Hospital.

Based on the above merits of the PhD thesis of Dr. Boyka Stoyanova, I recommend to the members of the esteemed scientific jury to vote positively and to award to Dr. Boyka Ilieva Stoyanova the educational and scientific degree "Philosophy Doctor" in the scientific specialty "Vascular Surgery", professional field 7.1 Medicine, field of higher education 7 Health and sports.

10.05.2023

Prepared by:



(Prof. Borislav Georgiev, MD)