

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

REVIEW

By prof. Veselin Petrov Petrov, MD, PhD,
Head of Vascular surgery Department MHAT Heart and Brain, Burgas
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

Regarding: dissertation work on the topic "Comparative analysis of treatment methods in chronic total occlusions of the superficial femoral artery" for awarding the educational and scientific degree "Doctor" to Dr. Boyka Ilieva Stoyanova, vascular surgeon at the Clinic for Vascular Surgery of the MHAT NHH , PhD student of independent training in the scientific specialty "Vascular Surgery", professional direction 7.1 Medicine, field of higher education 7 Health care and sports.

Scientific tutor - Prof. Mario Stankev, MD, PhD

The review was prepared according to the Law on the Development of the Academic Staff , the Regulations for the Application of the LAD and the Regulations for the Terms and Conditions for Acquiring Scientific Degrees and Holding Academic Positions at MHAT NHH EAD.

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. All presented materials are precisely arranged and described. There is no evidence of plagiarism.

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

Importance of the topic

Cardiovascular diseases are the number one cause of death worldwide, with peripheral arterial disease (PAD) taking one of the leading places with over 200 million affected by the disease. The prevalence and incidence of PAD are age-dependent, which, combined with the aging population, suggests that PAD will become a major socially significant disease. The resulting high rate of morbidity, disability and mortality will lead to greater and greater social and medical-economic damage not only in Bulgaria, but throughout the world. Among the diseases included in the PAD group, chronic total occlusions of the lower extremities with their most common localization – the superficial femoral artery, a. femoralis superficialis /AFS/. The modern approach to PAD requires early detection of risk factors, timely diagnosis and adequate treatment. To date, we have a wide range of therapeutic approaches, but there is still the question of systematization and optimization of behavior algorithms that lead to the best results for the patient.

In the context of what has been said so far, I consider the topic of the dissertation to be extremely relevant for the vascular community, because it raises the question of the opposition of the two main methods of treatment - operative and endovascular, as well as the resulting hybrid surgery. The present work provides a new reading of the globally debated

topic of choosing the most appropriate treatment in patients with chronic total AFS occlusions.

Structure of the PhD thesis

The dissertation was developed in accordance with the standards for the preparation of scientific work for the acquisition of a scientific and educational degree "Doctor". It is laid out on 233 pages and includes the following parts:

- title page – 1 page.
- used abbreviations – 2 pages
- content – 1 page
- introduction – 1 page
- literary review – 46 pages.
- purpose and tasks - 1 page
- materials and methods - 2 pages.
- results – 57 pages
- discussion – 81 pages
- conclusions, contributions - 3 pages.
- conclusion – 1 page
- used literature – 24 pages.

The dissertation is illustrated with 111 tables and 55 figures. The literary reference includes 276 sources, of which 5 are in Cyrillic and 271 are in Latin.

The literature review is prepared on 46 standard pages. It is very well structured and comprehensively developed. The author presents in depth the etiology and pathogenesis of the disease, as well as the anatomical features of the examined arterial segment and the historical development of vascular medicine on the subject. The diagnosis, the possible therapeutic approaches and the resulting complications are described in detail. Special and unsolved problems awaiting future answers are clearly stated.

The aim of the dissertation work is clearly and precisely formulated: "To carry out a comparative analysis of treatment methods for chronic total occlusions of a. femoralis superficialis".

In accordance with the formulated goal, 6 specific **tasks** have been identified:

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
2. To determine the influence of risk factors on patency in the three treatment methods
3. To determine the influence of previously performed reconstructions (upcoming, same and following segment) on the patency of the current reconstruction
4. To determine the influence of previous antiplatelet/anticoagulant therapy on the patency of the reconstruction
5. To determine the group of patients with MFA among those with PAD
6. To build a treatment algorithm for patients with CTO of AFS

Research methodology

449 patients with chronic total occlusions of a. femoralis superficialis, treated in the Vascular Surgery Department at the National Heart Hospital in May 2012 - April 2017, for a total of 5 years. A retrospective analysis was carried out and the patients were divided into three groups according to the type of treatment:

- patients who underwent open surgical treatment – 151
- patients who underwent endovascular treatment – 198

- patients who underwent hybrid treatment – 100

When familiarizing with the scientific work, the punctual analysis of the various trends in the treatment of patients is impressive - outlining the trend for "endo first" and a gradual "ebb" from operative treatment. The author describes in detail the techniques for carrying out operative, endovascular and hybrid treatment, presenting his own modifications in order to facilitate the methods and achieve better results.

A detailed **statistical analysis** is presented, for which the data were processed with the statistical package SPSS 20.0. A wide range of statistical methods were used.

The results of the dissertation are described in detail on 57 standard pages. They are distributed according to the type of treatment performed. They are richly illustrated through figures and tables including the main characteristics of the studied contingent, the type of reconstructions carried out, patency of the reconstructions and observed complications.

The **discussion** of the results follows the results and is 81 pages away. A strong impression is made by the detailed knowledge of the available guidelines for the treatment of patients with PAB and in particular those with chronic occlusions in the femoro-popliteal segment. The doctoral student describes in detail the differences in the indications for treatment of these patients imposed over the years and caused by the rapid development of the technological process. The influence of the risk factors and the possible ways to influence them are presented in detail. The author describes in detail the role of statins and antithrombotic therapy in patients with PAD. As extremely valuable I consider the discussion of the different types of reconstructions in operative, endovascular and hybrid treatment. I think they would be useful for the development of young specialists in the field of vascular surgery and angiology.

The discussion of the obtained results was carried out according to several criteria - assessment of revascularization and subsequent complications, post-procedural drug therapy and patency of the reconstructions. I was particularly impressed by the differentiation of patency results, particularly in the subgroups of patients with CLTI and those with diabetes mellitus. The analysis of the influence of the previous reconstructions and the previous antithrombotic therapy on the patency of the reconstructions is of interest.

Conclusions 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 substanced 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.

After evaluating the information available in the literature, as well as the data from the own analysis, according to the set **task 6**, Dr. Boyka Stoyanova builds and proposes an algorithm for the treatment of patients with chronic total occlusions of a. femoralis superficialis, as well as one for endovascular treatment in a femoral segment. A special emphasis in the presented algorithm is the behavior of patients with previous vascular reconstructions, which I consider useful given their steadily increasing number.

The contributions are divided into two groups - scientific and practical and confirmatory:

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 monographs, 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

To continue the collection and processing of the database after the completion of the dissertation work. To publish the resulting analysis data, which would be valuable for the development of future guidelines.

In conclusion, the dissertation work developed by Dr. Boyka Ilieva Stoyanova on the topic "Comparative analysis of treatment methods in chronic total occlusions of the superficial femoral artery" contains scientific results that represent an original contribution to science and meet the requirements for awarding educational and scientific degree "Doctor".

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. Veselin Petrov, MD, PhD)

