

# **OPINION**

for dissertation work

## **COMPARATIVE ANALYSIS OF TREATMENT METHODS FOR CHRONIC TOTAL OCCLUSIONS OF THE SUPERFICIAL FEMORAL ARTERY**

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Pursuant to Art. 9 and Art. 10 of ZRASRB, NJ, and the decision of the 1st meeting of the scientific jury, appointed by Order No. 111/01.03.2023 of the executive director of National Cardiology Hospital, Sofia, I was presented for opinion the dissertation work and abstract of Dr. Boyka Ilieva Stoyanova, a vascular surgeon at the Clinic for Vascular Surgery and Angiology at National Cardiology Hospital, Sofia.

The presented set of materials on paper and electronic media is in accordance with Articles 10 and 11 of the Law on the Development of the Academic Staff in the Republic of Bulgaria, Art. 32 of the PPZRASRB for the acquisition of the educational and scientific degree "Doctor" and includes all the necessary documents, formatted according to the requirements.

Vascular surgery has undergone enormous development over the years, and simultaneously with the optimization of the available operative techniques, new ones are also implemented (endovascular surgery), the material and technical base is improved and a number of innovations are introduced, which makes it possible to offer the three types of treatment. In recent decades, remarkable advances in technology have led to the increasingly widespread use of endovascular treatment in chronic total occlusions of AFS. The mini-invasiveness of the technique, its safety in high-risk patients, the relatively shorter hospital stay, and the effectiveness in terms of patency and preservation of the limb led to a gradual and progressive "moving away" from open surgery and the imposition of the strategy of "endovascular first" treatment. Although the vascular surgical community has

been searching for years for the “best” treatment for patients with infrainguinal peripheral arterial disease, there is currently no current large randomized clinical trial that compares the results of the three treatment methods – endovascular, operative, and hybrid. This once again proves the need to conduct a large randomized clinical trial comparing open and endovascular, and now hybrid surgery as a treatment method for peripheral arterial disease. So far, no scientific studies have been published on this problem in our country.

All this makes **the subject** of Dr. Boyka Ilieva Stoyanova's dissertation work: "Comparative analysis of treatment methods in chronic total occlusions of the femoral superficial artery", particularly relevant, useful, and very successfully chosen.

In her **introduction**, Dr. B. Stoyanova summarizes the scientific scope of the dissertation and emphasizes that one of the biggest challenges facing modern vascular medicine perhaps remains the systematization and optimization of behavior algorithms for different types of pathology, subject to good medical practice and supported by evidence. In her literature review, the dissertation student presents the scientific achievements on the topic of the dissertation work in the context of the goals and tasks set in the work.

Dr. B. Stoyanova's **overview** is comprehensive, with in-depth knowledge of the complex matter that is the basis of the dissertation. The dissertation presents the significance, frequency, and prevalence of peripheral arterial disease. It examines in detail the etiopathogenesis, clinical picture, diagnosis, and indications for conservative and operative treatment of chronic occlusions of AFS, which is the most common manifestation of peripheral arterial disease of the lower extremities. Dr. B. Stoyanova demonstrates extensive knowledge of conservative, operative, and endovascular treatment, as well as hybrid techniques applied in this field. It also discusses the complications of operative, endovascular, and hybrid treatment, all based on comprehensive information from published sources in the field. What is particularly valuable about Dr. B. Stoyanova's literature review is that it points out disagreements, raises questions that do not have a clear answer, and requires further research. It serves as a justification for the value of the dissertation and, more precisely, what are the expectations for its scientific and scientific-practical contribution.

**The aim** of the dissertation is precisely and briefly formulated, deducible from the literature review - "To conduct a comparative analysis of the treatment methods for chronic total occlusions of AFS". The eight tasks set by Dr. B. Stoyanova are subordinate to the goal. These are also the directions of research that have been analyzed in the process of the study.

A retrospective **analysis** of patients with chronic total occlusions of AFS, treated in the Clinic for Vascular Surgery at the National Cardiology Hospital, Sofia in the period from May 2012 to April 2017 inclusive, for a total of 5 years, was conducted.

Three groups of patients were included in the analysis, divided according to the type of treatment performed, as follows: patients who underwent surgical treatment - 151 patients, patients who underwent endovascular treatment - 198 patients, and patients who underwent hybrid treatment - 100 patients. Dr. B. Stoyanova describes each method precisely, in detail, with its main points, successive stages, and critical moments. To solve the set tasks, the doctoral student uses the following statistical methods: descriptive statistics, quantitative variables, categorical variables, Kolmogorov-Smirnov test, chi-square test, non-parametric Wilcoxon test, analysis of variance, non-parametric Kruskal-Wallis test, Kaplan analysis Mayer, Log Rank test.

**The results** obtained by Dr. B. Stoyanova are comprehensively and correctly described and are sufficient to fulfill the tasks set by the doctoral student.

In the study conducted by the doctoral student, the overall technical success in the three types of reconstructions amounted to 96.4%, and no statistically significant difference was found between the individual methods. The benefit of the performed revascularization is evaluated by the change in the ABI index, i.e. comparing baseline to post-procedure values. From the above results, it is clearly seen that all three revascularization techniques in chronic total occlusions of AFS provide an indisputable benefit to patients. The greatest benefit was reported for patients who underwent hybrid treatment for chronic total occlusions of AFS. The data obtained from this study show that, although with comparable post-procedural results and absolute benefit to the patient, the three techniques provide different durability of the reconstructions over time (at 5-year follow-up). Revascularization with the aim of maintaining primary assisted patency is most prevalent among endovascular treatment - 11.68%, followed by hybrid treatment - 7.14% and least common in surgical treatment - only 2.70%. The results obtained regarding the preservation of the limb (at 5-year follow-up) in the three treatment methods performed show comparable results in the first month – 96.69% in the operative, 97.98% in the endovascular, and 96.00% in the hybrid treatment.

This shows a comparable technical success rate of the described methods for the treatment of chronic total occlusions of AFS.

In **the discussion** of the results obtained in the study by the doctoral student, a critical analysis of her own results was made in the context of the literature data. On the other hand, the performed analysis reports the highest values of primary patency (both in the overall group and among patients with chronic limb-

threatening ischemia and diabetes) after endovascular treatment. Therefore, according to the doctoral student, all initial patients should be referred for endovascular treatment, regardless of the length of the occlusion ( $>$  or  $<$  25 cm) and its type (calcinosis), and not least, considering its minimally invasive nature and the lowest possible periprocedural risk. Upon careful preprocedural evaluation, a portion of these patients present with concomitant AFC/APF stenosis and should be referred for hybrid surgery.

Patients with previous endovascular treatment are divided according to the characteristics of the procedure performed – with POBA / DCB angioplasty or a stented segment up to 20 cm in length, as well as those with a stented segment  $\geq$  20 cm. The first group of patients should be re-referred for endovascular surgery. The second group of patients (stented area  $\geq$  20 cm) would benefit more from operative treatment, as it is considered to be technically challenging and would require a long scopic time and insertion of a large number of implants in case of endovascular intervention.

A similar stratification was applied to patients with a previous hybrid procedure - those with POBA / DCB angioplasty or a stented segment up to 20 cm in length, as well as those with a stented segment  $\geq$  20 cm. Again, the first group was referred for endovascular and the second for operative treatment. After previous surgical treatment, patients with bypass surgery should be referred again for open surgery (great technical difficulty for endovascular treatment, often available AFS ligatures), and those with semi-closed endarterectomy for endovascular treatment (due to the high rate of restenosis and subsequent short segment occlusions). Those with prior bypass surgery who are, however, assessed as high risk may be referred for endovascular therapy as an acceptable alternative to open surgery in patients with limited operative options.

As for the operative treatment, the doctoral student promotes the construction of a bypass with the use of an autogenous graft above all. The use of a synthetic graft leads to acceptable results, but in the opinion of the author, it should be applied only in the absence of a sufficient autogenous one. In individual cases, biological grafts should also be considered.

Endovascular treatment varies according to the capabilities of the operator and the material provision (available consumables) in the clinic, and unfortunately, the high price and the lack of reimbursement of the more specific devices remain major drawbacks.

**The conclusion** is well stated. It corresponds to the results obtained from the clinical trial and to their discussion in the previous chapter.

**The implication** is adequate, with a specific focus, without crossing the threshold of competence achieved by the conducted clinical research.

The dissertation student **points** out five contributions of a scientific-practical nature and four contributions of a confirmatory nature

**The bibliography** includes 276 well-selected articles and authors, arranged by their place of appearance in the text. A weaker Bulgarian participation is reported (only 5 citations), and of the remaining 271 in Latin, most were issued in the last 5-10 years.

The dissertation work of Dr. B. Stoyanova is well-arranged and illustrated, it is very easy to read. It is stylish and has few spelling mistakes.

In accordance with the requirements, Dr. B. Stoyanova has presented three publications in connection with the dissertation work and five participations in scientific forums on the subject.

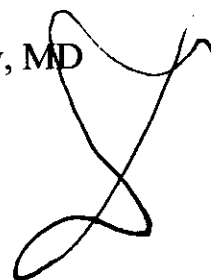
Dr. B. Stoyanova is a specialist in vascular surgery. Her clinical activity includes routine and advanced methods in the operative and endovascular treatment of vascular pathology. She possesses enviable awareness and oratorical skills, which define her as a fully formed professional with a scientific focus.

The dissertation work of Dr. B. Stoyanova is a quality product of a motivated doctor possessing a serious knowledge capacity. It presents in full a difficult, interesting, therapeutic problem with many still unsolved questions - treatment of chronic total occlusions of the superficial femoral artery.

The dissertation has certain contributions of theoretical, scientific, and scientific-practical importance. It includes a high level of practical knowledge of the problem, a perfectly performed research activity, and a professional analysis of the obtained results, which predetermines the routine use of the treatment algorithm proposed by the doctoral student in chronic total occlusions of AFS.

After getting acquainted in detail with the dissertation work of Dr. Boyka Ilieva Stoyanova, I believe that the work is dissertational, and innovative and will benefit vascular surgeons from the country in their daily work. The author has indisputable qualities, proven in her successful vascular-surgical practice in a leading medical institution, which is why I allow myself to recommend to the respected members of the scientific jury to vote positively and award Dr. Boyka Ilieva Stoyanova the educational and scientific degree "Doctor".

Prof. I. Lozev, MD



Sofia,

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