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To Chairman of Scientific Jury,  
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Executive Director of the NCH  
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## OPINION

by **Prof. Dr. Detelina Valchkova Lukanova, MD, PHD**

Head of the Department of Angiology at the NCH Medical Center

Chairman of the scientific jury for the competition for the acquisition of the educational and scientific degree "Doctor" in the field of higher education 7. "Health and sport", professional direction 7.1. "Medicine" and scientific specialty "Cardiovascular surgery" with code 03.01.49

on the submitted dissertation thesis and abstract on the topic:  
"Surgical methods of treatment in iliac occlusive disease-comparative analysis"

Author of the dissertation: Dr. Bistra Petrova Boneva, resident doctor at the Clinic for Vascular Surgery at the "National Cardiology Hospital", Sofia

Research supervisor: Professor Dr. Mario Draganov Stankev, MD, PHD

Cardiovascular diseases /CVD/ represent a group of diseases (coronary, cerebrovascular and peripheral arterial disease) that share common risk factors and lead to the development of atherosclerosis, and very often the process is multifocal with simultaneous involvement of all three vascular beds. CVDs represent a serious public problem, occupying the leading positions in statistics as a cause of mortality in the world.

Currently, more than 200 million people worldwide suffer from peripheral arterial disease (PAD). The prevalence of PAB is directly related to age, increasing by over 10% among patients in the sixth and seventh decades. The aging of the population and the continuous increase in the burden of risk factors inevitably lead to an increase in the number of patients with PAD and its recognition as a serious socially significant disease, which is associated with high morbidity, disability, mortality, and medico-economic costs. Iliac occlusive disease is a significant part of PAD of the lower extremities. No distal revascularization can be successfully implemented without adequate behavior to the aorto-iliofemoral segment providing blood inflow to the lower limb.

The therapeutic approach in patients with occlusive lesions in the iliac segment includes two main aspects. The first aims to reduce the overall cardiovascular risk given the multifocal nature of

atherosclerosis. The best medical therapy aims to influence known risk factors (arterial hypertension, dyslipidemia, diabetes mellitus) in combination with healthy lifestyle guidelines, smoking cessation, body weight reduction and daily physical activity. The second aspect concerns symptoms directly related to PAD (controlled exercise programs, vasodilators, endovascular, open or hybrid revascularization treatment).

Over the last decade, data from numerous studies and meta-analyses have been published, as well as practice guidelines endorsed by vascular surgical societies worldwide. They all discuss the effectiveness and safety of the different methods of revascularization – open, endovascular and hybrid. Vascular medicine has undergone significant changes and developments over the years, introducing new treatment techniques. Despite this progress, there are challenges in the systematization and optimization of management algorithms for the different localizations of vascular pathology.

Open surgery is still defined as the "gold standard" in treatment of occlusive lesions in the aorto-iliac segment. Its development in the 20th century was conditioned by optimization of instrumentation and suture materials, development of synthetic prostheses, refinement of vascular anastomoses, introduction of heparin and angiography as an imaging modality. Subsequently, the operative technique itself did not change significantly, but improvements were introduced with the aim of greater patency of the reconstructions and fewer peri- and postoperative complications. Operative treatment for lesions limited only to iliac arteries includes - aortofemoral, iliofemoral bypass and extra-anatomical bypass operations (femoral-femoral crossover bypass, axillo-femoral bypass). Factors such as operative access, choice of graft material and construction of the anastomoses are important when performing them.

Endovascular treatment for PAD, especially for lesions in large iliac arteries, is one of the fastest growing areas of modern medicine. There are several factors that align with it – minimally invasive, continuous improvement of devices, growing experience of operators. The expectation of the vascular surgical community is that in the near future, about 80% of all vascular interventions will be endovascular. The methodology used to treat chronic occlusions involving the iliac segment includes the following stages – selection of a site for percutaneous access, recanalization, vessel preparation (predilatation) and definitive treatment with or without stent/stent-graft placing to ensure that the vessel remains patent and provides orthograde blood flow to the tissues of the lower limb.

Hybrid surgery is a combination of open surgery and endovascular procedure, which is considered to combine the best of two approaches discussed so far. It has some significant advantages. The open access of the common femoral artery allows for one-stage treatment of the femoro-popliteal and iliac segments. Another advantage is access to the AFC and APF and the ability to surgically correct atherosclerotic changes in them, which aims to provide a sufficient outlet at least to the deep femoral artery. Hybrid surgery is particularly suitable for the so-called occlusive lesions with an inappropriate cap or occlusions without a "hammer" in which the probability of falling into the subintimal plane and even perforating the iliac artery is very high. Another advantage is the possibility of remote endarterectomy of long occlusions affecting both the common and external iliac arteries and thus drastically reducing the number of implants endovascular, as well as the absence of a large synthetic material such as the Dacron graft. Particularly suitable for hybrid

procedures are patients with subacute occlusions of the iliac segment, where thrombectomy and stenting are required.

All three treatment approaches have possible complications that must be managed appropriately.

Despite the enormous technological advances and the vast array of tools available to vascular surgery, it still faces many unsolved problems. Some of them are related to improving and popularizing the available techniques for the surgical treatment of chronic total occlusions in the aorto-ilio-femoral segment, while others focus on the search for new ones that would lead to better immediate and long-term outcomes for the patient's well-being.

The dissertation is presented on 206 printed pages and illustrated with 48 tables and 58 figures. The bibliography includes 286 literary sources, 8 in Cyrillic and 278 in English.

The content of the dissertation includes Introduction - 1 p., Literature review - 38 p., Aim and Tasks of the study - 1 p., Material - 5 p., Methods - 12 p., Results - 61 p., Discussion - 50 p., Limitations of the Study - 1 p., Conclusions - 2 p., Author Contributions - 1 p., Conclusion - 1 p., and Bibliography - 21 p.

The first pages of the literature review are dedicated to epidemiology, etiopathogenesis, and clinical manifestations of PAD. Further, focus is moved in detail on methods of treatment - conservative and invasive. Indications, contraindications, advantages, disadvantages, and complications of revascularization methods (open surgery, endovascular procedures, and hybrid surgery) are discussed. Special problems like patients with claudication and those with chronic limb-threatening ischemia are described. At the end of the review, the unsolved problems in the treatment of atherosclerotic lesions in the lower limb are summarized.

A great challenge remains the systematization and optimization of management algorithms for patients with chronic total occlusions in the iliac segment. The latter must be subjected to the well-established rules of good medical practice and supported by scientific evidence. That is why the topic of the thesis is extremely relevant. In Bulgarian literature, there are still no studies comparing the effectiveness - early and long-term, and the complications of the different methods of surgical treatment of this type of vascular pathology.

The aim of the thesis is well stated: to develop a treatment algorithm for patients with iliofemoral occlusive disease, considering risk factors, patient comorbidity, multifocal involvement of other vascular beds and the presence of previous reconstructions in the same segment.

The five tasks set correspond to the formulated goals above. Most important and with the greatest application in clinical practice are the second, third and fourth tasks: To study the interaction of the severity and stage of the disease in relation to choose operative approach and the patency of the reconstructions; To assess success, primary patency, and complications in patients undergoing the three types of reconstructions. To identify the alternative application of those three treatment methods and to determine the influence of risk factors on the patency of the reconstructions.

The materials and research methods used by the author are precisely described in detailed protocols for each type of revascularization strategy with the corresponding stages, accesses, and devices. Complications and their management are also described. Statistical processing methods are fully adequate to achieve set goals and tasks of the thesis. The obtained results are presented comparatively for the three methods, which facilitates the understanding of each studied parameter

in the context of the three considered revascularization strategies, despite the large volume of data presented. The latter are well illustrated in tables and diagrams.

In the discussion, the author was able to synthesize the results of the analyzes by critically comparing them with the recommendations of modern guidelines for the treatment of PAD, emphasizing the retrospective nature of the study and the time interval in which it was conducted (2009-2018). In the established sequence, the own results were compared with those of other authors presented in the literature review. It is impressive to discuss modern studies published in the last few years. It is emphasized that the basis of the good results achieved for the patients are, in addition to the specialists' team and the correct selection of patients, suitable for each type of the considered revascularization treatment, as well as the experience and qualifications of the operator.

The author defends his position that despite the presence of multiple terms used to evaluate the effect of revascularization, the patency of the reconstruction remains one of the important indicators for monitoring the outcome and comparing the individual revascularization strategies to build a therapeutic algorithm.

In primary patency, a smooth decline was observed for all three treatment methods in the 12 months period, with endovascular treatment being the best. Primary assisted patency was observed constant until the end of the first year in endovascular and hybrid treatment, where the latter proved to be better compared to open surgical treatment. Within one year of follow-up, primary assisted ambulation showed different trends. It is followed as a steeper increase with endovascular treatment within the third month, followed by a period of attenuation of the need for patency-assisted reintervention until the end of the first year. The next peak in the diagnosis of restenosis and the initiation of preventive treatment was observed after the 12th month. With the hybrid treatment, the frequency of diagnosed restenosis and the treatment performed for them increases relatively constantly. In open-label treatment, the peak incidence of these events is within the first year, preceded by a gradual increase.

In patients with iliac occlusions, the concomitant Cerebrovascular disease was 31.9%, and it was most common among those with hybrid treatment. Concomitant CAD was 16.2% without a significant difference in the endovascular and open groups and with about a 30% preponderance of the hybrid methodology. Simultaneous involvement of all three vascular beds was found in 1.2%.

The proposed therapeutic algorithm for operative, endovascular or hybrid treatment of occlusions in the iliac segment in primary patients and in those already intervened, presented at the end of the dissertation, is extremely valuable. It summarizes the results of the author's extensive research, as well as the recommendations contained in modern guidelines. Emphasis is placed on the group of patients with repeated revascularization, because there is no established consensus. The decision for those cases is individual and depends on many factors.

In the conclusion section, the author has shown the practical value of the conducted research. The most important of these are: The three revascularization methods show comparable rates of technical success, primary patency, and limb salvage, demonstrating their alternation with respect to these primary endpoints.; The severity of PAD, stage and clinical presentation have a statistically significant influence on the choice of revascularization approach. Endovascular

treatment is most advocated in patients with claudication, while cases with CLTI are predominantly treated with more aggressive revascularization strategies. The preoperative analysis should be strictly customized depending on the individual characteristics of the patient and the specifics of the clinical case. As in high-risk patients, endovascular and hybrid treatment are preferred. The latter is associated with better primary patency and a lower complication rate compared to open surgical treatment, at the cost of a more frequent need for reintervention to maintain patency. In high-risk patients, hybrid treatments are the preferred revascularization strategy.

The author's listed five own contributions with scientific-practical nature. Those are important with their applicability in daily clinical practice to improve the outcome of surgical revascularization in patients with occlusive lesions in the iliac segment.

As a weakness of the thesis, I agree with the author's opinion about the limitations of the study she stated. Its retrospective nature results in loss of follow-up of many patients, which distorts the curves of primary assisted and secondary patency in the whole group and subgroups with diabetes and CLTI.

Dr. Boneva meets the minimum national requirements under Article. 1, paragraph. 4 of the pertinent regulations, the rules for its implementation and the Rules for the conditions and procedures for acquiring scientific degrees and occupying academic positions at MBAL "National Cardiology Hospital" to the scientific activity of candidates for the acquisition of the educational and scientific degree "doctor" as with a required minimum of 80 points she collects 82 points.

In conclusion, I believe that the presented dissertation shows that the doctoral student Dr. Bistra Petrova Boneva possesses theoretical knowledge and professional skills in the scientific specialty Cardiovascular Surgery, demonstrating qualities and skills for independent conduct of scientific research.

Due to the above, I confidently give my positive assessment of the conducted research, presented by the above-reviewed dissertation work and abstract, and I propose to the honorable scientific jury to award the educational and scientific degree "doctor" to Bistra Petrova Boneva.

5.03.2024 г.  
Sofia

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/Professor Detelina Lukanova, MD, PHD/

