OPINION

on a dissertation thesis

Surgical Methods of Treatment for Iliac Occlusive Disease - A Comparative Analysis

by

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from

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In accordance with Article 10 of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), Scientific Jury, and the decision from the first meeting of the scientific jury appointed by order No. 70 dated 19.02.2024, by the Executive Director of National Cardiology Hospital, I was presented for opinion on dissertation thesis and abstract by Bistra Petrova Boneva, a vascular surgeon at the Clinic for Vascular Surgery at National Cardiology Hospital.

The set of materials presented on electronic media complies with Articles 10 and 11 of the Law on the Development of the Academic Staff in the Republic of Bulgaria and Article 32 of the Regulations for Implementation of LDASRB for acquiring the educational and scientific degree "Doctor". It includes all necessary documents, formatted according to the requirements.

In the context of the aging population and the increasing burden of risk factors, peripheral arterial disease (PAD) is becoming an increasingly significant social health issue, associated with substantial morbidity, disability, and significant healthcare and economic costs.

Despite the significant opportunities for treatment provided by endovascular techniques, the combination of an aging population and risk factors dictates the need for innovative and multimodal approaches. The development of vascular surgery, with a focus on endovascular techniques, reflects the current trends in the treatment of PAD. Despite efforts to promote a primary endovascular strategy, challenges arise when endovascular

intervention does not achieve the desired results. In such cases, open surgery, despite being "partially abandoned," continues to be applicable, especially for patients requiring an intensive and individualized approach.
The hybrid approach represents a promising solution that combines the advantages of both endovascular and open surgery. It may well be seen as the future of vascular surgery, offering a compromise between minimally invasive methods and traditional surgical intervention. With this approach, vascular specialists can choose the most appropriate strategy for each specific case, enriching the possibilities for successful treatment.

All three revascularization strategies – endovascular, surgical, and hybrid – should be considered as complementary elements in the vascular surgeon's arsenal. This approach is crucial, aiming to provide optimal and personalized treatment for patients with chronic ischemia of the lower limbs.

To date, no scientific studies have been published in our country comparing endovascular, surgical, and hybrid treatments in patients with occlusive disease in the iliac segment.
All this makes the topic of Dr. Bistra Petrova Boneva's dissertation, "Surgical Methods of Treatment for Iliac Occlusive Disease - A Comparative Analysis," timely, useful, and aptly chosen.

In her introduction, Dr. B. Boneva concisely defines the scientific scope of the dissertation and emphasizes its primary objective to present a comparative analysis of the revascularization treatment methods for iliac occlusive disease, examining the effectiveness and advantages of different approaches in modern vascular surgery.

In her literature review, the doctoral candidate presents scientific achievements related to the dissertation topic within the framework of the goals and tasks set in the scientific work. Dr. B. Boneva's review is comprehensive, showing an in-depth understanding of the complex subject matter at the core of the dissertation. She presents the significance, frequency, and prevalence of peripheral arterial disease. In detail, she examines the etiopathogenesis, clinical presentation, diagnostics, indications for conservative and surgical treatment of occlusive lesions in the infrarenal aorta and iliac arteries. Dr. B. Boneva demonstrates extensive knowledge regarding conservative, surgical, and endovascular treatment, as well as the hybrid techniques applied in this field. She also discusses the complications associated with surgical, endovascular, and hybrid treatments, all based on exhaustive information from published sources in this area. Particularly valuable in Dr. B. Boneva's literature review is the highlighting of disagreements, raising questions that do not have unequivocal answers and require

further studies. It serves as a justification for the dissertation's value and precisely what the expectations are for its scientific and practical contributions.
The aim of the dissertation is precisely and concisely formulated, deducible from the literature review conducted: "To develop a treatment algorithm for patients with iliofemoral occlusive disease, taking into account the risk factors, patient comorbidity, multifocal involvement of other vascular beds, and the presence of previous reconstructions in the same segment." The five tasks set by Dr. B. Boneva are aligned with this goal, guiding the research directions analyzed during the study.

A single-center retrospective analysis of patients admitted and treated for iliac occlusive disease at the vascular surgery clinic of NCH was conducted. The study period covers a 10-years period from January 2009 to December 2018. From the clinic's surgical logs, 521 patients who underwent 580 surgical interventions were selected. These interventions are distributed according to the applied treatment method as follows: endovascular recanalization and stenting of the iliac artery, or in short, endovascular treatment (EVT) – 182 (31.38%), hybrid surgical treatment (HST) – 183 (31.55%), and classical open surgical treatment (OST) – 215 (37.07%) in the aortoiliac segment.
To solve the tasks set, the doctoral candidate utilized the following statistical methods: Descriptive statistics; $\chi 2$-analysis (CHI-square test); Analysis of variance (ANOVA); Kaplan-Meier survival analysis; Log Rank test; Wilcoxon Signed Ranks Test. The results obtained by Dr. B. Boneva are thoroughly and correctly described and are sufficient to accomplish the tasks set by the doctoral candidate.

In studying the average patency of the reconstruction in days, she notes that for EVT, it is 276.12±356 days, for hybrid operations it is 262.43±360 days, and for OST, the average patency of the reconstruction is the highest, amounting to 471.74±71 days. Analyzing the patients who experienced early rethrombosis, related to the applied revascularization method, respectively, 6 cases with a relative share of 13.6% are observed in surgical treatment, one case with a relative share of 2.3% in endovascular, and two cases – 4.6% in hybrid treatment. The frequency of late thrombosis over the follow-up period is highest in open surgical treatment (30 cases, with a relative share of 68.1% of all thrombotic complications), followed by hybrid treatment (4 cases, 9.1% of all rethrombosis) and lowest in endovascular treatment (one case, 2.3%). Infectious complications are one of the most severe challenges after surgical treatment in vascular medicine. Regarding endovascular procedures, infections are rather casuistic. In the studied group, cases subjected to revascularization for IOD found 25 cases of infection at the surgical access site – 19 in the OST subgroup and 6 in the HST group.

Lower limb amputation, subjected to revascularization, is a primary endpoint in many studies. In the analysis conducted, rethrombosis of the index reconstruction led to limb

loss in eight cases, constituting 36.3% of all cases of major amputation, of which seven are in the surgical treatment subgroup with a relative share of 31.8%, one in the endovascular subgroup with a relative share of 4.5%, and none in the hybrid. 2/3 of the cases of lower limb amputation occurred with a patent iliofemoral reconstruction, but against the backdrop of infrainguinal vessel involvement by PAD. Three patients in the endovascular subgroup with a relative share of 13.6%, 6 cases with a relative share of 27.2% in the hybrid subgroup, and 5 cases (22.7%) in those subjected to open surgical treatment.

In the subgroup of patients with critical limb threatening ischemia (CLTI), the doctoral candidate notes that there is no difference in the patency rates of endovascular and hybrid reconstructions over time, and it remains relatively high with a preference for endovascular treatment. However, for patients with CLTI undergoing open surgery, a statistically significant difference and a higher risk of earlier loss of patency of the reconstruction are observed.

In the discussion of the study results, the doctoral candidate conducts a critical analysis of her own findings in the context of the literature. Dr. B. Boneva notes that in the modern medical world, the influence of industry and the evolution of technologies are factors that cannot be halted. They inevitably transform the processes of diagnosing a disease and change therapeutic strategies. Vascular surgery is no exception in this technologically advancing world. The material and technical base is being improved, image guidance and endovascular manipulation of distal lesions are introduced. Besides optimizing classic surgical techniques, new endovascular ones are being implemented, and combinations of both methods are emerging, offering significant advantages. This evolutionary process shifts the traditional practice of open surgeries and introduces endovascular procedures as the first choice of treatment strategy. Technological innovations allow surgeons to perform precise interventions using minimally invasive methods, which reduce surgical trauma and recovery time for patients, thereby shortening their hospital stay. However, vascular surgeons face the challenge of mastering technically all these different surgical techniques by presumption and choosing a specific treatment method for the particular medical case.

In the modern medical community, it is unthinkable to circumvent the rules of good medical practice or to ignore the guidelines. These are continuously updated based on randomized and controlled studies, aiming to practice evidence-based medicine.

This retrospective study aims to contribute to a better understanding of the multifactorial disease process and the choice of an alternative surgical approach. According to the doctoral candidate, the leading consideration in treating PAD should be the patient's

overall condition and the stage of their disease. The choice of treatment strategy varies depending on whether the patient is a claudicant, a patient with CLTI, or a patient with ongoing loss of tissue from the distal part of the limb.
The doctoral candidate concludes that most models of aorto-iliac disease can be successfully treated with endovascular approaches and the implantation of appropriate stents. Open surgery is often reserved for long-segment occlusions in the iliac segment or after the failure of a previous endovascular procedure. The choice of an open surgical procedure to ensure sufficient orthograde blood flow should be based on a combination of factors such as the potential risk to the patient, the anatomical pattern of the disease, and other clinical factors. Anatomical bypass (e.g., aortofemoral/iliofemoral bypass) is always preferred over any extra-anatomical reconstruction. In patients with CLTI and concomitant iliac and femoral-popliteal segment involvement, iliac reconstruction should precede distal reconstruction. She recommends the application of the endovascular approach as the first choice in patients with CLI with moderate to severe disease manifestations (GLASS stage I A), involvement of the aortoiliac arterial segment, and a medical history of prior intervention. Surgical treatment is appropriate for a patient with CLTI, falling into the medium-risk group and with proven extensive aorto-iliac involvement (GLASS stage 2) or after an unsuccessful previous endovascular procedure.

The data from the comparative analysis conducted by the doctoral candidate prove that over time, endovascular treatment has become the first method of choice, especially in patients in the earlier stages of the disease, while the more traumatic surgical treatment is chosen in advanced stages of peripheral arterial disease (PAD), explained by the extensive spread of the atherosclerotic process in the vessels of the lower limb. Regarding the hybrid surgical approach, the stage of the disease is not the leading criterion for choice, but rather the concomitant diseases and the involvement of the common femoral artery by the atherosclerotic process. Although many comparative analyses of results from endovascular and open surgical treatments in different arterial segments have been published, the scientific world, according to the doctoral candidate, needs prospective studies linking the stage of PAD with the choice of surgical approach in occlusive arterial disease.

The doctoral candidate develops and proposes a treatment algorithm for patients with occlusions in the iliac segment, emphasizing the treatment possibilities following previous reconstructions in the same arterial segment.

The candidate also notes some limitations of the study. The conducted study is non-randomized and retrospective. Some of the patients were treated more than ten years ago, and it was not always possible to extract all the necessary data from the patient

documentation. Given the retrospectively collected data for the examined cases, it is expected that not all are complete.

The conclusion is well-formulated. It matches the results achieved from the clinical study and their discussion in the previous chapter.

The ten conclusions made are adequate, with specific direction, without exceeding the competence threshold achieved by the clinical study.

The doctoral candidate authoritatively points out five contributions of scientific-practical character.

The references include 286 well-chosen articles and authors, arranged according to their appearance in the text. There's a lesser participation from Bulgarian sources (only 8 citations), and of the remaining 278 in English, most are published in the last 5-10 years.

Dr. B. Boneva's dissertation is well-organized and illustrated, making for a very readable document. It is stylistically coherent and free of spelling mistakes.

Corresponding to the set academic standards and criteria for the successful completion of a doctoral degree, the doctoral candidate Dr. B. Boneva has demonstrated a significant contribution to the scientific community through the presentation of four full-text publications, one in English and the other three in Bulgarian. This multilingual approach ensures the wide access and dissemination of the research results both nationally and internationally.

The documents and materials presented by the candidate and reviewed by me meet the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria.

Dr. B. Boneva is a well-established vascular surgery specialist. Her clinical activity includes routine and avant-garde methods for the operative and endovascular treatment of vascular pathology. She possesses commendable knowledge, which identifies her as a fully formed professional with a scientific orientation.

Dr. B. Boneva's dissertation is a quality product of a motivated physician with a serious capacity and knowledge. She presents in full volume a difficult, interesting therapeutic problem with many unresolved questions - the treatment of occlusive lesions in the infrarenal aorta and iliac arteries.

The dissertation makes specific contributions of theoretical, scientific, and scientific-practical significance. It includes a high level of practical knowledge on the problem, perfectly conducted research activity, and a professional analysis of the obtained results, which predetermine the routine use of the treatment algorithm for iliac occlusive disease proposed by the doctoral candidate.

After thoroughly reviewing Dr. Bistra Petrova Boneva's dissertation, I consider the work to be dissertation-worthy, innovative, and will be utilized by vascular surgeons in their daily work in the country. The author has undeniable 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 to award Dr. Bistra Petrova Boneva the educational and scientific degree "Doctor."

Sofia
26.03.2024

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