

To:
THE CHAIRMAN OF THE SCIENTIFIC JURY
AT
MULTI-DISCIPLINARY HOSPITAL FOR ACTIVE TREATMENT
“NKB” EAD
SOFIA

REVIEW

by

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Re: PhD Thesis titled:

**"Surgical Methods of Treatment in
Iliac Occlusive Disease -
Comparative Analysis"**

of

Dr. Bistra Petrova Boneva

for the award of PhD educational and scientific degree

PhD programme "Vascular Surgery"

Multi-Disciplinary Hospital for Active Treatment “National Hospital of
Cardiology” EAD, Sofia, Clinic of Vascular Surgery

Thesis Supervisor:

Prof. Dr. Mario Stankev, MD, PhD

According to a decision of the scientific jury appointed by Order No 70/19.02.2024 of the Executive Director of Multi-Disciplinary Hospital for Active Treatment “National Hospital of Cardiology” (MHAT “NKB”), Sofia, I present to its members this review.

Brief background information and professional realization

Dr. Bistra Boneva graduated in medicine in 2013. In 2019 she acquired a medical specialty in vascular surgery, and in 2020 she graduated as a Master in Public Health and Health Management. In the same year, Dr. Boneva also acquired a certificate of competency in endovascular and vascular surgery. Since 2023 she has been enrolled as a PhD student at the Vascular Surgery Clinic of MHAT “NKB”.

Structure of the PhD thesis

The PhD thesis is written on 236 standard pages and is illustrated with 48 tables and 58 figures. The bibliographical reference list includes 286 literary sources, of which 8 in the Cyrillic alphabet and 278 in the Latin alphabet.

Literary Review

The literary review is comprehensive, the topics discussed therein are well structured and its topical relevance is impressive.

The literary review systematically introduces current knowledge and existing problems related to epidemiology, clinic, diagnosis and treatment of the peripheral arterial disease (PAD). The different classifications and the classic terms as well as the newly-introduced terms of the recent years related to its clinical manifestation are discussed in detail. The data on the natural development of PAD and its connection with other clinical manifestations of multifocal atherosclerosis (MFA) are also of interest. Significant attention is paid to the modern algorithms for the treatment of PAD and the management of risk factors in MFA. A significant part of the literary review is focused on the analyses for finding a solution for revascularization, the ways of treatment according to the anatomical localization and the clinical presentation of PAD, as well as the comparative assessments between the different types of treatment.

Purpose and objectives of the PhD thesis

The purpose of the scientific work is properly formulated - to develop an algorithm for treatment in patients with iliofemoral occlusive disease, taking into account the risk factors, comorbidities of the patient, multifocal involvement of other vascular pools and the presence of previous reconstructions in the same segment for the selection of a treatment approach.

The following objectives are determined for the completion of this purpose:

1. To examine the interaction of the risk factors, the severity and stage of the disease and their impact on the involvement of adjacent vascular pools and on the choice of a surgical approach and survival ability of the reconstruction.
2. To assess the success, primary patency and complications in patients undergoing the three types of reconstructions.
3. To optimize the pre-operative analysis of patients with PAD in order to select optimal surgical strategy.
4. To identify the alternative application of the three methods of treatment.
5. To assess the benefit of the hybrid approach to open-label surgical treatment in patients with damages.

Clinical material and methods

The study was conducted at the Clinic of Vascular Surgery, MHAT "NKB", for the period January 2009 – December 2018 and represents a single-center retrospective analysis of patients, who were admitted and underwent interventions on the occasion of iliac occlusive disease. The clinical material presented includes 521 patients, who underwent 580 interventions. According to the applied method of treatment in the aorto-iliac segment, the patients were allocated as follows: endovascular treatment (EVT) was performed in 182 patients (31.38%), hybrid surgical treatment (HST) in 183 (31.55%) and classic open surgical treatment (OST) in 215 (37.07%) of them.

The selection of patients was based on the Fontaine classifications and the anatomical TASC II classification, and the evaluation of the proposed surgical intervention was based on vascular surgical discussion with consideration of the patient's medical history and clinical status, both in terms of his vascular suffering and in terms of the general condition and the constellation of comorbidities.

In her presentation, Dr. Boneva described in detail the ways to perform the three types of interventions that are the subject of this work.

The patients' follow-up was conducted according to a well-defined protocol, and the complications that occurred were evaluated precisely according to strict and categorically accepted criteria in the field of vascular surgery.

For the processing of clinical material, results obtained and comparative assessments, the PhD student used the following statistical methods:

specialized statistical software package SPSS 20.0 (Statistical Package for Social Science), descriptive statistics, CHI-square test, Cramer's coefficient, dispersion analysis (ANOVA), Kaplan-Meier survival analysis, Log Rank test, Wilcoxon Signed Ranks Test.

Here we should point out that the clinical material presented in Dr. Boneva 's PhD thesis offers a modern statistical sample, characterizing the Bulgarian patient with atherosclerosis from the first quarter of the 21 century.

Outcomes

The registered outcomes are presented correctly, and their good structuring in the PhD thesis facilitates their detailed comparison.

In the statistical processing, some connections are established, which are of interest from a scientific and medical point of view, and which may be in support of the treatment of this type of pathology. Such are, for example, the established relatedness between sex, the degree of hypertension, smoking, the presence of TIA, etc., and the type of intervention performed. The conducted analysis of patients demonstrates that in those, who are in the second stage of CAI (chronic arterial insufficiency), and those with CRF (chronic renal failure), preference for performing more sparing interventions (EVT) is registered.

Of practical interest are also the data on the average duration of preserving the patency of the reconstruction in the three types of interventions, which for vascular surgeons can be an accurate reference what to expect from the treatment procedures in this anatomical segment. Very important in this direction are the results of the analyzed data, which show that any revascularization undertaken in the iliac segment brings a 50% risk of loss of patency after the fifth year.

The reported complications, thromboses and mortality are strongly in favor of the hybrid and endovascular type of treatment – another advantage that should be highlighted.

The analysis conducted of the patency of the reconstruction in claudicants and patients with chronic limb-threatening ischemia (CLTI), provides information of better initial outcomes in claudicants - an advantage that is reduced with the progress of time.

The presented comparative analysis between the three revascularization strategies in the cases with clinical presentation of limb ischemia also demonstrates the advantages of HST and EVT in the treatment of this type of lesions.

Statistical analyzes of the impact of MFA, diabetes mellitus and previous reconstructions on strategy choices and subsequent patency also offer useful scientific and practical data.

In conclusion, we must point out that the analyses performed of the presented outcomes are correctly planned and conducted and provide multi-layered essential information both on the complexity of the clinical course of MFA and on the many facts that we need to consider when determining our treatment approaches.

Conclusions

In her PhD thesis, Dr. Boneva presents the following conclusions from the performed clinical and scientific work.

1. Among the studied risk factors, the greatest weight on the choice of surgical approach were established to have the male sex, smoking, the presence of arterial hypertension and chronic renal failure, the concomitant involvement of the MFA of the carotid vascular pool. The higher assessment of the ASA class, patient's age, the presence of diabetes mellitus and dyslipidemia, as well as the concomitant involvement of other vascular pools (coronary and visceral) are considered as independent risk factors. There is no statistically significant difference in the mean patency of the reconstructions in the three groups, depending on the known risk factors studied.
2. The severity of the PAD stage and the clinical manifestation have a statistically significant but weak correlation in terms of the choice of revascularization approach. EVT is most common in limb ischemia, while CLTI cases are predominantly

intervened using more aggressive revascularization strategies. The severity of the PAD stage and the clinical manifestation have a statistically significant impact on the patency of the reconstructions, where the cases of CLTI lose patency significantly earlier.

3. The three treatment methods showed comparable frequencies of technical success, primary patency and limb rescue, which proves their alternativeness in relation to these primary endpoints. The most common and specific complications are observed in OST, followed by HST, which should be taken into account when choosing these revascularization strategies.
4. The pre-operative analysis should be strictly personalized depending on the individual patient characteristics and the specifics of the clinical case. In high-risk patients, EVT and HST have an advantage. There is a need to improve the systematic post-operative monitoring and the evaluation of outcomes, including possible complications and improvement of the patient's quality of life.
5. HST is associated with better primary patency and lower incidence of complications compared to OST, at the cost of a more frequent need for reintervention to maintain the patency. In high-risk patients, HST is the preferred revascularization strategy. HST allows simultaneous intervention through one surgical approach of different arterial segments responsible for the blood supply to the limb.

Contributions

The contributions described by the PhD student stem from the presented clinical material and the registered conclusions and are presented as follows:

- For the first time in Bulgaria, such a large single-center clinical study is conducted, which compares endovascular, surgical and hybrid treatment in patients with occlusive disease in the iliac segment.
- The study allows to recommend in a convincing and scientifically reasoned way the strategy of primary administration of EVT for lesions not engaging the AFC, or HST in extensive spread of the disease with involvement of the AFC, and open surgery should be maintained as a treatment option after conducted endovascular or hybrid revascularization.

- Systematic scientific analysis and statistical results strongly prove that OST should be used in patients with long life expectancy and with minimal burden of comorbidities and risk factors.
- The conclusion that HST is the most acceptable revascularization strategy in high-risk patients with extensive spread of the disease is of great scientific and practical importance.
- For the first time, an algorithm for the treatment of patients with occlusions in the iliac segment is proposed, which emphasizes treatment options after previously performed reconstructions in the same arterial segment;

Publications related to the PhD thesis

In accordance with the requirements, the PhD thesis presents 4 full-text publications (1 in English and 3 in Bulgarian) and 1 scientific report, presented in an international forum.

Conclusion:

The presented PhD thesis and author's abstract are written and structured in accordance with the criteria for acquiring the educational and scientific degree "PhD" under the current regulatory framework.

The presented PhD thesis shows in-depth scientific knowledge, professional skills and experience in the development of scientific topics in the field of vascular diseases. Impressive are also the demonstrated skills of the PhD student for statistical processing of clinical data and interpretation of the results obtained.

With regard to the facts presented in the review, I give my positive evaluation of the presented PhD thesis and I would like to propose to the honored members of the scientific jury to vote positively for the award of the scientific and educational degree "PhD" to Dr. Bistra Petrova Boneva in the specialty "Vascular Surgery".

Reviewer:



(Assoc. Prof. Dr. Dimitar Petkov, MD)

15. 03. 2024