

REVIEW OF A THESIS

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Subject: dissertation submitted for the award of the educational and scientific degree "Doctor" in the doctoral programme "Cardiology", professional field 7.1. Medicine, area of higher education 7. Healthcare and Sports, entitled: "Concomitant carotid pathology in patients undergoing invasive cardiac diagnostic procedures" submitted by Dr Tsvetan Hristov Zhelev

I. Procedure for the Announcing Public Defence

The dissertation was reviewed and approved for public defence by the Departmental Council of the First Department of Internal Diseases at the Medical University – Varna. By Order No. R-109-204/03.06.2026 of the Rector of the Medical University – Varna, I was appointed as a member of the Scientific Jury. Subsequently, pursuant to Minutes No. 1/11.06.2026, I was elected Chair of the Scientific Jury and assigned to prepare the present review. For this purpose, I was provided with all the required documentation by the University's Doctoral School. The present review has been prepared in accordance with the requirements of the Academic Staff Development in the Republic of Bulgaria Act (ASDRBA), the Regulations for its Implementation, and the Regulations for Academic Staff Development of the Medical University – Varna.

II. Brief Biographical Information about the PhD Candidate

Dr Tsvetan Hristov Zhelev graduated from the Medical University – Varna in 2007, obtaining the Master's degree in Medicine. In 2020, he completed a second Master's degree in Healthcare Management and Medical-Social Care. In 2014, he acquired the specialty of Cardiology, followed one year later by a specialty in Interventional Cardiology. Following a competitive selection procedure, Dr Zhelev was appointed Assistant Professor at the First Department of Internal Diseases in 2017. In 2018, he enrolled in the doctoral programme in Cardiology.

Since November 2007, he has been working at the Second Clinic of General and Interventional Cardiology at St Marina University Hospital, Varna.

During the period from February to October 2008, he completed postgraduate clinical training in Cardiology at Hadassah Medical Center, Jerusalem, Israel. Dr Zhelev is certified in both Basic and Advanced Echocardiography.

III. Scientometric Evaluation of the Publications Related to the Dissertation

In support of the present procedure, Dr Zhelev has submitted two full-text publications, comprising one original research article and one review article. The submitted publications adequately reflect the principal findings of the dissertation and fulfil the minimum scientometric requirements established by the Medical University – Varna for the award of the Doctor of Philosophy (PhD) degree.

IV. Structure of the Dissertation

The submitted dissertation is well structured and includes all mandatory components required of a doctoral thesis, presented in a logical and coherent sequence, namely: Introduction; Literature Review; Aim, Objectives and Hypotheses; Materials and Methods; Results and Discussion; Conclusion; Conclusions; and Scientific Contributions. The relative proportions of the main sections are appropriate, with the following distribution: Literature Review : Aim, Objectives and Materials and Methods : Results and Discussion = 4 : 1 : 3. The dissertation is illustrated with 21 figures and 7 tables, all of which have been carefully selected and provide substantial scientific value. They complement the text without duplicating the information already presented. They provide a solid basis for a comprehensive and well-argued discussion.

V. Literature Support

The bibliography comprises 201 references, including 7 publications in Bulgarian and 194 international publications. The number of references is entirely adequate for the scope of the dissertation and demonstrates the candidate's familiarity with both classical and contemporary literature relevant to the research topic.

VI. Relevance and Significance of the Dissertation

The dissertation addresses a highly relevant scientific problem of considerable social, clinical and economic importance. Carotid atherosclerosis represents one of the leading causes of ischaemic stroke, with more than one-third of all strokes resulting from atherosclerotic lesions of the extracranial cerebral arteries, including the carotid and vertebral arteries. Approximately one in every two patients with asymptomatic but significant carotid stenosis will experience a major cardiovascular event—including stroke, myocardial infarction or peripheral vascular complications—within five years. The importance of this clinical problem is convincingly supported in the literature review, where Dr Zhelev critically summarizes and discusses numerous contemporary publications, predominantly published during the last decade. Despite the growing body of evidence in this field, several important issues remain insufficiently clarified, including the identification of patients at highest risk for carotid atherosclerosis and the optimisation of diagnostic algorithms for its timely detection.

In this context, the scientific problem addressed in the present dissertation is undoubtedly timely, clinically relevant and of considerable practical significance.

VII. Evaluation of the Individual Sections of the Dissertation

The Literature Review extends over 55 pages and is organised into six major sections covering: the relevance of the research topic; common risk factors for concomitant carotid and coronary atherosclerosis; prevalence of concomitant carotid and coronary artery disease; current consensus statements and clinical guidelines; contemporary diagnostic approaches to carotid and coronary atherosclerosis; and conclusions drawn from the literature review. The literature review demonstrates the author's comprehensive knowledge and critical understanding of the current state of research concerning concomitant carotid pathology. Conclusions are provided after each major section; however, their presentation could have been more systematically organised and more directly aligned with the overall aim and objectives of the dissertation. The principal aim of the study is to determine and validate the relationship between the severity of cardiovascular disease and the severity of carotid atherosclerosis in order to optimise preventive, diagnostic and therapeutic strategies in patients with coronary artery disease. The aim is clearly formulated and is supported by three well-defined research objectives: To analyse the risk profile of patients with concomitant cardiovascular and cerebrovascular atherosclerosis; To investigate the presence of an exposure-dependent relationship between cardiovascular risk factors and the different degrees of carotid and coronary atherosclerosis; To evaluate the correlation between cardiovascular and cerebrovascular pathology.

Based on the evidence presented in the literature review, the candidate has also formulated two research hypotheses, which are logically derived from the existing scientific knowledge.

The Materials and Methods section describes the study design, study setting, observation period, inclusion and exclusion criteria, clinical protocol, diagnostic methodology—including both invasive and non-invasive investigations—and the statistical methods applied. The information is presented in an appropriate level of detail and provides a clear understanding of the methodological framework of the study.

The Results are presented together with the Discussion, an approach which I consider more appropriate and scientifically justified than presenting these sections separately. This structure facilitates the interpretation of the findings and enhances the logical flow of the dissertation. The results are presented clearly, systematically and consistently, following the predefined research objectives. The characteristics of the study population are analysed from several perspectives. Separate analyses are performed according to sex, while the study population is further divided into three subgroups according to the severity of carotid artery disease: Group A – patients with at least one carotid stenosis $\geq 50\%$; Group B – patients without significant carotid stenosis ($\geq 50\%$) but with at least one non-significant ($< 50\%$) carotid atherosclerotic plaque; Group C – patients without detectable carotid atherosclerotic lesions. The relationship between coronary and carotid atherosclerosis is comprehensively evaluated, including the coexistence of carotid and coronary artery disease. Furthermore, the cardiovascular risk profile of patients with and without carotid stenosis in the presence of concomitant coronary artery disease is analysed, together with the assessment of carotid stenosis severity using both ultrasonographic and angiographic methods.

The Discussion provides an appropriate interpretation of the obtained results and compares them with the currently available scientific evidence.

The Conclusion successfully summarises the most important findings of the study together with their scientific interpretation. The Conclusions could have been presented in a more systematic manner and more directly linked to the predefined research objectives.

The candidate identifies thirteen scientific contributions, including four original contributions and nine contributions of a confirmatory nature. Overall, these contributions are supported by the presented results and statistical analyses.

Given the study design and sample size, such conclusions would benefit from a more cautious interpretation. This particularly applies to statements such as: "We confirmed the existing evidence that male sex is more frequently affected by the atherosclerotic process."

VIII. Critical Remarks

The principal limitation of the dissertation is related to the relatively small study population, which additionally represents a selected hospital-based cohort. This inevitably limits the generalisability of the findings to the broader population and warrants a certain degree of caution when interpreting the conclusions.

IX. Overall Evaluation and Recommendation

The dissertation entitled "Concomitant carotid pathology in patients undergoing invasive cardiac diagnostic procedures", submitted by Dr Tsvetan Hristov Zhelev has been prepared in accordance with the generally accepted requirements for a doctoral thesis. The dissertation is supported by publications reflecting its principal scientific findings and fulfils the requirements of the Academic Staff Development in the Republic of Bulgaria Act (ASDRBA), the Regulations for its Implementation, and the Regulations for Academic Staff Development of the Medical University – Varna for the award of the Doctor of Philosophy (PhD) degree. Based on the above considerations, I give a positive evaluation of the dissertation and recommend that the Scientific Jury award Dr Tsvetan Hristov Zhelev the educational and scientific degree "Doctor" in the doctoral programme "Cardiology".

June 23, 2026
Varna

Signed:

Prof. Mariya Negreva, MD, PhD, DSc

Заличено на основание чл. 5,
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