

OPINION

by

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regarding a dissertation submitted for the award of the Educational and Scientific Degree
Doctor

Field of Higher Education: 7. Health Care and Sports

Professional Field: 7.1. Medicine

Scientific Specialty: Cardiology

Dissertation Title:

"Concomitant Carotid Pathology in Patients Undergoing Invasive Cardiac Diagnostics"

submitted by

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Scientific Supervisor:

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With order N: 109-204/03.06.2026 of the Rector of MU-Varna I am chosen as a member of the scientific jury and according to order N: 1/11.06.2026 r. I am also required to prepare a statement on the procedure of acquiring educational degree "Doctor" with candidate Dr Tsvetan Hristov Zhelev.

Brief Information on the Professional Development and Qualifications of the Doctoral Candidate: Dr Tsvetan Zhelev graduated from the Medical University of Varna in 2007. Since that year he has been working as a physician at the Second Department of Invasive Cardiology, St Marina University Hospital, Varna. In 2008 he undertook specialised training in Cardiology at Hadassah Hospital, Jerusalem, Israel. He obtained a specialty in Cardiology in 2014 and in Invasive Cardiology in 2015. Since 2017 he has been serving as an Assistant Professor in the First Department of Internal Diseases.

Relevance of the Topic: Ischaemic stroke remains one of the leading causes of mortality and disability in developed countries. More than one-third of all strokes are associated with atherosclerotic changes in the extracranial cerebral arteries. The carotid and coronary arteries are among the vascular territories most frequently affected by atherosclerosis. These arterial systems share similar characteristics, risk factors, and mechanisms of plaque formation despite their different anatomical locations. Coronary atherosclerosis is recognised as an independent predictor of carotid atherosclerotic disease. Furthermore, the severity of carotid atherosclerosis correlates with both the number and severity of affected coronary arteries. Consequently, the identification of carotid stenosis during invasive cardiac diagnostics is important for risk stratification in patients with coronary artery disease, particularly those with multivessel involvement. Digital subtraction angiography (DSA) remains the gold standard for the diagnosis of vascular diseases. The combination of invasive and non-invasive diagnostic modalities may facilitate therapeutic decision-making, especially in asymptomatic patients with multifocal atherosclerosis.

Structure of the Dissertation: The dissertation comprises 119 pages and is presented in accordance with the established academic requirements. It contains 21 figures and 11 tables. The dissertation includes: Introduction and Literature Review – 56 pages; Aim and Objectives – 1 page; Materials and Methods – 13 pages; Results and Discussion – 33 pages; Conclusions and Contributions – 3 pages. The bibliography includes 201 references, seven of which are in Cyrillic script. The dissertation abstract contains six figures and ten tables.

Literature Review: The literature review provides a comprehensive analysis of current scientific knowledge concerning: Risk factors for coronary and carotid atherosclerosis; Studies evaluating the prevalence of concomitant coronary and carotid disease; Current consensus statements and clinical guidelines; Diagnostic approaches to carotid and coronary atherosclerosis.

Aim and Objectives: The author formulates the principal aim of the study as a logical continuation of the literature review: To determine and validate the correlation between the severity of cardiovascular pathology and the severity of carotid atherosclerosis, with the objective of optimising preventive, diagnostic, and therapeutic strategies in patients with coronary artery disease. The doctoral candidate proposes the following hypothesis: There is a moderate correlation between the severity of coronary and carotid atherosclerosis, and an exposure-dependent relationship exists between cardiovascular risk factors in patients with cardiovascular and cerebrovascular atherosclerotic disease.

Materials and Methods: A total of 299 patients were included in the study. Information was collected regarding: Demographic characteristics; Clinical characteristics; Cardiovascular risk factors. The following investigations were performed: Lipid profile assessment; Renal function evaluation; Echocardiography; Coronary angiography; Carotid angiography. Additionally, carotid duplex ultrasonography was performed in 70 patients. Modern statistical methods were applied for data analysis and interpretation.

Results and Discussion: Among the most significant findings are:

- Concomitant carotid pathology is common among patients with coronary artery disease.
- Men predominate in the groups with moderate and severe carotid stenosis, whereas both sexes are equally represented among patients without carotid stenosis.
- A clear relationship was demonstrated between the severity of arterial hypertension—defined by the number of antihypertensive medications required for adequate blood pressure control and the severity of carotid atherosclerotic disease.
- A significant association was established between the accumulation of cardiovascular risk factors and the severity of carotid involvement.
- A statistically significant positive correlation was demonstrated between the severity of coronary artery disease and the severity of carotid atherosclerosis ($r = 0.367$; $p < 0.001$).
- A characteristic high-risk profile for carotid disease was identified: male sex, age above 55 years, diabetes mellitus, poorly controlled hypertension requiring at least four antihypertensive medications, and clinically manifest coronary artery disease.
- Differences were observed between ultrasonographic and angiographic assessment of carotid stenosis severity.
- No transient or permanent complications related to invasive carotid angiography were recorded among the 299 examined patients.

The obtained results confirm the proposed hypotheses regarding the existence of a statistically significant relationship between coronary and carotid pathology and the exposure-dependent influence of cardiovascular risk factors.

The author proposes a diagnostic protocol for carotid ultrasound screening in:

- Patients with the identified high-risk profile;
- Patients with documented coronary atherosclerosis, regardless of stenosis severity;
- Patients with previous ischaemic stroke or transient ischaemic attack.

In cases where carotid stenosis is detected during screening, invasive coronary angiography including assessment of the supra-aortic vessels is recommended.

Scientific Contributions: Among the proposed contributions, I consider the following to be the most significant:

- Identification of a clinical profile associated with a high probability of concomitant carotid and coronary stenotic disease.
- Development of a practical diagnostic algorithm for carotid atherosclerosis in patients referred to cardiology departments.
- Demonstration of a statistically significant gradient relationship between hypertension severity and carotid atherosclerotic burden.
- Establishment of a predictive model indicating a high probability of significant carotid disease in patients requiring intensive antihypertensive therapy combined with additional cardiovascular risk factors.
- Confirmation of a statistically significant relationship between carotid stenosis severity and coronary atherosclerotic disease ($p < 0.001$).
- Confirmation of a positive correlation between the severity of coronary and carotid atherosclerosis ($r = 0.367$; $p < 0.001$).
- Demonstration of the need for routine carotid ultrasonography in cardiology practice.
- Confirmation of previously reported discrepancies between carotid duplex ultrasonography and digital subtraction angiography in the assessment of carotid stenosis severity.

Publications and Scientific Communications: In connection with the dissertation, Dr Zhelev has presented two scientific publications. The scientific output fulfils the formal requirements; however, I believe that the collected material provides sufficient grounds for additional publications and presentations at scientific meetings.

Conclusion: The research conducted by Dr Tsvetan Zhelev addresses important and contemporary issues in cardiology, angiology, and interventional cardiology. The results support the need for a comprehensive evaluation of patients at high risk of atherosclerotic vascular disease, including: assessment of traditional cardiovascular risk factors; use of validated risk modifiers for risk reclassification; application of both non-invasive and invasive imaging techniques. In my opinion, the dissertation fully complies with the requirements of the Academic Staff Development Act of the Republic of Bulgaria and its implementing regulations for the award of the Educational and Scientific Degree Doctor. For these reasons, I recommend that the esteemed Scientific Jury vote positively and award Dr Tsvetan Zhelev the Educational and Scientific Degree Doctor.

Varna, 25 June 2026

Assoc. Prof. Atanas Angelov, MD

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