REVIEW

by Assoc. Prof. Stefan Naydenov Naydenov, MD, PhD
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Regarding: The doctoral dissertation entitled **"Clinical Significance of Pentraxin 3 in Patients with Ischaemic Heart Disease Not Eligible for Revascularisation"** by **Dr Dimitar Tihomirov Hristov**, resident physician and doctoral student at the Department of Cardiology and Rheumatology, Faculty of Medicine, Prof. Dr Paraskev Stoyanov Medical University of Varna, submitted for the award of the educational and scientific degree **"Doctor"** in Professional Field 7.1 Medicine, Doctoral Programme in Cardiology (code 03.01.47).

Pursuant to Order No. R-109-299/20 August 2026 of the Rector of the Medical University of Varna and the decision of the Faculty Council of the Faculty of Medicine at the Medical University of Varna (Minutes No. 63/17 August 2026), and in accordance with the Act on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of the Act on the Development of the Academic Staff in the Republic of Bulgaria, and Article 2, paragraphs 2 and 3 of the Regulations on the Development of the Academic Staff at the Medical University of Varna, a scientific jury was appointed to conduct the procedure for the award of the educational and scientific degree "Doctor".

The procedure for the preparation and defence of the doctoral dissertation of Dimitar Tihomirov Hristov complies with the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria, its implementing regulations, and the Regulations on the Development of the Academic Staff at the Medical University of Varna.

I have no conflict of interest in relation to the present procedure. I have found no evidence of plagiarism in the scientific work of Dr Dimitar Tihomirov Hristov.

The doctoral dissertation of Dr Dimitar Hristov comprises a total of 126 pages, distributed as follows: one title page; table of contents, 2 pages; list of commonly used abbreviations, 3 pages; introduction, 2 pages; literature review, 38 pages; aim and objectives of the study, 1 page; participants and methods, 6 pages; results and discussion, 48 pages; pharmacoeconomic analysis, 2 pages; conclusions, 1 page; contributions, 1 page; final conclusion, 1 page; study limitations, 1 page; future perspectives, 1 page; list of publications related to the dissertation, 1 page;

acknowledgements, 1 page; appendices, 2 pages; and bibliography, 14 pages. The structure and opening pages of the individual sections are presented in the table of contents.

The dissertation contains 30 figures and graphs and 23 tables. The bibliography includes 211 references.

Overall, the dissertation follows a conventional structure, with the proportions between its individual sections broadly complying with the generally accepted national academic requirements.

RELEVANCE OF THE TOPIC

The topic of the dissertation is relevant from both theoretical and scientific-practical perspectives. Ischaemic heart disease remains a leading cause of morbidity, disability, and mortality and represents a major medical and public health problem. Despite contemporary pharmacological and interventional treatment options, some patients with chronic coronary syndrome have neither a clinical indication nor a technically feasible option for revascularisation; therefore, the assessment of their residual risk is particularly important.

Traditional cardiovascular risk factors and established prognostic models cannot fully explain individual differences in clinical course and the occurrence of adverse events. Current concepts identify chronic low-grade vascular inflammation as a major mechanism in the initiation, progression, and destabilisation of the atherosclerotic process. This highlights the need to identify vascular-specific biomarkers that could complement clinical assessment and improve risk stratification in patients with ischaemic heart disease.

Pentraxin 3 is a promising inflammatory biomarker; however, its clinical and prognostic significance in patients with chronic coronary disease who are not eligible for revascularisation remains insufficiently clarified. The selected topic is therefore timely, scientifically relevant, and potentially applicable in clinical practice for individualising the monitoring and pharmacological treatment of this high-risk patient population.

KNOWLEDGE OF THE SUBJECT

The literature review demonstrates the doctoral candidate's thorough knowledge of contemporary concepts regarding the pathogenesis of atherosclerosis and coronary artery disease.

The principal cellular, molecular, and immunological mechanisms involved in the initiation, progression, and complications of the atherosclerotic process are examined systematically. The pathophysiological features of obstructive coronary atherosclerosis, vascular remodelling, impaired coronary reserve, and their relationship with the clinical manifestations of myocardial ischaemia are presented. The author demonstrates sound knowledge of the methods used for the clinical assessment of anginal symptoms and provides a well-reasoned presentation of the

capabilities and limitations of the Canadian Cardiovascular Society classification. Particular attention is devoted to the Seattle Angina Questionnaire as a validated disease-specific instrument for evaluating physical limitation, angina frequency, treatment satisfaction, and quality of life.

The principal groups of inflammatory biomarkers, their biological characteristics, and the requirements that a biomarker must fulfil to be incorporated into clinical practice are analysed in detail. The doctoral candidate correctly distinguishes systemic inflammatory markers, such as C-reactive protein, from pentraxin 3 as a potentially more specific marker of local vascular inflammation. The available evidence concerning the diagnostic and prognostic value of pentraxin 3 in acute coronary syndromes, chronic coronary syndrome, and after percutaneous coronary intervention is presented and critically discussed. The author acknowledges the inconsistencies among individual studies, the absence of universally accepted reference values, and the influence of renal function, inflammatory diseases, and concomitant therapy on biomarker concentrations. The insufficiently investigated significance of pentraxin 3 in symptomatic patients with angiographically documented coronary atherosclerosis who are not eligible for revascularisation is clearly identified, logically supporting the aim and objectives of the dissertation.

CHARACTERISTICS OF THE RESULTS AND DISCUSSION

The "Results and Discussion" section is structured logically and presents the original findings in direct relation to the stated objectives and the available scientific evidence. The study cohort is characterised in detail with respect to demographic parameters, traditional cardiovascular risk factors, comorbidities, pharmacological treatment, and angiographic status. The use of the validated Bulgarian version of the Seattle Angina Questionnaire permits a standardised assessment of anginal symptoms, functional limitation, and quality of life. The results demonstrate a statistically significant inverse association between plasma pentraxin 3 concentrations and physical capacity, as assessed using the relevant questionnaire domain. When patients were stratified according to the severity of physical limitation, significantly higher pentraxin 3 levels were observed in the group with more severe anginal symptoms.

The identified cut-off value of 1.1025 ng/mL demonstrated 68% sensitivity and 74.5% specificity in distinguishing patients with severe symptoms from those with mild symptoms, although the overall discriminatory ability of the biomarker was relatively limited. Analyses of the other domains of the Seattle Angina Questionnaire complement the assessment of the relationship between baseline vascular inflammation, the frequency of anginal symptoms, and quality of life. At the same time, no statistically significant association was found between pentraxin 3 concentration and the number of coronary arteries affected by intermediate stenoses. This negative result is interpreted appropriately and cautiously, without drawing unsupported conclusions

regarding a direct relationship between the biomarker and the anatomical severity of coronary atherosclerosis. The author suggests that clinical symptoms may be determined not only by epicardial stenoses but also by microvascular dysfunction and other mechanisms of myocardial ischaemia.

The results of the prospective clinical follow-up, with a median duration of 16 months, aimed at identifying rehospitalisations due to worsening anginal symptoms, are of particular importance. A pentraxin 3 cut-off value of ≥0.9205 ng/mL demonstrated 81.8% sensitivity and 55.1% specificity for predicting such rehospitalisations. Patients above this threshold had an approximately 5.5-fold higher likelihood of rehospitalisation than patients with lower biomarker concentrations. These findings support the potential use of pentraxin 3 in identifying a subgroup of patients who may require more intensive antianginal and lipid-lowering therapy and closer clinical monitoring. The discussion is analytical, compares the findings with those reported by other authors, acknowledges the limitations of the study, and substantiates the need for subsequent validation of the identified cut-off values in larger, independent patient cohorts.

COMMENTS AND RECOMMENDATIONS

1. I recommend revising the wording of the dissertation title. In its current form, "...patients with ischaemic heart disease who are not eligible for a revascularisation procedure" does not clarify whether the patients had no clinical indication, lacked a technically feasible option, or were considered unsuitable for revascularisation. Possible titles include: "Clinical and Prognostic Significance of Pentraxin 3 in Patients with Ischaemic Heart Disease Not Eligible for Coronary Revascularisation" or "Clinical and Prognostic Significance of Pentraxin 3 in Patients with Ischaemic Heart Disease Without an Indication for Revascularisation".
2. I recommend the following revisions and structural changes to the dissertation:

- The title of the chapter "Participants and Methods" should preferably be replaced with the more established scientific term "Materials and Methods". I propose the following sequence within this chapter:

- First subsection: "Study Population and Study Design", incorporating the text from the current "Study Design" section and presenting the principal demographic and clinical characteristics of the study population.
- Second subsection: "Inclusion and Exclusion Criteria".
- Third subsection: "Diagnostic Methods", followed by a systematic presentation of the clinical, laboratory, and instrumental methods used, organised into separate subheadings.

- A separate subsection entitled "Statistical Methods", clearly describing the statistical analyses performed.

- The current chapter "Results and Discussion" should be divided into two separate chapters: "Results" and "Discussion". This would provide a clearer distinction between the presentation of the original data and their interpretation in the context of the available scientific literature.
- The "Pharmacoeconomic Analysis" section would be more appropriately included as a separate subsection of the "Results" chapter, provided that it presents original findings from an analysis performed by the author. If its content is predominantly interpretative, it should be included in the "Discussion" chapter.
- The title "Weaknesses of the Study" should be replaced with the more appropriate scientific term "Study Limitations". This section should preferably be placed at the end of the "Discussion" chapter, immediately before the "Future Perspectives" section.
- There is no need for the "Conclusion" to be presented as a separate chapter. Its content may be included as a brief summarising paragraph at the end of the "Discussion" chapter, introduced, for example, by the phrase "In conclusion…".
- The "Discussion" chapter should be followed by a separate chapter entitled "Conclusions", comprising approximately 10–12 clearly formulated conclusions that derive directly from the most important original findings and do not contain new interpretations or recommendations.
- After the "Conclusions", I recommend the following sequence of final sections: "Contributions of the Dissertation", "Bibliography", "Publications Related to the Dissertation", "Acknowledgements", and "Appendices".

This reorganisation would improve the logical sequence, methodological clarity, and overall academic structure of the dissertation.

3. The "Introduction" should be reduced to approximately one page and should focus on the relevance of the problem, its public health significance, and the scientific rationale for conducting the study.

- The sentence:

"In 2020, 244.1 million people worldwide suffered from ischaemic heart disease. Men were affected to a greater extent, while the geographical distribution showed a higher incidence of the disease and higher mortality in North Africa, the Middle East, Eastern Europe, and Central Asia"

should preferably be revised as follows:

"In 2020, the number of patients with ischaemic heart disease worldwide reached 244.1 million. The disease was more prevalent among men and was associated with higher morbidity and mortality in North Africa, the Middle East, Eastern Europe, and Central Asia."

- The "Introduction" should provide a concise summary of specific epidemiological data on morbidity and mortality due to ischaemic heart disease, including STEMI, in Bulgaria and the Member States of the European Union. These indicators may be compared with data from the United States and, if necessary, other regions of the world. The information should be synthesised in no more than two or three sentences, avoiding an excessive accumulation of statistical data.
- A substantial portion of the "Introduction", beginning with the sentence "In the middle of the twentieth century..." and ending with "Establishing the association...", is predominantly historical and theoretical in nature. It would therefore be more appropriately included in the "Literature Review" chapter.
- The final part of the "Introduction" should contain two or three transitional sentences that clearly outline the unresolved scientific problem, the insufficient evidence regarding the clinical and prognostic significance of pentraxin 3, and the rationale for conducting the present study.

A suitable concluding passage for the section could be:

"Despite the accumulating evidence regarding the role of inflammation in the pathogenesis and progression of coronary atherosclerosis, the clinical and prognostic significance of pentraxin 3 in patients with ischaemic heart disease who are not eligible for revascularisation remains insufficiently understood. There is also insufficient evidence concerning the relationship between plasma levels of this biomarker, the severity of anginal symptoms, quality of life, and the risk of subsequent adverse clinical events. This provides the rationale for conducting the present study."

4. I recommend the following structural changes to the "Literature Review" chapter:

- The subsection "Biomarkers of Vascular Inflammation" represents a logical continuation of the discussion of the inflammatory pathogenesis of atherosclerosis. It should therefore be placed immediately after "Pathogenesis of Obstructive Coronary Atherosclerosis" and before "Clinical Assessment of the Severity of Anginal Symptoms". This would create a clearer sequence, progressing from the pathophysiological mechanisms of the disease, through their objective assessment using biomarkers, to the clinical evaluation of symptoms.
- At the end of the chapter, I recommend adding a separate subsection entitled "Conclusions from the Literature Review", containing 10–12 brief and clearly formulated conclusions.

These should synthesise the principal findings from the literature analysed, outline the existing controversies and unresolved scientific questions, and substantiate the need for the present study. The conclusions should not merely repeat the content of the individual subsections but should establish a logical transition to the aim, objectives, and research hypothesis of the dissertation.

An appropriate sequence for the principal subsections could be:

5. Inflammation as a Component of the Pathogenesis of Atherosclerosis
6. Pathogenesis of Obstructive Coronary Atherosclerosis
7. Biomarkers of Vascular Inflammation
8. Pentraxin 3 and Ischaemic Heart Disease
9. Pentraxin 3 and Statin Therapy
10. Clinical Assessment of the Severity of Anginal Symptoms
11. Limitations of Pentraxin 3 as a Marker of Vascular Inflammation and Unresolved Scientific Questions
12. Conclusions from the Literature Review

5. I recommend the following clarifications and corrections in the "Materials and Methods" chapter:

- The study design should be defined unambiguously at the beginning of the methodological section. It should be specified whether the study is single-centre, observational, analytical, and prospective cohort in design. Its two components should be clearly distinguished: the cross-sectional analysis of baseline clinical, laboratory, and instrumental parameters and the subsequent prospective follow-up for rehospitalisation. This distinction is essential because it determines the types of conclusions that may be drawn and the level of evidence provided.
- A more convincing justification of the sample size is required. An a priori calculation of the required number of participants should be presented based on the expected effect size and incidence of the primary endpoint. If such a calculation was not performed, a post hoc assessment of statistical power should be provided. The small cohort size limits the reliability of the correlation, ROC, and regression analyses. In this context, the observed correlation between PTX3 and physical limitation, $\rho = -0.258$, although statistically significant, represents a small effect and should not be interpreted as a strong or clinically compelling association.

- The absence of a control group is a major methodological limitation. This should be clearly stated in both the "Materials and Methods" and "Study Limitations" sections. The absence of a control group precludes direct comparison with patients without coronary atherosclerosis, patients who have undergone revascularisation, or healthy individuals, and limits the ability to interpret PTX3 levels more definitively.
- The primary endpoint should be defined more precisely. The wording "rehospitalisation due to worsening anginal symptoms" is clinically relevant but contains an element of subjectivity. The diagnostic criteria for worsening angina, the method used to confirm events, whether an independent adjudicator was involved, and the criteria used to distinguish cardiovascular from non-cardiovascular causes of hospitalisation should be specified. It should also be stated how multiple rehospitalisations in the same patient were handled.
- If unstable angina and fatal and non-fatal myocardial infarction were included in a composite endpoint, this should be stated prospectively and unambiguously in the methodological section. The individual components should be defined precisely, the rationale for combining them should be provided, and it should be clarified whether the analysis was based on time to first event or on the total number of events.
- The duration of follow-up was variable, with a median of 16 months and an interquartile range of 9–23 months. With such variability, conventional logistic regression does not account for time to event or censoring. Kaplan–Meier analysis, the log-rank test, and a Cox regression model would be more appropriate and would permit a more accurate assessment of the relationship between PTX3 and time to first rehospitalisation.
- The current subsection "4.2. Study Design" should not be presented as a separate narrative section if its content is conveyed primarily through a diagram. In that case, the graphical representation should be labelled "Figure … Study Design", with a brief explanation in the text immediately before or after the figure.
- The subsection "Structured Interview" should preferably be replaced with the more clinically precise term "Medical History". This subsection should systematically describe the data collected regarding symptoms, risk factors, comorbidities, family history, current treatment, and the use of the Seattle Angina Questionnaire.
- The "Statistical Analysis" section should begin by clearly identifying the statistical software used, the method for determining the required sample size, and the principles applied in the descriptive and comparative analyses. I propose the following wording:

"All data were processed using the statistical software package …, version … . The minimum required sample size was determined a priori using G*Power, version …, based on a predefined statistical significance level of $\alpha = 0.05$, a desired statistical power of $1 - \beta = \ldots$, an expected effect size of …, and an expected incidence of the primary endpoint of … . The analysis indicated that at least … participants were required to achieve the predefined statistical power."

The sample-size calculation should not be linked directly to "ensuring external validity" or "generalisation to the Bulgarian population". Statistical power determines the probability of detecting a true effect but does not, in itself, guarantee representativeness or external validity. The generalisability of the results also depends on the method used to select participants, the characteristics of the study cohort, whether the study is single-centre or multicentre, and the extent to which the cohort corresponds to the target population.

The text may continue as follows:

"Categorical variables, including nominal and ordinal parameters, were presented as absolute frequencies and relative proportions expressed as percentages. Normally distributed quantitative variables were described using the mean and standard deviation, whereas non-normally distributed variables were described using the median and interquartile range from the 25th to the 75th percentile, as well as minimum and maximum values. The distribution of the variables was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests and, where appropriate, graphical assessment.

The statistical significance of differences between categorical variables was analysed using Pearson's χ^2 test and, when expected frequencies were small, Fisher's exact test. An independent-samples t-test was used to compare two independent groups with respect to normally distributed quantitative variables, whereas one-way analysis of variance was used to compare more than two groups. For non-normally distributed quantitative variables, the Mann–Whitney U test and the Kruskal–Wallis H test were used, as appropriate. When a statistically significant difference was identified among more than two groups, the post hoc tests used for multiple comparisons should also be specified. A two-sided level of statistical significance of $p < 0.05$ was adopted for all analyses."

Depending on the analyses actually performed, the section should additionally specify:

- the correlation method used—Pearson's or Spearman's correlation;
- the ROC analyses, AUC values, and 95% confidence intervals;
- the method used to determine optimal cut-off values, for example, the Youden index;
- the univariable and multivariable regression models;
- the method used to select covariates;

- the assessment of multicollinearity and model fit;
- the methods used for time-to-event analysis, if Kaplan–Meier analysis and Cox regression were applied.

The statement in the dissertation that the odds ratio is equivalent to relative risk requires mandatory correction. The odds ratio and relative risk are distinct statistical measures. The odds ratio may approximate the relative risk only when the event analysed is rare, but it should not be described as equivalent to relative risk.

Appropriate wording would be:

"The results of the logistic regression analysis were presented as odds ratios (ORs) and their corresponding 95% confidence intervals. The OR expresses the change in the odds of the event of interest associated with the presence or change of the respective predictor and should not be interpreted as a relative risk, except as an approximation when events are rare."

This terminological correction should be applied consistently throughout the "Materials and Methods", "Results", "Discussion", and "Conclusions" sections.

6. Results

I recommend the following corrections and additions to the "Results" chapter:

- The absence of a control group represents a major limitation in the interpretation of the findings. Without a comparison group comprising healthy individuals, patients without angiographically documented coronary atherosclerosis, or patients who have undergone revascularisation, it is impossible to determine the extent to which the measured PTX3 concentrations are specific to the study population. The current design permits analysis of associations among variables within the cohort but does not allow definitive comparisons among different clinical phenotypes.
- In the absence of a control group, the overall cohort should at least be stratified by sex. Demographic, clinical, laboratory, and instrumental parameters may be presented comparatively in tables with the columns "Overall Population", "Men", and "Women", together with the exact p-value for the statistical significance of differences between the two sexes.
- The PTX3 cut-off value of ≥ 0.9205 ng/mL was derived using ROC analysis and subsequently evaluated in the same relatively small cohort. This approach creates a risk of optimistic overestimation of the diagnostic and prognostic performance of the model. The reported sensitivity of 81.8% and specificity of 55.1% indicate good sensitivity but limited specificity. Therefore, the identified cut-off value should be described as exploratory rather than as a parameter ready for immediate clinical application. Internal validation using

bootstrap analysis or cross-validation is recommended, followed by external validation in an independent patient cohort in a subsequent study.

- The clinical significance of some ROC analyses is presented more definitively than the results permit. An AUC of 0.654 for distinguishing patients with severe from those with mild anginal symptoms indicates poor discriminatory ability. PTX3 therefore cannot independently and reliably determine the severity of angina. Cautious wording such as "shows potential", "may contribute to clinical assessment", and "requires further validation" should be used consistently in the results, discussion, conclusions, and contributions.
- In tables containing quantitative variables, data should be presented according to their distribution. For normally distributed data, an appropriate format is "mean ± standard deviation (minimum–maximum)", whereas non-normally distributed data should be presented as "median (IQR; minimum–maximum)". This principle should be applied consistently, including in Table 2.
- Figure 6 should include the exact p-value for the statistical significance of the observed between-group differences. Generalised expressions such as $p < 0.05$ or p = N.S. should be avoided when the exact value is available.
- In tables containing categorical variables, data should be presented as n (%). A separate column containing the exact p-value should be included for each comparison, and the statistical test used should be specified in the table heading or footnote.
- The data in Table 5 should also be presented as n (%), with a separate column showing the exact p-value.
- The "Results" chapter should not contain subsections entitled "Discussion". This chapter should present the original findings objectively, without detailed comparison with published evidence or extensive pathophysiological interpretation. The text from the existing "Discussion" subsections should be transferred to and organised thematically within a separate "Discussion" chapter, while retaining the relevant thematic subheadings where appropriate.
- The presentation of the results should be organised consistently according to the stated objectives and predefined endpoints. For each analysis, the number of patients included, the statistical test applied, the effect size, the exact p-value, and, where appropriate, the 95% confidence interval should be reported.

These corrections would improve the transparency, reproducibility, and scientific credibility of the results and reduce the risk of overinterpretation.

7. Discussion and conclusions

The "Discussion" chapter should include a more detailed analysis of the influence of potential confounding factors on plasma PTX3 concentrations. Biomarker levels may be affected by age, sex, renal function, obesity, diabetes mellitus, smoking, heart failure, pharmacological therapy, and the presence of subclinical inflammation. The author has appropriately applied exclusion criteria for a number of diseases and conditions that may increase PTX3 concentrations; however, this approach limits external validity and the generalisability of the findings to the real-world multimorbid population with ischaemic heart disease. This limitation should be emphasised more clearly in both the discussion and the conclusions.

The independence of the prognostic value of PTX3 from the treatment administered has also not been demonstrated. Statin and antianginal therapy may simultaneously influence anginal symptoms, inflammatory activity, and the likelihood of subsequent rehospitalisation. The type, dose, and intensity of lipid-lowering and antianginal treatment, changes to the therapeutic regimen at discharge, and adherence to the prescribed treatment during follow-up should therefore be presented in greater detail. Without statistical adjustment for these therapeutic factors, the independent prognostic contribution of PTX3 cannot be convincingly established. The conclusions in this regard should be phrased cautiously and should emphasise the associative rather than causal nature of the observed relationships.

8. Study limitations

The absence of a control group must be added to the stated study limitations. The lack of a comparison group comprising healthy individuals, patients without angiographically documented coronary atherosclerosis, or patients who have undergone revascularisation limits the ability to assess the specificity of the observed PTX3 concentrations for the clinical population studied. The design permits analysis of associations among variables within the cohort but does not allow definitive comparisons among different clinical phenotypes.

9. Linguistic, stylistic and technical corrections

A final linguistic, stylistic, and technical revision of the dissertation is required. I recommend the following corrections:

- Table titles should be placed above the respective tables, with explanatory notes immediately below them.
- It is not necessary for every subsection to begin on a new page.
- All terms and notations should be presented in Bulgarian or explained at first use; for example, "mean ± one standard deviation" should be used instead of the isolated notation "mean ± 1 SD".

- The term “patients” should be used consistently instead of “sick persons”.
- The use of “pentraxin 3” and “PTX3” should be standardised, with the full term written out at first mention and followed by the abbreviation in parentheses.
- A uniform format should be applied to decimal places, units of measurement, p-values, confidence intervals, and statistical abbreviations.
- Original results and their interpretation should not be combined within the same paragraphs. The results should be presented objectively in the relevant chapter, while their interpretation should be confined to the “Discussion”.
- The bibliography should be checked for consistency of referencing style, duplicate references, technical inaccuracies, and complete correspondence between in-text citations and the reference list.

My comments and recommendations are advisory in nature only. They do not diminish the scientific or practical value of the dissertation but are intended to improve its methodological precision, logical structure, and academic presentation. The identified inaccuracies may be corrected during the final revision before the dissertation is submitted for public defence.

CONCLUSION

The doctoral dissertation submitted by Dr Dimitar Tihomirov Hristov constitutes an independent scientific study addressing a relevant and important problem and contains original scientific and applied scientific findings. The doctoral candidate demonstrates the necessary theoretical knowledge and the ability to conduct clinical research and to analyse and interpret the resulting data. The dissertation fulfils the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria, its implementing regulations, and the Regulations on the Development of the Academic Staff at the Medical University of Varna.

This provides me with sufficient grounds to vote **in favour** of awarding **Dr Dimitar Tihomirov Hristov** the educational and scientific degree **“Doctor”** in Professional Field 7.1 Medicine, Doctoral Programme in Cardiology.

Заличено на основание чл. 5, §1, б. „В“ от Регламент (ЕС) 2016/679

18 Sep 2026

Signature:

/Assoc. Prof. Stefan Naydenov, MD, PhD/