

STATEMENT

From Assoc. Prof. Vasil Dimitrov Velchev, MD, PhD

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Regarding the doctoral thesis for awarding the educational and scientific degree Philosophy Doctor in 7. Healthcare and Sports – higher education area, Professional field 7.1 Medicine, scientific speciality Cardiology. I have been tasked to prepare a position statement as a member of the Scientific Jury for the procedure for obtaining a PhD degree according to Order N: P-109-367/08.08.2023 of the Rector of the Medical University – Varna (Minutes Summary № 1/1/11.08.2023).

Thesis subject: APPLICATION OF ECHOCARDIOGRAPHIC METHODS FOR FUZZY STRATIFICATION DETERMINING THE VOLUME OF SURGERY IN PATIENTS WITH ISCHEMIC MITRAL REGURGITATION

by Daniela Stoyanova Panayotova, MD

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Research Consultant: Prof. Natalia Nikolova, MD, PhD

Relevance of the thesis

With the ageing population in Bulgaria and Europe, ischemic heart disease (IHD) is becoming increasingly prevalent. Modern interventional and medication treatment methods enable more patients to survive the acute phase of myocardial ischemia and, respectively, to develop complications. One of these complications that has been shown to affect patients' length and quality of life is ischemic mitral regurgitation. In the field of cardiology and cardiac surgery practice, there is no consensus on the management of patients with indications for surgical revascularization if the patient has severe chronic secondary mitral regurgitation (MR). In this sense, the issue of how best to refine the indications for surgical correction of ischemic MR in IHD patients is relevant and important for clinical practice.

The thesis is presented in 170 pages, structured in 6 sections, almost each of which is subdivided into topics. The main text of the thesis has two appendices – Appendix 1 with 94 pages and Appendix 2 with 40 pages. It is structured according to the requirements: Introduction – 2 pages; Literature review – 59 pages; Aim and tasks – 1 page; Materials and methods – 65 pages; Results and their application – 20 pages; Conclusions and contributions – 4 pages; References – 27 pages, including 324 titles, 5 of which are in Bulgarian, and the rest – in the English language. A licensed EndNote program was used to prepare the references. The doctoral thesis is illustrated with 32 tables, 15 figures and 42 mathematical formulae. The echocardiographic images presented in the text are Dr. Panayotova's personal work.

In **the introduction**, the PhD student elucidates the significance of the issue of ischemic mitral regurgitation in patients undergoing open heart surgery for revascularization. According to the doctoral student, there is no consensus on standardized algorithms for determining in which patient ischemic MR should be corrected and how so – whether a single-stage Mitral Valve Repair (MV Repair) should be performed together with coronary artery bypass grafting (CABG), or whether the surgery should be limited to revascularization only.

The literature review includes 12 main sections, some further subdivided into topics concerning different aspects of aetiology, pathophysiology, diagnosis, treatment methods – medication and surgical, percutaneous interventions, etc. Attention is paid to the controversy in the guidelines on the type of surgical treatment – valve prosthesis or MV plasty, as well as to the different data in randomized and non-randomized studies, which raises a number of questions for cardiologists and cardiac surgeons involved in the treatment of this type of complications of IHD. The structuring and subjects addressed in the literature review show a wealth of clinical experience and an excellent grasp of the issues. Focus is given to modern mathematical data processing methods, providing more exact data for assessing the issues examined.

Based on the literature review, Dr. Panayotova has arrived at conclusions regarding the significance of IHD and its associated issues in the present day. Ischemic MR significantly impacts the life-span and quality of life for those suffering from this complication. This suggests that these patients should undergo an echocardiography during the period of acute ischemia and at follow-up thereafter.

The **thesis aims** to use appropriate echocardiographic and clinical parameters to improve the quality and to digitize the certainty in the individualized choice of surgical treatment (combined CABG + MV Repair or isolated CABG surgery). Additionally, by applying fuzzy sets, it is aimed at the diagnosis of the medical condition (relatively preserved or relatively impaired) of IHD patients complicated by chronic ischemic mitral regurgitation. The goal is distinctly outlined and focuses on the digitization of data to optimize the type and volume of surgical treatment.

The five tasks the doctoral student sets are precisely defined and closely associated with the stated goal. The search for evidence of the positive effect of revascularization alone or combined with mitral valve repair on the extent of MR is noteworthy.

The clinical materials for the research include patient data of 169 patients operated on in the period 2007 – 2022 in the Cardiac Surgery Clinic at St. Marina University Hospital – Varna, where the doctoral student works. In 85 patients, the surgical intervention was combined with revascularization and MV plasty (MV Repair + CABG). In the remaining 84 patients, there was only isolated CABG surgery. The first pool of patients was divided into Group A and the second – into Group B. The group distribution was based on demographic, clinical and echocardiographic criteria. Echocardiography in each patient was performed preoperatively, in the early (5 to 30 days) and remote (6 to 54 months) postoperative period. A database including more than 70 parameters was constructed for each patient. Based on these data, patients in each major group, A and B, were divided into subgroups, A1 and B1, including patients with relatively preserved general and cardiac status, and A2 and B2, including patients with relatively impaired status. A 6-step Main algorithm (MA) is proposed to divide patients into groups A and B, and a 6-step Auxiliary algorithm (AAA) is proposed to divide group A patients into subgroups A1 and A2. A 7-step Auxiliary algorithm (AAB) is proposed to divide group B patients into subgroups B1 and B2. Several tables illustrate this patient allocation.

The **Results** section compares patients with similar characteristics using the "pseudo-control groups" method. In order to determine to what extent each patient bears the characteristics of one or another group and subgroup – "affiliation degree"- the "fuzzy samples" methods have been applied. Some patients are very suitable for the given procedure, and their affiliation degree would be 1. Other patients are unsuitable for that procedure; their affiliation score in the grading would be 0. Patients with subgroup affiliation degrees less than 0.5 were designated as outliers (atypical group members). The characteristics of such patients do not

affect the characteristics of the groups and subgroups. These patients may be subject to alternate decisions regarding the type and amount of surgical procedures.

The algorithms used to assign patients to groups and subgroups are illustrated by creating 49 examples (Appendix 1). These examples can serve as a practical guide for applying the algorithms by cardiologists and cardiac surgeons.

The results of surgical treatment on the integral indices "regurgitation fraction" and "degree of mitral regurgitation" are evaluated in this section. For this purpose, the "fuzzy pseudo-control groups" method, detailed in Appendix 2, was applied. Sophisticated mathematical models were used in the data processing, for which Dr. Daniela Panayotova was assisted by her research consultant Prof. Natalia Nikolova.

Four **conclusions** are logically derived from the overall material and its exposition, the statistical analyses performed, and the data interpretation. They confirm the value of the set goal and the tasks to achieve it. Utilizing the suggested algorithms provides guidelines for refining the indications for including patients in a group for isolated revascularization or combined surgery with MV plasty.

Contributions claims

The contributions of Dr. Panayotova's thesis are aimed at creating algorithms for more accurate stratification of patients into groups and subgroups appropriate for different surgical interventions. For this purpose, the use of a number of clinical and echocardiographic parameters is proposed. The parameters' analysis is aided by a 6-step algorithm determining the volume of surgery the patient is best suited for. Auxiliary 6- and 7-step algorithms determine each patient's affiliation degree to the appropriate subgroup according to the general and cardiological condition of patients. This may have clinical and prognostic significance. The positive impact of surgical intervention and mitral valve repair, particularly on the integral parameters "regurgitation fraction" and "degree of mitral regurgitation", is demonstrated. The existing CSC database at St. Marina University Hospital of patients with IHD complicated with IMR has been updated and expanded with new medical features – a prerequisite for furthering research in this area.

The **thesis summary** meets the requirements, and its contents corresponds to the thesis.

Conclusion

Dr. Daniela Panayotova's thesis is an in-depth study based on clinical data accumulated over 15 years. It concerns critical and relevant issues of the volume of surgical treatment in patients with IHD complicated by significant ischemic MR. The proposed stratification algorithms can refine the indications and volume of surgical intervention. The examples in Appendix 1 are a good representation of the utilization of the algorithms. They may facilitate the specialists involved in this type of treatment and may contribute to better outcomes in cardiology and cardiac surgery practice, respectively.

Dr. Panayotova has shown proficiency in constructing and using scientific databases, conducting research and summarising their results.

Considering all that has been conveyed thus far, the relevance and importance of the problems researched in the thesis, I submit my POSITIVE assessment and propose the Honourable Scientific Jury to vote positively for awarding the educational and scientific degree Philosophy Doctor to Dr. Daniela Stoyanova Panayotova in the scientific speciality Cardiology.

September 24th, 2023

Respectfully:

Sofia



Assoc. Prof. Vasil Velchev, MD, PhD