STATEMENT

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Regarding the doctoral thesis
for awarding the educational and scientific degree
in higher education area 7. Healthcare and Sports
7.1. Medicine– professional field,
Scientific speciality Cardiology

Doctoral thesis on the subject of

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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I have been appointed as a member of the Scientific Jury, pursuant to Order No. P-109-367/08.08.2023 of the Rector of the MU-Varna and accordingly, based on the protocol N: 1/11.08.2023, I have been tasked to prepare a position statement on the procedure for awarding the educational and scientific degree Philosophy Doctor to the candidate Dr. Daniela Stoyanova Panayotova.

Brief data on the professional development and qualifications of the PhD student: in 1986, Dr. Daniela Panayotova graduated from the Medical University of Sofia. In 1993 and 1998, she obtained Certificates of completion of special training in Internal Medicine and Cardiology, respectively. Since 2005, she has worked as a cardiologist at the Cardiac Surgery Clinic at St. Marina University Hospital – Varna. Since 2018, Dr. Panayotova has been an assistant professor at the Department of Cardiovascular Surgery and Angiology, Medical University of Varna. Her publishing activity is mainly related to the problems of diagnosis and treatment of heart surgery patients. She has co-authored several textbooks and manuals.

Relevance of the subject

Ischemic heart disease (IHD) is among the most prevalent heart conditions. When IHD is further complicated by ischaemic mitral regurgitation, the prognosis of patients deteriorates significantly. There are two approaches when surgical treatment is necessary – isolated revascularisation/coronary artery bypass graft (CABG) or combined treatment (revascularisation + mitral valve repair). There is no consensus on the optimal approach in patients with moderate to severe ischaemic mitral regurgitation (IMR). Some patients are suitable for a particular procedure, and others are not, but the decision is unclear and ambiguous for one-third of the patients. The studies performed so far are with relatively small groups and are difficult to compare because they differ in the diagnostic criteria and surgical techniques involved.

This unresolved problem impels the core of the research to develop a personalised patient stratification algorithm. The algorithm aims to aid the decision on the surgery volume for patients with IMR. The idea consists of building three fuzzy algorithms that result in the affiliation degree of each patient to a particular fuzzy subgroup. The approach is individualised to a considerable extent and reduces the risk of incorrect decisions.

Thesis structure

Dr. Daniela Panayotova's thesis is organised according to the requirements. It is presented in 170 pages and is illustrated with 15 figures, 32 tables and 42 mathematical formulas. The thesis includes an introduction and literature review (60 pages), aim and tasks (1 page), materials and methods (59 pages), results and discussion (14 pages), and conclusions and contributions (3 pages). The bibliography contains 324 sources, of which 5 are in Cyrillic.

Literature review

In the literature review, Dr. Panayotova discusses in detail the problem of secondary mitral regurgitation: definition, epidemiology, pathophysiology, classification, and diagnosis. The chapter on the diagnosis of secondary mitral regurgitation discusses the possibilities of various invasive and non-invasive imaging modalities.

Dr. Panayotova provides detailed information on the echocardiographic evaluation of the disease, reviewing both conventional and cutting-edge modalities of the method. A separate chapter is devoted to perioperative echocardiographic evaluation in IHD patients, including secondary mitral regurgitation. Current treatment options for IMR are presented – conservative, interventional, and surgical. The chapter on surgical treatment discusses the different surgical approaches and the outcomes and potential complications, respectively.

Based on the literature review, Dr. Panayotova concludes that IMR has overtaken aortic valve stenosis in prevalence in recent years. Current treatment of acute myocardial infarction, even when the infarct-related artery is vascularised on time by percutaneous coronary intervention, does not always prevent the development of IMR. This necessitates that all affected patients be accurately assessed in the early and remote post-incident period for the presence of IMR. There is still no consensus on the optimal strategy for the treatment of IMR in the short and long term. There are no straightforward algorithms for tailoring the treatment approach for patients with IMR.

Aim and tasks

The PhD student establishes the research aim as a logical continuation of the literature review. This study aims to use appropriate echocardiographic and clinical parameters to improve the quality and to digitise the certainty in the individualised 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.

Materials and methods

The research is based on patient data from the Cardiac Surgery Clinic at St. Marina University Hospital – Varna. The study included 169 patients with IHD and significant chronic IMR treated surgically. Of the included patients with CHD and significant chronic IMR, 85 had a combined intervention – revascularisation + mitral valve repair (MVR + CABG), and 84 had isolated revascularisation (CABG).

The parameters analysed were demographics, risk factors for atherosclerotic vascular disease, history of myocardial infarction, history of coronary intervention, coronary anatomy, functional class, comorbidities, etc. Echocardiographic evaluation of the heart and, specifically, of the IMR was an important part of the evaluation of patients. Dr. Panayotova gives detailed information about the assessed parameters illustrated with figures, which are her own material. Many parameters are specific and used primarily by specialists involved in the preoperative assessment of patients indicated for cardiac surgery.

Sophisticated mathematical models have been used to analyse the data and develop algorithms, for which the PhD student has been assisted by her research advisor, Prof. Natalia Nikolova, MD, PhD.

Results, discussion and conclusions

The following parameters were recorded and archived for each patient: 20 identifiers, 18 anamnestic and ultrasonographic preoperative parameters, and 13 dimensional (triple) parameters. Each tridimensional parameter represents three different values at different time points. Thus, each patient is described by a 75-dimensional record of the following parameters.

All 75 measurement records were analysed, and patients were divided into 4 groups: A1, A2, B1, and B2. However, this division does not explain to what extent each patient is suitable for one of the two main surgical interventions. 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. The affiliation grading score would be between 0 and 1 for the remaining patients. The scoring of patients undergoing isolated revascularisation (CABG) is not clear but ambiguous. The same applies to group A patients undergoing combined surgery. This led to the development of a basic fuzzy classification algorithm that provides the degree of affiliation to groups A and B.

This algorithm aims to establish the process of identifying the type of surgical treatment for patients with IHD complicated with IMR, which can be either isolated revascularisation (CABG) or revascularisation combined with mitral valve reconstruction (MV Repair + CABG). The choice of surgical treatment is formalised using the 6-step Main algorithm. For patients in groups A and B, a corresponding algorithm applied after the basic one is proposed.

Dr. Panayotova offers a complete system of examples for all possible combinations of the algorithm outcomes. The system contains 49 examples, each showing a specific or fictitious patient classified by the Main algorithm into one of the A or B groups. If the patient is classified with group A, the classification into subgroups A1 and A2 according to Algorithm AAA is presented. If the patient is classified in group B, the classification in subgroups B1 and B2 according to Algorithm AAB is presented.

Dr. Panayotova draws the following conclusions:

- The algorithms applied in this research calculate only the maximum value of four possible coefficients that predetermine the classification of a patient to a particular subgroup.
- If the maximum value of μ is less than 0.5, the patient is considered an outlier and does not participate in the following calculations. Thus, the characteristics of the subgroup can be more adequately estimated.
- Based on the different affiliation degrees, a different stratification of patients into groups and subgroups can be created, hence a different treatment recommendation.
- For the purposes of this study, we decided that four subgroups were an appropriate balance between the homogeneity achieved within the subgroups and the size of the resulting subgroup samples.

Contributions

Of the proposed contributions, I consider the following to be the most significant:

- For patients with IHD complicated by IMR, a 6-step fuzzy algorithm (MA) has been created. For each patient, the algorithm identifies the affiliation degrees to two inhomogeneous groups: A (CABG and mitral valve repair) or B (isolated CABG).
- Two conditional fuzzy algorithms were created to homogenise groups A and B stratification. If MA has unconditionally classified a patient into group A, the 6-step conditional fuzzy algorithm AAA computes the conditional affiliation degrees of the patient into two homogeneous subgroups by medical status: A_1 (relatively preserved) or A_2 (relatively impaired). If the MA has unconditionally classified a patient into group B, then the 7-step conditional fuzzy algorithm AAA calculates the conditional affiliation degrees of the patient to two homogeneous subgroups by medical status: B_1 (relatively preserved) or B_2 (relatively impaired).
- The MA, AAA and AAB algorithms are organised into a diagnostic-stratification system that determines the patient's subgroup (A_1, A_2, B_1 or B_2) for each patient with IHD complicated by IMR and his/her absolute affiliation degree in that subgroup.
- A complete system of 49 examples for all possible combinations of MA, AAA and AAB algorithms' outputs is created. It illustrates the application of the created fuzzy algorithms in a medically understandable way. In practical terms, such a system facilitates and personalises the decision-making approach to a complex medical situation such as IHD complicated with significant chronic IMR.

Thesis-related publications and scientific communications: Dr. Panayotova submitted four publications, one of which was published in an impact factor journal.

Conclusion

Dr. Daniela Panayotova's scientific inquiry focuses on an interesting yet incompletely resolved issue in cardiology and cardiac surgery.

The proposed algorithm for a personalised assessment of IHD patients indicated for surgical treatment is innovative and a prerequisite for further research. Dr. Panayotova's thesis fully meets the requirements for awarding the educational and scientific degree "Philosophy Doctor". This provides grounds to confidently propose to the esteemed scientific jury to vote positively for awarding the scientific degree "Philosophy Doctor" to Dr. Daniela Panayotova.

Varna, 17/09/2023

Assoc. Prof. Atanas Angelov, MD, PhD