O P I N I O N

by Prof. Dr. Plamen Georgiev Panayotov, PhD.

Medical University "Prof. Dr. P. Stoyanov "- Varna

Department of Cardiovascular Surgery and Angiology

Dissertation for the award of PhD "**Doctor**" In the field of higher education 7. Healthcare and sports, professional field 7.1. "Medicine", for scientific specialty and doctoral program "Cardiovascular surgery", code: 03.01.49. Approved members of the Scientific Jury according to order №641 /26.11.2021 of the Executive Director and the Procurator of the hospital Acibadem City Clinic UMHAT Tokuda EAD, Sofia.

Topic: "SURGICAL TREATMENT IN PATIENTS WITH PROSTHETIC VALVE

ENDOCARDITIS "

To Dr. Ivilin Plamenov Todorov

Cardiac Surgeon at the Clinic of Cardiac Surgery of ACIBADEM CITY CLINIC

UMBAL TOKUDA EAD,

assistant at the Medical Faculty of Sofia University "St. Kliment Ohridski "from 2019.

PhD student in free form of education at the Clinic of Cardiac Surgery of Acibadem City Clinic UMHAT Tokuda, Sofia.

Supervisor: Assoc. Prof. Dr. Dimitar Nikolov, PhD.

The candidate's career profile.

Dr. Ivilin Plamenov Todorov was born on July 30, 1982. He graduated from the National High School of Natural Sciences and Mathematics "Acad. L. Cholakov ". In 2007 he completed his higher education in Medicine at the Medical University in Sofia. He started working at the Clinic of Cardiac Surgery at Acibadem City Clinic University Hospital Tokuda - Sofia in October 2010, where he still works. In 2014 He has a specialty in cardiac surgery and has short-term specializations in cardiac surgery clinics in Europe.

General description of the presented materials materials.

I have been presented in electronic and printed form a dissertation and abstract, which meet the requirements of ZRASRB and the Regulations for its implementation in "Acibadem City Clinic University Hospital Tokuda" - EAD, Sofia. I am provided with copies of 2 of the dissertation-related publications in digital version.

The topic of the dissertation is topical and dissertable - prosthetic endocarditis (PVE) remains a serious problem in cardiac surgery, which is associated with difficulties in diagnosis and medical treatment and carries a high perioperative risk. Early and long-term

postoperative results depend to a large extent on timely and accurate indications for surgical treatment. In this sense, the search for appropriate laboratory tests, clinical and echocardiographic indicators, as well as the assessment of risk factors for adverse treatment outcomes can be particularly useful in future work not only of the dissertation but also of cardiologists and cardiac surgeons in the country.

The dissertation is presented on 132 pages, structured in 5 main sections with additional points in most of them. The main sections are: Introduction - 1 page; Literary review - 37 pages; Purpose and tasks - 1 page; Clinical material and methods - 22 pages; Own results - 28 pages; Discussion of the results - 12 pages; Conclusions and recommendations - 2 pages Bibliography - includes 208 titles, of which 11 in Bulgarian and 197 by foreign authors. 38 have been published in the last 10 years. The dissertation is illustrated with 38 tables, 5 diagrams and 15 figures and 9 photos from clinical practice. Contributions according to the author: with scientific-applied and original character - 7; with confirmatory character - 5;

In the **introduction,** the dissertation substantiates the significance of the problem with PVE . There is no consensus worldwide on diagnosis and treatment, including the exact timing of surgery.

The literature review includes 12 sections, some of which have subsections, such as the pathogenesis, clinical features, diagnostic methods (10 subsections, including new diagnostic methods), surgical and medical (7 subsections on various microbial agents) treatment. Data on the results of PKE treatment are cited. The last point of the literature review is "Challenges and future perspective", in which the author makes 11 logical and generalizing conclusions, which is a positive quality of this dissertation.

The main goal of the dissertation is "To compare the clinical characteristics and results of surgical treatment of patients with early and late prosthetic valve endocarditis with emphasis on nosocomial PVE, in order to determine the factors leading to high risk of complications and nosocomial mortality." clearly defined and emphasizes the possibilities for prevention, timely diagnosis and treatment of PVE.

The 5 tasks set by the author are specific and directly related to the set purpose.

The **clinical material** of the dissertation includes a retrospective study of data for 79 patients operated with PVE in a period of about 11 years. in cardiac surgery, where the dissertation works. These patients are part of a total of 330 cardiac reoperations performed during the same period in this institution. Excluded from the study were patients operated on for PVE after COVID-19 infection due to insufficient worldwide data on possible links between these conditions. Patients with PVE are divided into 2 groups - group 1 with early PVE (EPVE) including 33 (41.77%) patients, and group 2 with late PVE (LPVE) - 46 (58.23%) patients. The data were collected retrospectively from medical records at Tokuda Hospital. The follow-up is for a period of 2 months after the operative intervention, as the data are from coupons for check-ups, telephone interviews and contact with GPs. The division of patients into 2 groups is in accordance with the most common criteria for early and late PVE in time, with a limit of 365 days after the initial valve prosthesis.

All patients had blood cultures and material from the infected valve prosthesis examined, but no clear correlation was found between the two.

The surgical technique of PVE re-operations is described in detail and illustrated with photographs. The details of planned and emergency surgery are well given, as well as the criteria for the need for peripheral cannulation, or readiness for such before sternotomy. The merit of the author of the dissertation is the inclusion in the study of patients with previous coronary surgery with a passable LIMA graft. After 2015, "LIMA angiographic balloon occlusion" is applied.

The dissertation includes patients who underwent a course of antibiotic treatment and elective surgery, as well as those in whom surgery was performed in a short time or urgently without time for a sufficiently long course of antibiotics.

All patients had echocardiographic assessment of cardiac function and valvular pathology, with a predominance of transesophageal (TEE) over transthoracic (TTE) echocardiography. This is in line with current practice in such patients.

The information about the parameters studied in the dissertation is collected and processed with modern methods, including SPSS v.16 and a package of basic statistical methods used in medical practice.

In the sections "**Own results**" and "**Discussion of results**" Dr. Todorov analyzes the results of his study, giving demographic characteristics of patients and types of heart surgery to which they are subjected. There are tables and diagrams that give a clear idea of the results of comparisons of the two groups of patients and statistical analyzes. The difference in mortality found in the study is impressive - it is about three times higher in patients with reoperation for late PVE than in patients with early PVE. The analysis of over 30 indicators, as a statistically significant difference in the comparison between survivors and deceased patients was found in 12 of these indicators. Reoperation with replacement of two or more valves, followed by severe heart failure requiring IABP, urgency of surgery, preoperative sepsis and shock, aortic cross-clamping times, and CPB time have been found to be most prevalent.

A difference was found in the microbiological characteristics of early and late PVE. In both groups of patients the cases with negative blood cultures are very high - 54% in group 1 and almost 61% in group 2. To verify the cause of infection in more than half of the patients did not help and sent for testing material from explanted infected valve.

Significant part of dissertation is given to the approach to a patent LIMA graft - patients are divided into group. A -with catheter balloon occlusion and group B— without such occlusion during the operation. As a result of the collected and processed information, it is concluded that the balloon occlusion of the arterial graft during the operation is

relatively low-risk procedure with good results in terms of myocardial protection and postoperative laboratory parameters.

In the final section "**Conclusions and recommendations**" are 10 conclusions that follow logically from the overall material and its presentation, statistical analyzes and interpretation of data. Confirm the value of the goal and the tasks to achieve it, using a panel of predictive criteria for unfavorable outcome. Emphasis on the diagnostic predominance of TEE over TTE. Routine transcatheter intraoperative temporary occlusion of a permeable arterial graft is introduced.

Critical remarks and recommendations.

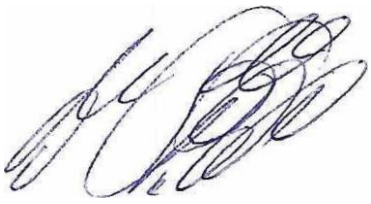
There are no literature sources published in the last 5 years.

Contributions with scientifically applied and original character - I consider significant and the seven described by the author - are based on a relatively large series of patients, which is an achievement of the scientific papers published in Bulgarian practice.

Contributions of a confirmatory nature - I consider the contributions indicated by the author in five points to be significant.

Conclusion - The dissertation of Dr. Ivilin Todorov is a thorough study of significant clinical material for an 11-year period, which concerns important and current issues for prosthetic valve endocarditis - early and late.

Based on all the above, the relevance and importance of the issues studied in the dissertation, I give my **POSITIVE** assessment and invite the Honored Scientific Jury to vote positively for the award of educational and scientific degree "**Doctor**"- PhD of Dr. Ivilin Plamenov Todorov in the scientific specialty and a doctoral program in Cardiovascular Surgery.



December 29, 2021 Prepared:

Varna Prof. Dr. Plamen Panayotov, PhD.