

R E V I E W

By Prof. Dr. Kiril Vasilev Draganov, DSc

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on the doctoral thesis for awarding the educational and scientific degree of '**Philosophy Doctor**'

Field of Higher Education: 7. Healthcare and Sports, direction 7.1. Medicine

Scientific Specialty: Cardiac Surgery

Author: Pavlin Lyubenov Manoilov, MD

Doctoral Form: Independent study

Institution: Department of Cardiovascular Surgery and Angiology, Cardiac Surgery Clinic, Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

Thesis Subject: Epidemiology, Risk Factors and Clinical Presentation of Wound Infections After Sternotomy. Prevention and Treatment Trends in the Cardiac Surgery Clinic

Research supervisor: Prof. Plamen Panayotov, MD, PhD, Department of Cardiovascular Surgery and Angiology, Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

I was appointed as a member of the scientific jury for the defence of the above-mentioned doctoral thesis by Order № R-109-1/ 02.01.2025 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, Prof. Dimitar Raykov, MD, DSc.

At its first meeting, I was appointed as a reviewer.

1. Overall presentation of the procedure and the doctoral candidate

The doctoral candidate Pavlin Lyubenov Manoilov, MD, submitted the required documentation on electronic media. It fully complies with the current regulations in the country as stated by the Development of Academic Staff in the Republic of Bulgaria Act (DASRBA) and the Rules and Regulations for Academic Staff Development at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

At the end of the thesis, Dr. Manoilov provided a list of 9 scientific forum presentations and 7 full-text publications (pp. 110 –111).

Notes and remarks on the documentation

The thesis defence procedure and related documents meet the requirements of the current regulations in the Republic of Bulgaria.

Brief biographical data

Dr. Pavlin Lyubenov Manoilov graduated from Medical University – Pleven in 1991. From 1991 to 1997, he worked as an occupational physician in the Lyaskovets Clinic, Veliko Tarnovo region. Subsequently, until 2009, he was a surgeon at Dr. Stefan Cherkezov Regional Hospital, Veliko Tarnovo. For two years, from 2000 to 2002, he was an auditor at the Regional Health Insurance Fund, Veliko Tarnovo. From 2009 to 2011, he specialised in cardiac surgery at Ospedale Niguarda, Milan, Italy. In 2011, Dr. Pavlin Manoilov joined the Cardiac Surgery Clinic at St. Marina University Hospital – Varna, and since 2019 has been an assistant professor at the Department of Cardiovascular Surgery and Angiology, Medical University "Prof. Dr. Paraskev Stoyanov" – Varna. He has acquired certificates in two specialities – in Surgery (1999) and in Cardiac Surgery (2018).

2. Relevance of the subject

The thesis holds significance for Bulgarian medicine in terms of both its scientific and practical application. Wound complication issues, their occurrence, timely diagnosis, treatment and prevention in surgical interventions, particularly in cardiac surgery, have been analysed in numerous past, present, and likely future studies. According to the literature, superficial and deep sternotomy infection rates after cardiac surgeries range from 0.4% to 15.0%, with mediastinitis affecting 1.0 – 5.0% of patients. Mortality for deep infections ranges from 9.1% to 14.0%, and for mediastinitis reaches a shocking 47.0%. Adverse infection consequences after cardiac surgery include: extended hospital stay; significant human and financial resource expenditure; long-term patient quality of life deterioration; and potentially fatal outcomes. The presence of risk factors for wound complications in cardiac operations is something surgeons need to be aware of, yet influencing these factors is challenging. These risk factors could be: advanced-age patients; polymorbid conditions; obesity; diabetes; generalized vascular damage, etc. While some risk factors are unalterable, certain pre-operative, operative, and post-operative measures can significantly reduce infectious complication risks.

These various factors motivated the research conducted by the doctoral candidate.

3. Problem understanding

The literature review is presented on 57 pages (from page 8 to page 64 inclusive).

Dr. Manoilov comprehensively examined contemporary information regarding wound infections in cardiac surgery. After a brief historical overview of the issue, the main points of the pathogenesis of the complication are indicated. Essential for practice are the definitions of Oakley and Wright, according to which two types are distinguished according to localisation, clinical presentation and severity: *sternal dehiscence* (characterised by the absence of clinical or microbiological infection evidence) and *mediastinal wound infection* with two subtypes – superficial wound infection or mediastinitis with/without mediastinal sepsis and with/without unstable sternum.

The review extensively addresses the social and economic aspects of surgical site infection, the classification and diagnostic methodologies with references to significant international research studies from the United States, United Kingdom, Japan, and Germany.

Key sections in the literature review include: risk factors for sternal infections (pages 25–34), microbiological considerations (pages 34–37) and treatment options and modern antiseptic characteristics (pages 37–43). Innovative treatment perspectives are presented. The review introduces the Negative Pressure Wound Treatment (NPWT) method, representing a contemporary approach to wound management.

The review concludes by consolidating prevention methods across three critical stages: pre-operative, intra-operative and post-operative.

The literature review comprises 50% of the thesis and significantly exceeds the standard 25–30% volume. Some introductory information is perceived as overly basic. Some of the figures are personal case study photographs (also not accepted to be included in the literature review). Despite minor limitations, the extensive review demonstrates Dr. Manoilov's comprehensive understanding and commitment to thorough scientific investigation.

4. Research objective, tasks, and methodology analysis

The thesis aims to minimise the risk of sternal wound infections after cardiac surgery and to optimise the management of this serious complication. To achieve his objective, Dr. Pavlin Manoilov formulated / tasks. Six of these tasks are precise, clear, and allow for in-depth scientific investigation. I consider Task #5 redundant (To present the frequency of wound

infections in the Cardiac Surgery Clinic, Varna over a nine-year period), significantly overlapping with Task #1 (... analysis of own results and study of the epidemiology of postoperative wound infections in the Clinic of Cardiac Surgery – Varna). Task #5 is also inconsistent with the findings of the two studies (Study 1 and Study 2) mentioned below in "Material and Methods", and conducted over a period of 3 and 1 year respectively. Indeed, on pages 75–76, the incidence of sternal wound infections at the doctoral student's institution is presented over a 9-year period in tabular form. However, this data lacks commentary (the narrative is absent), is not subjected to statistical evaluation, and is not analysed. Therefore, it cannot serve as a basis for discussion, for formulating conclusions and recommendations. In one sentence in the "Discussion" section, on page 79, a decrease from 7.45% at the beginning of the period to 1.47% at the end is found.

The research material subjected to processing and analysis is relatively large for the scale and volume of Bulgarian cardiac surgery. There are 118 (101 + 17) patients with sternal wound infection included and 101 without such infection after cardiac surgery (based on a total of 1859 interventions performed). For the purposes of the study, they were divided into three groups (cohorts) in which two retrospective studies were performed:

- ✓ Study 1, Target group of n=101/1354 cases, over a 3-year period;
- ✓ Study 2, Target group of n=17/505 cases, over a 1-year period;
- ✓ Control (reference) group, n=101 cases, without development of wound infection but with similar other indicators to the other two groups.

Study 2 was conducted after implementing the Prevention of Wound Infections Protocol after cardiac surgery at the Cardiac Surgery Clinic, St. Marina University Hospital – Varna (hereinafter referred to as "the Protocol").

In all patients, the doctoral candidate investigated 17 potential risk factors for the development of infectious complications. They are presented in tabular form (Tables 12 – 28 inclusive), as absolute numbers for qualitative indicators (without calculated percentages) or average values for quantitative ones (without minimum-maximum values indicated). The tables do not include explanatory comments, and the figures have not been subjected to statistical processing.

The statistical methods used to analyse the results and assess reliability (significance) are standard for this type of scientific output, with descriptive statistics predominating.

5. Characteristics and evaluation of the thesis and its contributions

The thesis is 133 pages long. The visualisation is rich – 50 tables, 24 figures (pictures) and 1 diagram. There are two diagrams, but one of them (on page 78) is not numbered and titled. Some pictures (e.g., those numbered 2–8) are placed in the "Discussion" chapter, without a specific connection to the text. It would be appropriate for them to be included in the methods and/or results sections.

The bibliography is comprehensive, current, and representative, including 335 sources.

The notes and comments on the literature review, aim and tasks, materials and methods were mentioned earlier in the review. Here, I will focus on the achieved results, their presentation and discussion, conclusions, and contributions.

The results are important from a practical perspective. They are presented in descriptive and tabular form.

In Study 1 and Study 2 (before and after the protocol implementation, respectively), the frequencies of deep and superficial wound infections were 1.32% versus 1.18% and 6.13% versus 2.17%. This shows that a decrease was registered after the Protocol implementation.

Three out of 17 investigated risk factors significantly influenced the occurrence of postoperative wound infection in Study 1: diabetes mellitus; BMI > 25; duration of artificial lung ventilation. These are presented in Tables 30 and 31, with the latter repeating three rows from the previous table and, in my opinion, is redundant.

In Study 2, the significant risk factors were also three: chronic heart failure; duration of artificial lung ventilation; low albumin levels. The information is tabulated in Tables 34 and 35, and the comment for the second table corresponds closely with that for Tables 31 and 30.

I highly appreciate the data provided by the doctoral student in the discussion section regarding the financial and social implications of sternal wound infections after cardiac surgery. There is information for 11 cases, 6 of which were rehospitalized, with a significant imbalance between revenues and treatment costs.

The supplemented and adapted Protocol for Preventing Wound Infections, implemented in the Cardiac Surgery Clinic at St. Marina University Hospital – Varna, is one of the most valuable aspects of the thesis. It was developed based on the protocol proposed by P. Vogt et al., which contains 16 preventive measures distributed across three main stages of a cardiac patient surgical treatment: pre-, intra-, and post-operative. The protocol used in the institution of the doctoral candidate contains detailed activities and measures described in 10 sections, numbered with Roman numerals. The protocol is thoroughly presented in the Discussion section.

Comparing the results obtained before and after the Protocol implementation (Table 37, page 75) establishes a significant reduction in the frequency of this complication ($P = 0.0007$), which represents clear evidence of its effectiveness and functional value.

A relatively innovative method for treating deep sternal infections after cardiac surgery is the application of Negative Pressure Wound Therapy (NPWT). In the clinic where Dr. Manoilov works, the methodology was used in 109 cases with excellent results, including patients with decubital wounds in the sacrum area or severe lower limb infections after saphenous vein harvesting for venous autograft. Emphasis is similarly placed on applying closed incision Negative Pressure Wound Therapy (ciNPWT) as a preventive measure for patients with significant risk factors for sternal infections. This approach requires additional research to establish itself as routine, as discussed by the doctoral candidate.

On pages 108–109, Dr. Pavlin Manoilov presents 11 conclusions, which logically wrap up the thesis. Some conclusions are confirmatory, in line with literature data, while others result from a comprehensive analysis of the obtained original results. Conclusions No. 4 (*The introduction of the Prevention of Wound Infections Protocol reduced these complications in the Cardiac Surgery Clinic – Varna.*) and No. 5 (*Strict adherence to the Prevention of Wound Infections Protocol could lead to a stable trend of decreasing wound infection frequency*) are almost identical to me. Conclusion No. 9 (*Introduction of new programs, products, and technologies based on new research that could contribute to reducing wound complication frequency*) probably refers to the same Protocol.

The doctoral candidate presents 3 thesis contributions, which are precisely and clearly formulated.

6. Assessment of the publications and the doctoral candidate's personal contribution

With respect to the publications authored by Dr. Manoilov, I would like to offer the following comments. Not all titles are related to the thesis subject. Moreover, most of them are partially or entirely repetitive. For example: presentation 4.1.1. (Heart Tumors and Cysts) and publication 4.2.1. (Tumors and Cysts of the Heart); presentation 4.1.2. (Risk Factors for Wound Infection in Cardiac Surgery – Brief Literature Review, Own Experience, Risk Models) and publications 4.2.2. (Risk Factors for Wound Infection in Cardiac Surgery – Brief Literature Review, Risk Models) and 4.2.3. (Risk Factors for Wound Infection in Cardiac Surgery -

Literature Review, Own Experience, Risk Models); presentation 4.1.8 (Implantation of a Hemodialysis Catheter Directly in the Right Atrium Due to Exhaustion of Vascular Access) and publications 4.2.5. (Implantation of a hemodialysis catheter directly in the right atrium due to exhaustion of vascular access) and 4.2.6 (Haemodialysis catheter placement directly in the right atrium due to exhausted vascular access options).

Nevertheless, the number of original and non-repetitive scientific works related to the thesis subject meet the requirements for obtaining the educational and scientific Philosophy Doctor degree. In this regard, I can point out presentation 4.1.3. (Prevention of wound infections in the Cardiac Surgery Clinic, St. Marina University Hospital – Varna; Study, Experience, Results), 4.1.9. (Results of Prevention and Treatment of Chest Wound Infections After Sternotomy for a 9-Year Period) and publications 4.2.4. (Results of prevention and treatment of sternal wound infections after sternotomy over a 9-year period), 4.2.7. (Application of NPWT in patients after cardiac surgery - Literature Review and Own Experience).

After a detailed review of the thesis and the related publications, I highly evaluate the overall work of Dr. Pavlin Lyubenov Manoilov on the issues of diagnosis, treatment, and prevention of infectious complications after sternotomy. I consider the thesis to be a sufficiently in-depth study. Its research, the obtained results, their analysis, the conclusions and the contributions validate the personal merits of the doctoral candidate.

7. Critical remarks and recommendations

The critical remarks regarding Dr. Pavlin Manoilov's thesis were pointed out in the individual sections of the review. Despite these critical observations, I believe that the conducted research possesses the necessary qualities for such scientific production, and I give a positive assessment of the efforts made by the doctoral candidate.

8. Thesis summary

The thesis summary meets the requirements in terms of volume and content, providing a clear understanding of the essential aspects of the research, and sufficiently detailing the achieved results and formulated conclusions.

CONCLUSION

The thesis by Dr. Pavlin Lyubenov Manoilov on the subject of “Epidemiology, Risk Factors, and Clinical Presentation of Wound Infections After Sternotomy. Prevention and Treatment

Trends in the Cardiac Surgery Clinic” contains scientific and practical applications that make a distinct contribution to scientific knowledge. They meet the requirements of DASRBA and the Rules and Regulations for Academic Staff Development at the Medical University "Prof. Dr. Paraskev Stoyanov" –Varna. The submitted documentation and thesis results fully correspond to the specific requirements, they are original, and no plagiarism has been established.

The thesis demonstrates that the doctoral candidate possesses in-depth theoretical knowledge and professional skills, showcasing qualities and abilities for independent scientific research.

Based on the above, I give my positive assessment of the conducted research and propose to the esteemed scientific jury to award the educational and scientific degree of Philosophy Doctor to Dr. Pavlin Lyubenov Manoilov, for which I confidently cast my POSITIVE vote.

Reviewer:

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
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20/01/2025

(Prof. Kiril Draganov, MD, DSc)