

## REVIEW

by Academician Prof. Dr. Grigor Angelov Gorchev, MD, DSc, specialist in Obstetrics and Gynaecology, Surgery and Oncology, Professor at the Medical University of Pleven, Academician of the Bulgarian Academy of Sciences

of a dissertation submitted for the award of the scientific degree **“Doctor of Sciences”**

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Title of the dissertation: **“Modern Surgical Approaches in Malignant Diseases of the Gastrointestinal Tract- Clinical and Epidemiological Aspects in Northeastern Bulgaria”**

Field of higher education: 7. Healthcare and Sports, Professional field: 7.1 Medicine

The dissertation consists of 248 pages and is illustrated with 3 panels of photographic material, 29 figures, and 61 tables, as well as Appendices provided on electronic media.

The bibliography comprises 1068 references, cited as follows: 171 references listed in the Literature Review, Part I; 33 references listed in the Literature Review, Part II; 796 references used in the preparation of the PICOS analysis; and 68 references distributed across the remaining chapters of the dissertation.

### 1. RELEVANCE OF THE SCIENTIFIC PROBLEM

Malignant diseases of the gastrointestinal tract represent one of the most serious health threats in the modern world. They are among the leading causes of mortality and disability in both developed and developing countries. According to data from international epidemiological registries, colorectal carcinoma is the third most common cancer worldwide and the second leading cause of cancer-related mortality. A similar trend is observed in other neoplasms of the gastrointestinal tract,

including gastric cancer, pancreatic cancer, and hepatocellular carcinoma. The situation in Bulgaria is particularly concerning, where unfavorable trends in cancer incidence and mortality have been observed. Available data indicate that Bulgaria is among the few countries in the European Union where an increase in cancer-related mortality has been recorded over the past decade. This underscores the need for in-depth scientific research aimed at improving the diagnosis and treatment of oncological diseases. In this context, the study of contemporary surgical approaches in gastrointestinal neoplasms is of particular importance. Surgical treatment remains the main therapeutic method for a large proportion of these diseases, and treatment success depends on multiple factors, including the stage of the disease, the surgical technique used, the presence of comorbidities, and the quality of postoperative care. A particularly relevant aspect of modern oncology is the development of multimodal therapeutic strategies that combine surgical treatment with chemotherapy, targeted therapy, and immunotherapy. This approach enables a significant improvement in both patient survival and quality of life.

## **2. SIGNIFICANCE OF THE RESEARCH**

The dissertation of Prof. Dr. Kostadin Angelov fits exceptionally well within the contemporary scientific trends in the field of oncological surgery. A particularly valuable aspect of the study is the analysis of the clinical and epidemiological characteristics of gastrointestinal neoplasms in Northeastern Bulgaria. Such regional studies are of great importance, as they make it possible to identify specific trends and characteristics in disease incidence that may be associated with demographic factors, socio-economic conditions, lifestyle, and access to healthcare services.

The results of such studies can be used in the development of national and regional programs for the prevention and early diagnosis of oncological diseases.

## **3. STRUCTURE AND SCOPE OF THE DISSERTATION**

The dissertation is presented in a substantial volume and includes all the necessary structural elements.

The work contains: an extensive literature review; clearly formulated aims and objectives; a detailed description of the methods used; a systematic presentation of the results; an in-depth discussion; and well-substantiated conclusions, as follows:

1. Introduction- 3 pages
2. Literature Review- 116 pages
3. Aim and Objectives- 1 page
4. Materials and Methods- 4 pages
5. Analysis of the Research Results- 72 pages
6. Discussion of the Results and Conclusions of the Dissertation- 14 pages
7. Contributions- 2 pages
8. Recommendations- 1 page
9. Scientific Publications Related to the Dissertation- 2 pages
10. References- 19 pages
11. Appendices- provided on electronic media

The structure of the dissertation is logical and well organized. The presentation is clear and consistent, which facilitates the comprehension of the information presented.

#### **4. ANALYSIS OF THE LITERATURE REVIEW**

The literature review is exceptionally comprehensive and covers a wide range of scientific publications related to gastrointestinal oncology. The author examines the main etiological factors that play a role in the development of gastrointestinal

neoplasms. Among these, particular attention is given to smoking, alcohol consumption, dietary factors, and chronic inflammatory diseases.

In esophageal carcinoma, for example, smoking and alcohol consumption have been identified as major risk factors, with their effect being synergistic and significantly increasing the risk of developing the disease. The author also discusses the role of gastroesophageal reflux disease as a leading risk factor for the development of esophageal adenocarcinoma.

## **5. RESEARCH METHODOLOGY**

The methodological approach of the study is well developed and includes the use of modern statistical methods.

Particular attention is devoted to the analysis of comorbidities in patients with gastrointestinal neoplasms. The presence of comorbidities may significantly influence the outcomes of surgical treatment, as well as the risk of postoperative complications. The analysis of comorbidities was performed using codes from the International Classification of Diseases (ICD), which allows for a standardized assessment of accompanying diseases.

## **6. ANALYSIS OF CLINICAL RESULTS**

The obtained results demonstrate clearly defined trends in the structure of gastrointestinal neoplasms in the studied region. Particularly noteworthy is the analysis of the length of hospital stay for the different diagnoses. For example, in patients with rectal carcinoma, the average hospital stay is approximately 9 days, which is relatively close to the values reported in the international literature. This result indicates that the surgical treatment of these patients is performed at a high professional level and meets the contemporary standards of oncological surgery.

## **7. DISCUSSION OF THE RESULTS**

The discussion section of the dissertation represents one of its strongest aspects. The author analyzes the obtained results in the context of the existing scientific literature, comparing them with data from international clinical studies.

Particular attention is given to the role of minimally invasive surgery in the treatment of gastrointestinal neoplasms. This approach is associated with several advantages, including:

1. reduced surgical trauma
2. faster patient recovery
3. shorter hospital stay
4. lower risk of postoperative complications.

## **8. SCIENTIFIC CONTRIBUTIONS**

The scientific contributions of the dissertation may be systematized into several main directions:

### **8.1. ORIGINAL CONTRIBUTIONS OF SCIENTIFIC-THEORETICAL AND METHODOLOGICAL SIGNIFICANCE**

5. For the first time in Bulgaria, surgical oncological pathology has been analyzed through the framework of Health Technology Assessment (HTA) by means of a retrospective observational study of electronic medical records derived from real clinical practice.

6. For the first time in the scientific literature, a systematic review of scientific publications following the PRISMA standard has been conducted for the evaluation of surgical oncological practice in diseases of the gastrointestinal tract.
7. For the first time in international surgical research practice concerning oncological gastrointestinal diseases, a study assessing clinical effectiveness based on the PICOS framework has been conducted.
8. For the first time in Bulgaria, a narrative observational study of contemporary surgical approaches to the treatment of malignant diseases of the gastrointestinal tract has been carried out at both international and national levels, based on an analysis of scientific publications by Bulgarian authors.
9. For the first time in Bulgaria, an epidemiological study of malignant diseases of the digestive tract has been conducted on the basis of a systematic analysis of data from the European Cancer Information System (ECIS) and the International Agency for Research on Cancer of the World Health Organization (IARC/GLOBOCAN).
10. For the first time in Bulgaria, a local-regional longitudinal retrospective study of malignant diseases of the gastrointestinal tract has been conducted, covering one of the six administrative regions of the country.
11. An original author-designed protocol for a retrospective study has been developed, together with a unique research toolkit for conducting systematic reviews of scientific publications aimed at evaluating surgical interventions.
12. An original author-modified version of the PICOS framework intended for the evaluation of oncological gastrointestinal diseases has been developed. In addition to the standard five elements- P (Population), I(Intervention), C (Comparator), O (Outcome), and S (Study Design)- the modified instrument includes Tumor type, TNM classification, ECOG performance status, and Type

of surgery (radical/palliative). This modified version of the PICOS framework (which may be referred to as a'Modo Angelov) represents an original contribution of international significance. Without the inclusion of these additional elements in the PICOS framework, the assessment of the clinical effectiveness of surgical interventions would not be possible.

## **8.2. CONTRIBUTIONS OF SCIENTIFIC-APPLIED SIGNIFICANCE**

1. The study enriches the knowledge of medical specialists regarding the practical application of retrospective studies based on electronic medical records, both for the purposes of the healthcare system and for fundamental medical science and clinical practice.
2. The scale of the processed data and the obtained results are generalizable and extrapolatable at both national and international levels.
3. The study identifies three main future directions:
  - the transition toward minimally invasive surgery;
  - the critical importance of precise lymphadenectomy and pathological assessment;
  - the increasing focus on the optimization of perioperative management.
4. National and international epidemiological data demonstrate persistent geographical differences in incidence and outcomes, with higher rates of gastric cancer and colorectal carcinoma observed in Eastern Europe and East Asia. These differences highlight the need for regionally adapted screening programs and therapeutic protocols.
5. The future of surgical oncology in gastrointestinal diseases is increasingly determined by multidisciplinary collaboration, molecular tumor profiling, and the integration of digital tools for surgical navigation and planning. These

factors encourage the application of precision medicine and the personalization of surgical treatment according to the individual characteristics of each patient.

6. Innovative surgical techniques and their added benefits are presented and analyzed in depth.
7. A relationship is demonstrated between the lack of precise tumor staging in the scientific literature and a fundamental methodological shortcoming, observed not only at the national but also at the international level.

### **8.3. CONTRIBUTIONS OF A CONFIRMATORY NATURE**

13. Based on the systematic review of 171 scientific publications, it has been confirmed that:
  1. esophageal cancer is an aggressive malignant disease with a poor prognosis despite significant advances in multimodal therapy;
  2. the prognosis for gastric cancer remains unfavorable, primarily due to late diagnosis;
  3. the prognosis for small bowel cancer is highly variable and is determined mainly by tumor histology and the stage at diagnosis;
  4. malignant tumors of the colon, rectum, and anal canal, although anatomically adjacent, represent distinct disease entities with unique epidemiological, etiological, molecular, and clinical characteristics;
  5. malignant tumors of the colon continue to have the highest incidence among gastrointestinal tract tumors;
  6. pancreatic cancer remains one of the most lethal malignancies, characterized by challenging epidemiology, late diagnosis, and complex molecular biology despite advances in pharmacological therapies;

7. cancers of the gallbladder and bile ducts are aggressive malignancies with increasing incidence, particularly with regard to intrahepatic cholangiocarcinoma;

8. despite significant progress, the treatment of liver cancer continues to represent a major clinical challenge.

## **9. BIOGRAPHICAL DATA**

Prof. Dr. Kostadin Georgiev Angelov, MD, PhD, MHM, MF was born on 7 June 1977 in the city of Sliven, Bulgaria. In 2004 he graduated in Medicine from the Medical University of Sofia, and in 2006 he obtained a Master's degree in Public Health and Health Management. In 2010 he acquired the specialty in Surgery. In 2014 he successfully defended his dissertation and obtained the educational and scientific degree "Doctor" (PhD) in the scientific specialty Surgery. In 2015 he was elected Associate Professor, and in 2020 he was elected Professor at the Medical University of Sofia. His academic career is associated with the Department of Surgery at the Faculty of Medicine, Medical University of Sofia, where he successively held the positions of Assistant Professor, Associate Professor, and Professor. In his teaching activity, Prof. Angelov delivers lectures and practical training in surgery to students of Medicine and Dental Medicine, as well as training for intern physicians, residents, and doctoral students. He actively participates in the education and training of young specialists, serving as a scientific supervisor of PhD students and medical residents, and is the author of numerous reviews and expert opinions in procedures for awarding scientific degrees and academic positions.

Prof. Angelov's research activity is focused on the problems of modern surgery, with a particular contribution in the field of the surgical treatment of malignant diseases of the gastrointestinal tract. He is the author of a significant number of scientific publications in Bulgarian and international scientific journals, some of which have been published in journals with impact factor and indexed in international scientific databases such as Web of Science, Scopus, and ResearchGate.

His scientific works have received considerable attention in the scientific literature and have been widely cited.

Prof. Angelov actively participates in the scientific and academic community, being a member of several scientific and professional organizations, including the Bulgarian Surgical Society, the International Gastric Cancer Association, the International Society of Surgery, and the European Society for Medical Oncology. He has also participated in the editorial activities of scientific journals, including serving as Secretary and Editor-in-Chief of the journal “KHIRURGIYA” (Surgery), the official journal of the Bulgarian Surgical Society.

His teaching and scientific activities have been highly appreciated by both the academic community and students. In 2012, he was awarded “Best Lecturer” by medical students, and in 2015 he received the “Prof. Dr. Parashkev Stoyanov” Award for outstanding achievements in medical science and teaching.

## **10. ADDITIONAL DOCUMENTS**

1. An extended abstract of the dissertation in Bulgarian, prepared in accordance with the requirements of the Medical University of Varna, and in English;
2. An application to the Rector for the initiation of the defense procedure;
3. A professional (academic) curriculum vitae signed by the candidate;
4. A certified copy of the diploma for the completed educational qualification degree “Master”, together with its supplement;
5. A certified copy of the diploma for the acquired educational and scientific degree “Doctor (PhD)”;
6. A completed standardized report demonstrating compliance with the minimum requirements for obtaining the scientific degree “Doctor of Sciences”, including both paper and electronic versions of the supporting documents, issued by the Medical University of Varna;

7. A report on the original scientific contributions;
8. A declaration of originality of the dissertation and absence of co-authorship claims;
9. A declaration of authenticity of the submitted documents;
10. A list of publications related to the topic of the dissertation (no fewer than 10 publications), signed by the candidate;
11. Copies of the publications related to the topic of the dissertation;
12. Completed information cards of the National Centre for Information and Documentation (NACID) in Bulgarian and English;
13. A summary of the dissertation in English;
14. A similarity report of the dissertation and the scientific works submitted within the procedure for obtaining the scientific degree “Doctor of Sciences”, compared with scientific materials available online, including scientific databases and internet sources, issued by the Medical University of Varna.

The listed documents provide the following information:

The present dissertation is an original independent scientific work, which shows 0% similarity with the dissertation submitted for the educational and scientific degree “Doctor (PhD)” and 3% similarity with internet sources. These data demonstrate the genuine scientific contribution and the high standards that Prof. Angelov applies in the preparation of his scientific work.

A total of 24 scientific publications have been presented, 15 of which are related to the dissertation, as well as one chapter in a monograph. These scientific works do not require additional reviewing within this procedure, as they have already been published in journals where each publication undergoes peer review prior to official publication. The total number of points accumulated by Prof. Angelov from these scientific publications is 2180.85, which exceeds the minimum requirements for

obtaining the scientific degree “Doctor of Sciences” by more than twenty times, demonstrating the value and significance of the candidate’s scientific output. His scientific works have been cited more than 130 times. The total impact factor of Prof. Angelov’s publications is 59.706, with 24 publications in total, 10 of which participate in the present procedure.

The main contributions of these 24 scientific publications can be summarized in the following areas:

1. Inflammatory bowel diseases;
2. Laparoscopic rectal resection;
3. Predictors of colorectal anastomotic insufficiency;
4. Minimally invasive techniques in the treatment of hiatal hernias;
5. Bariatric surgery;
6. Surgical treatment of malignant diseases of the gastrointestinal tract;
7. Laparoscopic surgery of the adrenal gland;
8. Intraoperative brachytherapy in patients with breast cancer.

## **11. CONCLUSION**

The dissertation of Prof. Dr. Kostadin Angelov represents a significant scientific study that contributes to the development of modern oncological surgery.

The work is characterized by:

- high scientific value;
- in-depth analysis;
- substantial clinical material;

- practically applicable results.

## 12. FINAL ASSESSMENT

Based on the above, I consider that the dissertation entitled “Contemporary Surgical Approaches in Malignant Diseases of the Gastrointestinal Tract- Clinical and Epidemiological Aspects in Northeastern Bulgaria”, together with the submitted additional documents, fully meets the requirements for the awarding of the scientific degree “Doctor of Sciences.”

Therefore, I propose to the esteemed scientific jury that the scientific degree “**Doctor of Sciences**” be awarded to **Prof. Dr. Kostadin Georgiev Angelov, MD.**

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