

REVIEW

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OF THE DISSERTATION

"Modern Surgical Approaches in Malignant Diseases of the Gastrointestinal Tract- Clinical
and Epidemiological Aspects in Northeastern Bulgaria"

by **Prof. Dr. Kostadin Georgiev Angelov, MD,**
for the award of the scientific degree "Doctor of Sciences."

The present review is prepared in accordance with the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of the Act on the Development of the Academic Staff in the Republic of Bulgaria, and the Regulations for the Development of the Academic Staff at the Medical University "Prof. Dr. Paraskev Stoyanov"- Varna.

The materials submitted to me for review- the dissertation, extended abstract, publications, reports, and accompanying documents- address important problems related to malignant neoplasms of the gastrointestinal tract.

The introduction of the dissertation outlines the reasons for the relevance of the problem and the choice of the dissertation topic.

The dissertation comprises 248 pages and is illustrated with three panels of photographic material, 29 figures, and 61 tables, as well as appendices on electronic media.

The literature used includes 1068 sources, cited as follows: 171 sources presented in the Literature Review, Part I; 33 sources presented in the Literature Review, Part II; 796 sources used in the preparation of the PICOS analysis; and 68 sources distributed throughout the remaining chapters of the dissertation.

In the context of contemporary oncological morbidity, malignant diseases of the gastrointestinal tract represent a significant medical and social problem both globally and

nationally. The increasing incidence of these diseases, combined with their high mortality rate and serious socio-economic consequences, determines the need for in-depth clinical, epidemiological, and organizational research. In this regard, the presented dissertation clearly demonstrates scientific and practical significance.

It is particularly important that the author examines the problem not only from a clinical perspective, but also through the prism of public health and Health Technology Assessment. This integrative approach allows for a more comprehensive interpretation of the obtained results and creates prerequisites for formulating practically applicable recommendations aimed at optimizing the diagnostic and therapeutic process.

An additional value of the study lies in the regional analysis of morbidity in Northeastern Bulgaria, which contributes to a more precise understanding of the local characteristics of oncological pathology and provides a basis for the planning of regional health policies.

The literature review demonstrates a thorough knowledge of contemporary scientific publications devoted to the epidemiology, diagnosis, and surgical treatment of malignant diseases of the gastrointestinal tract. The wide scope of the sources used reflects a systematic and critical approach to the selection and analysis of scientific information.

A particularly strong impression is made by the analytical approach used in interpreting the published data. The author does not limit the discussion to a purely descriptive presentation of results but conducts a comparative analysis of various international and national studies. In this way, the main trends in the development of surgical techniques are outlined, including minimally invasive approaches, multimodal treatment, and the integration of personalized medicine into oncological surgery.

The literature analysis clearly demonstrates that advances in surgical technologies and improvements in diagnostic methods significantly influence patient survival and quality of life. At the same time, the author correctly emphasizes that the success of treatment depends not only on the surgical technique itself but also on early diagnosis, a multidisciplinary approach, and the effective organization of the healthcare system.

The literature review examines the epidemiology, etiology, pathogenesis, pathoanatomy, clinical presentation, diagnosis, principal instrumental investigations, staging, operative and non-operative treatment, possible postoperative complications, follow-up,

prognosis, palliative treatment, and other aspects of carcinomas of the gastrointestinal tract, including esophageal cancer, gastric cancer, small intestine cancer, colorectal cancer, pancreatic cancer, gallbladder and bile duct cancer, and liver cancer. The analyses of the health problem "malignant diseases of the gastrointestinal tract" are based on data from 171 scientific publications.

The objective of the dissertation is clearly and precisely formulated:

To analyze the clinical and epidemiological aspects of malignant diseases of the gastrointestinal tract in Northeastern Bulgaria and the outcomes of modern surgical approaches used in their treatment, and to analyze surgical approaches through the prism and standards of Health Technology Assessment.

To achieve the above objective, the following seven tasks have been formulated:

1. To conduct an epidemiological study of malignant diseases of the gastrointestinal tract in Bulgaria based on literature data.
2. To analyze modern surgical approaches for the treatment of malignant diseases of the gastrointestinal tract.
3. To conduct an epidemiological study of malignant diseases of the gastrointestinal tract in Northeastern Bulgaria.
4. To evaluate the clinical aspects and to classify and stage malignant diseases of the gastrointestinal tract in Northeastern Bulgaria according to their localization and progression.
5. To analyze modern surgical approaches for the treatment of malignant diseases of the gastrointestinal tract in Northeastern Bulgaria.
6. To assess the locoregional characteristics and social significance of malignant diseases of the gastrointestinal tract at both micro- and macro-levels.

7. To forecast the main trends in the development of morbidity from malignant diseases of the gastrointestinal tract in the short- and long-term at regional and national levels.

The methodological approach applied in the dissertation is characterized by systematic organization and scientific justification. The inclusion of a large number of patients over an extended time period allows for the derivation of statistically reliable and clinically meaningful conclusions.

The use of combined methods- clinical, epidemiological, and statistical- enables a multidimensional analysis of the studied problem. This approach allows not only the assessment of the frequency and structure of the diseases, but also the monitoring of trends in their development and the outcomes of the applied surgical approaches.

Particularly positive is the application of the PICOS methodology in the analysis of the scientific literature, which is characteristic of modern systematic reviews and meta-analyses. This approach enhances the scientific value of the research and ensures greater objectivity in the interpretation of the results.

Prof. Angelov has used clinical material covering an 11-year period (01.01.2013-31.12.2023), with a total of 2,103 patients included in the analysis. The patients were operated on at the Clinic of General and Operative Surgery of University Hospital "St. Marina" EAD, Varna.

A variety of statistical methods were applied for data processing, including: descriptive statistical analysis; frequency analysis- one- and two-dimensional frequency distributions according to categorical and metric variables; and the use of the specialized statistical software IBM SPSS Statistics.

Available Bulgarian publications show that minimally invasive and robot-assisted operations performed in Bulgaria demonstrate the typical benefits of minimally invasive surgery (MIS), including reduced blood loss, faster recovery, shorter hospital stay, and in some cases adequate lymph node dissection. These findings support the hypothesis that most of the benefits described in the international literature are also applicable to the Bulgarian population. However, Bulgarian publications mainly describe implementation, early results, and validation of scales, while the lack of large randomized controlled trials (RCTs), meta-analyses, and long-term data means that the level of scientific evidence remains limited.

Minimally invasive techniques such as laparoscopy and robotic surgery are gradually replacing open procedures in the treatment of many localized gastrointestinal tumors, as they improve postoperative recovery without compromising treatment effectiveness in appropriately selected patients.

In esophageal cancer, minimally invasive esophagectomy (MIE) is increasingly being adopted as a method for reducing postoperative morbidity while maintaining comparable long-term outcomes.

In rectal cancer, total mesorectal excision (TME) remains the standard of treatment, while newer approaches such as transanal TME (TaTME) and robotic TME are still under evaluation for improving the quality of resection and reducing conversion rates.

For hepato-pancreato-biliary tumors, extended and synchronous resections (including resections of liver metastases), as well as a multidisciplinary treatment approach (neoadjuvant therapy combined with surgery), are increasingly applied in selected groups of patients.

Nevertheless, several issues remain under discussion, including cost-effectiveness, the learning curve associated with robotic surgery, optimal patient selection for organ-preserving procedures, and the role of neoadjuvant therapy prior to surgical intervention.

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.

The future of gastrointestinal surgical oncology is increasingly determined by multidisciplinary collaboration, molecular profiling of tumors, and the integration of digital tools for surgical navigation and planning. These factors promote the application of precision medicine and the personalization of surgical treatment according to the individual characteristics of each patient.

Through the present dissertation, for the first time in Bulgaria and on such a scale, an attempt has been made to analyze surgical oncological pathology through the instrumentarium of Health Technology Assessment (HTA) by means of a retrospective observational study of electronic medical records.

The obtained results are presented in a systematic manner and illustrated through a

substantial volume of tables and graphical materials, which facilitates their interpretation and analysis. The data make it possible to trace both the frequency of different localizations of gastrointestinal neoplasms and the specific features of their clinical course.

Particularly valuable is the comparative analysis between national statistical data and the results of the study conducted in Northeastern Bulgaria. This approach makes it possible to highlight specific regional characteristics of disease incidence, as well as potential differences in diagnostic and therapeutic practices.

The discussion of the results demonstrates a thorough understanding of the complexity of oncological processes and emphasizes the importance of early diagnosis and timely surgical treatment. The author correctly highlights the role of the multidisciplinary approach in the treatment of these patients, involving collaboration between surgeons, oncologists, gastroenterologists, radiologists, and pathologists.

The regional analysis of morbidity in Northeastern Bulgaria represents a significant contribution of the dissertation. The study of local demographic, social, and health-related factors allows for a better understanding of the mechanisms influencing the distribution of malignant diseases of the gastrointestinal tract.

The results indicate the presence of certain regional differences both in the incidence of specific cancer localizations and in the stage at which the disease is diagnosed. This underscores the necessity of developing targeted preventive and screening programs tailored to the specific characteristics of the population.

From a practical perspective, these findings can serve as a basis for optimizing regional health policies and improving the organization of oncological care.

Dr. Angelov formulates two key conclusions in his dissertation:

1. Contemporary literature in surgical oncology is clearly up-to-date (approximately 64.7% of the publications date from the 2020s). However, the predominance of retrospective study designs remains pronounced, which limits the levels of evidence and increases the risk of systematic bias typical of observational studies.
2. A geographical concentration of publications in Asia (predominantly Japan and China) is observed. This fact should be taken into account when extrapolating results to other

populations, considering potential epidemiological, clinical, and organizational differences.

The main conclusion of the dissertation is that: there are serious gaps in the prevention of malignant diseases. Indirectly, it can be argued that there is delayed diagnosis and late seeking of specialized medical care.

The author proposes the following original contributions in the dissertation, which I fully accept:

1. For the first time in Bulgaria, surgical oncological pathology has been analyzed through the instrumentarium of Health Technology Assessment (HTA) by means of a retrospective observational study of electronic medical records from real clinical practice.
2. For the first time in the scientific literature, a systematic review of scientific publications following the PRISMA standard has been conducted to evaluate surgical oncological practice in diseases of the gastrointestinal tract.
3. For the first time in international surgical oncological research on gastrointestinal malignancies, a study evaluating clinical effectiveness based on the PICOS framework has been conducted.
4. For the first time in Bulgaria, a narrative observational study of modern surgical approaches for the treatment of malignant diseases of the gastrointestinal tract has been carried out at both international and national levels, based on the analysis of scientific publications by Bulgarian authors.
5. For the first time in Bulgaria, an epidemiological study of malignant diseases of the digestive tract has been conducted based on 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).

6. For the first time in Bulgaria, a locoregional longitudinal retrospective study of malignant diseases of the gastrointestinal tract has been conducted, covering one of the six administrative regions of the country.
7. An original author-designed protocol has been developed for the retrospective study, introducing a unique research instrumentarium for conducting systematic reviews of scientific publications for the evaluation of surgical interventions.
8. An original author-modified version of the PICOS framework for evaluating 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 PICOS (a'Modo Angelov) represents an original contribution of international significance. Without the inclusion of these additional elements, the evaluation of the clinical effectiveness of surgical interventions would be impossible.

RECOMMENDATIONS

I make the following recommendations regarding the dissertation:

1. The results should be published with a focus on the methodology of surgical research and the application of PRISMA and PICOS.
2. The PICOS analysis according to Angelov and Appendix 2 may be considered a separate original scientific work, and I recommend that it be published independently.

SCIENTOMETRIC INDICATORS OF THE SUBMITTED DOCUMENTS

Prof. Angelov presents 24 scientific publications, of which 15 are directly related to the dissertation and one is a chapter in a monograph. All publications have undergone peer review during the publication process.

The total number of points accumulated by Prof. Angelov through these publications is

2180.85, compared to the minimum requirement of 100 points. These scientific works have been cited more than 130 times, according to the Scopus database.

Prof. Angelov presents a total of 24 publications in journals with an Impact Factor, 10 of which are fully relevant to the present procedure. The total Impact Factor of his publications is 59.706.

Scientific contributions include research in the following areas: surgery of esophageal cancer, gastric cancer, pancreatic cancer, and liver cancer; hepatobiliary surgery; surgery of colon and rectal cancer; lymph node dissection in gastric cancer; insufficiency of colorectal anastomoses; inflammatory bowel diseases and their surgical treatment; laparoscopic adrenal surgery; intraoperative brachytherapy in patients with breast cancer; minimally invasive techniques in the treatment of hiatal hernias; bariatric surgery.

According to the similarity report of the dissertation, the following results are established:

1. 0% similarity between the dissertation submitted for the scientific degree "Doctor of Sciences" and the previous dissertation for the PhD degree
2. 3% similarity between the dissertation and internet sources

BIOGRAPHICAL DATA

Kostadin Angelov was born on 7 June 1977 in the city of Sliven. He completed his secondary education at Ivan Vazov Secondary School in Nova Zagora. He graduated from the Medical University – Sofia with a Master's degree in Medicine in 2004 and a Master's degree in Public Health and Health Management in 2006. He began working at University Hospital "Alexandrovska" as a hospital orderly in 2000, and in 2005 he won a competition for a residency position in surgery. His career as a physician began in the Emergency Department-Shock Room of Emergency Medical Services in Sofia, where he worked as a resident physician. In 2006, he won a competition for the position of assistant professor at the Department of Surgery, Faculty of Medicine, Medical University- Sofia. In 2010, he obtained

his specialty in surgery. From 2006 to 2011, he served as Head of Educational Activities at the Department of Surgery, Medical University- Sofia, and from 2008 to 2011, he was Chief Administrative Physician at the Clinic of Surgery, University Hospital "Alexandrovska"- Sofia. Since 2006, he has been a volunteer with the Bulgarian Red Cross and an instructor in first aid training, and between 2009 and 2012 he was a member of the Sofia City Council of the Bulgarian Red Cross. In 2013, he won a competition for Executive Director of University Hospital "Alexandrovska", which he managed until 2020. In 2014, he defended his dissertation and obtained the educational and scientific degree "Doctor (PhD)" in Surgery, with the dissertation titled: "Optimization of the Operative Approach and Lymph Node Dissection in Patients with Gastric Cancer." In 2015, he obtained a Master's degree in Finance at the University of National and World Economy, and in the same year he was elected Associate Professor, and later Professor in 2020. Between 2014 and 2020, Prof. Angelov served as: Member of the Board of the Association of University Hospitals for Active Treatment in Bulgaria; Member of the Faculty Council of the Faculty of Medicine at Medical University- Sofia; Member of the Academic Council of Medical University- Sofia; Secretary of the Bulgarian Surgical Society; Subsequently Secretary and Editor-in-Chief of the journal "Surgery", the official publication of the Bulgarian Surgical Society; Chief Secretary of the Bulgarian Surgical Society; Member of the State Examination Commission for the specialty "Surgery"; Advisor to the Parliamentary Committee on Health; and Chief Coordinator of the Expert Council on Surgery at the Ministry of Health.

In 2020, he was elected by the National Assembly as Minister of Health, serving until May 2021. Since then, he has been a Member of Parliament, serving as Vice-Chair and Chair of the Parliamentary Health Committee, and currently as Deputy Speaker of the National Assembly.

Since March 2023, Prof. Angelov has also been a Visiting Professor of Surgery at the Department of General and Operative Surgery, Medical University- Varna.

As a lecturer, he has delivered numerous lectures in surgery to medical students, dental students, interns, residents, and doctoral candidates. He has published extensively in Bulgarian and international journals indexed in major scientific databases. In 2012, he was recognized as "Best Lecturer" by the graduating class of medical students, and in 2015 he

received the “Prof. Dr. Paraskev Stoyanov” Award for achievements in medical science and education. He serves as scientific supervisor of doctoral candidates and surgical residents, and is the author of numerous reviews and expert opinions in academic competitions for scientific degrees and academic positions. His scientific activity is visible in Web of Science, Scopus, ResearchGate, and Google Scholar. He has 24 publications in journals with an Impact Factor, with citations ranging between 515 and 10,248 across different databases.

Prof. Angelov is a member of Bulgarian Surgical Society; Bulgarian Medical Association; International Gastric Cancer Association (IGCA); International Society of Surgery (ISS); and European Society for Medical Oncology (ESMO). He has received numerous awards, including: Distinguished Contributor of the Bulgarian Red Cross; Physician of the Year (2018) in the category “Management of Medical Activities” by the Sofia Medical Association; Gold Medal of the Bulgarian Red Cross; Award from the Bulgarian Association of Healthcare Professionals for contribution to healthcare development; “Person of the Year 2020” Award from the National Association for Spinal Muscular Atrophy, among many others.

In conclusion, it should be emphasized that the presented dissertation represents a large-scale and in-depth scientific study dedicated to one of the most significant problems of modern surgery and oncology. The author demonstrates a high level of professional competence, analytical thinking, and a profound knowledge of the scientific literature.

The research is distinguished by a clearly formulated scientific concept, well-structured methodology, and well-founded scientific conclusions. The obtained results have both theoretical and practical value, as they contribute to a better understanding of the epidemiological and clinical characteristics of malignant diseases of the gastrointestinal tract and to the optimization of modern surgical approaches in their treatment.

A particularly valuable contribution of the study is the analysis of regional characteristics of morbidity in Northeastern Bulgaria, which provides important information for the development of effective strategies for prevention, early diagnosis, and treatment. The results of the research may serve as a basis for future scientific studies and for improving clinical practice.

All of the above provides sufficient grounds to conclude that the dissertation fully meets the requirements for scientific research at a high academic level and represents a significant

contribution to the fields of surgery, oncology, and public health.

Therefore, based on the above and with full professional conviction, I consider that the dissertation "Modern Surgical Approaches in Malignant Diseases of the Gastrointestinal Tract – Clinical and Epidemiological Aspects in Northeastern Bulgaria", submitted by Prof. Dr. Kostadin Georgiev Angelov, MD, for the scientific degree "Doctor of Sciences", represents a completed scientific work fully complying with the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its implementation, and the Regulations for the Development of the Academic Staff at the Medical University "Prof. Dr. P. Stoyanov"- Varna.

For these reasons, as an external reviewer, I respectfully propose to the distinguished scientific jury to vote positively **for awarding the scientific degree "Doctor of Sciences" to Prof. Dr. Kostadin Georgiev Angelov, MD.**

REVIEWER:

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

Prof. Dr. *Angel* Uchikov, DSc

Заличено на основание чл. 5,
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