## REVIEW

## by Assoc. Prof. Dr. Nikolay Vassilev Belev, MD, PhD

Department of Propaedeutics of Surgical Diseases Medical University - Plovdiv

of dissertation work

## " Transabdominal laparoscopic treatment of adrenal tumors in adults and children"

to: Dr. Stefan Blagovestov Mihaylov

for awarding the scientific and educational degree "Doctor" in the scientific specialty "General Surgery"

Scientific supervisor: Assoc. Prof. Dr. Veselin Marinov Marinov, MD, PhD, BSc.

The dissertation has been discussed and approved for public defense by the Department Council of the Department of General and Operative Surgery at the Medical University of Varna, with a report from the Department Council numbered 7/27.06.2025. Additionally, according to Order R-109-302/14.07.2025 issued by the Rector of the Medical University of Varna, I have been appointed as a member of the scientific jury for the dissertation defense.

The submitted materials, both in paper and electronic formats, comply with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LAADRB) and the Regulations on the Development of the Academic Staff at the Medical University "Prof. Dr. Paraskev Stoyanov"-Varna.1. General presentation of bibliographical dates.

Dr. Stefan Blagovestov Mihaylov was born in 1996 in the town of Dryanovo. He graduated from secondary school in 2015 at the National Aprilov High School with a German language focus. He earned his Medical degree in 2021 from MU-

Varna. Since 2022, he has been specializing in Pediatric Surgery at the University Hospital "St. Marina" - Varna, where he currently works as a resident in the First Clinic of Surgery at the University Hospital "St. Marina" - Varna and as a regular assistant at the Department of General and Operative Surgery at MU "Prof. Dr. Paraskev Stoyanov" - Varna.2. Relevance of the topic

With advances in imaging diagnostics and endocrinology, the detection of adrenal tumors has become more frequent, highlighting the need to improve surgical methods. Similar studies are relatively scarce in Bulgarian scientific literature, underscoring the importance of this study, which systematically assesses the effectiveness, safety, and benefits of transabdominal laparoscopic treatment of adrenal tumors, as well as promotes this approach in Bulgarian clinical practice. Additionally, adrenal tumors pose a significant medical challenge due to their varied clinical presentations—from incidental findings to hormonally active or malignant neoplasms. The transabdominal approach is especially favored because it offers a larger surgical field and clearer anatomical visualization, making it easier to remove larger or more complex tumors and providing better access to vascular structures. It also has several advantages over traditional open surgery, including less blood loss, shorter hospital stays, faster recovery, and improved cosmetic outcomes. These benefits have been demonstrated in both adults and children, establishing laparoscopic adrenalectomy as the preferred method.3. Knowledge of the problem

Dr. Stefan Mihaylov demonstrates a thorough understanding of the subject across general clinical, endocrinological, oncological, resuscitation, and surgical aspects. The patients are categorized based on the hormonal activity of the tumors in a well-reasoned manner. Detailed algorithms are provided for preoperative preparation, intraoperative monitoring, and management of expected postoperative issues. The surgical procedures were performed by the same team using standardized laparoscopic techniques, highlighting a high level of surgical expertise in addressing the problem.4. Research methodology.

Dr. Mihaylov's study is retrospective and single center. It was conducted at the University Hospital "St. Marina" - Varna and covers the period from 01.01.2008 to 31.12.2024. The patient population includes 82 individuals who underwent transabdominal laparoscopic adrenalectomy. The material is well described and supplemented with figures and tables. During this period, 82 laparoscopic adrenalectomies were performed for adrenal gland tumors. The patients were

divided into four homogeneous groups based on the hormonal activity of the tumor, enabling a statistically reliable analysis. The study's methodology is clear and aligns with the objectives. The protocol for preoperative diagnosis, surgical approach, postoperative follow-up, and statistical tools used are all thoroughly described.5. Evaluation of the dissertation.

The dissertation is presented in a volume of 220 pages and contains 38 tables and 50 figures. It complies with the accepted requirements for the structure of a dissertation. It includes the following chapters: Introduction (3 pages), Literature review (92 pages), Aim and objectives (1 page), Material and methods (16 pages), Results of own research (43 pages), Analysis and discussion of own results (22 pages). Conclusion and conclusions (4 pages), Bibliography (28 pages). Bibliography includes 426 titles in Latin and two articles by Bulgarian authors.

The dissertation candidate clearly defines the goal of analyzing the outcomes of transabdominal laparoscopic adrenalectomy in both adults and children. To accomplish this, six tasks must be completed. Six conclusions have been drawn logically from these tasks. The studied patient group shows heterogeneity concerning clinical features associated with excess hormone production. Additionally, patients often present with significant comorbidities, with most having arterial hypertension even before surgery. This condition requires clarification of its cause, demanding an active diagnostic approach and thorough preoperative assessment. I highlight the anatomical variations in blood supply and adrenal gland location, which significantly influence surgical technique. Arterial and venous anomalies are more common in right-sided lesions, necessitating careful assessment during dissection. In this context, transabdominal access offers excellent visualization, enabling identification and control of anatomical structures despite individual differences. The presence of hormonally active tumors, particularly pheochromocytomas and corticosterone-producing neoplasms, correlates with increased intraoperative hemodynamic instability. Despite mandatory preoperative medication, effective hemodynamic management during surgery is essential, as it greatly reduces the risk of intraoperative complications. The results are presented in a clear analytical format. The role of transabdominal laparoscopic adrenalectomy in the surgical treatment of adrenal tumors in both adults and children was evaluated. Surgical procedures were performed in 82 patients, divided into four groups based on the tumor's hormonal activity. In the studied group, a slight preference for leftsided adrenalectomies was observed—51.2% (n=42) of cases—compared to 48.8% (n=40) for right-sided procedures. The average tumor size was  $50.57 \pm 41.01$  mm.

The smallest tumors were in Group 2 ( $26.23 \pm 10.93$  mm), while the largest tumors appeared in Group 4 (67.15  $\pm$  61.11 mm). Notably, there was no statistical difference in blood loss between the groups, indicating that hormonal activity does not significantly influence intraoperative blood loss. Classical hypercortisolism is associated with centripetal fat accumulation and impaired carbohydrate metabolism, with the highest mean BMI recorded in patients from Group 3—31.74  $\pm$  19.0 kg/m<sup>2</sup>. The analysis did not find a statistically significant difference in BMI between the groups (F(3)=0.53, p=0.666). Although the patients' mean age was relatively young, a notable feature was the presence of significant comorbidities. Obesity was statistically significant among the groups, with the highest prevalence in Group 3 (85.71%, n=18; p=0.0134). Borderline statistical significance was observed regarding COPD/Asthma, with the highest percentage in Group 4 (30.77%) and the lowest in Group 3 (4.76%) (p=0.0599). It was noted that five patients, or 9.8% of all patients, did not require antihypertensive therapy. Further analysis revealed that in the pheochromocytoma group, only one patient needed a triple-drug regimen. Conversely, all patients in Group 2 required antihypertensive treatment, with only one on monotherapy. There is a strong positive correlation, with higher BMI associated with longer operative time; the results were statistically significant in both tests (p < 0.001). The discussion follows the structure of the Results chapter, helping the reader clearly understand how the author's findings compare to data in the broader literature. The material highlights the larger size of the operated tumors. Many studies show that tumor size is linked to a higher rate of intraoperative complications, especially in cases of neoplasms without hormonal activity or clinical symptoms, which are often diagnosed late when tumors are larger. In pheochromocytomas, larger tumors are associated with higher plasma levels of catecholamines and an increased potential for their release into the circulation, leading to subsequent effects. The Conclusion chapter correctly states that the effectiveness and applicability of laparoscopic transabdominal access in treating adrenal tumors extend to a wide range of patients, including those with increased anesthetic risk, overweight individuals, and large lesions. The data emphasize the importance of an individualized approach to preoperative assessment and planning to enhance safety and improve surgical outcomes.6. Literature reviewThe literature review is well organized and includes the following sections: Historical review; Anatomy and topography of the adrenal gland; Physiology and pathophysiology; Diseases of the adrenal gland, including surgical treatment; Indications for adrenalectomy; Evolution of surgical approaches; Applications in adults; Applications in the pediatric population; Complications; The situation in Bulgaria; and a critical analysis of the literature. The review covers articles from 1951 to 2025, with a focus on the most recent five years.

## 7. Contributions.

I would like to highlight the contribution of the dissertation work: a modern and statistically reliable study of the application of transabdominal laparoscopic access as a method for treating adrenal tumors has been conducted. For the first time in Bulgaria, an analysis of the results of transabdominal laparoscopic adrenalectomy in adults and children has been performed. Additionally, a comparison of the outcomes of transabdominal laparoscopic adrenalectomy across different pathological and functional conditions of the adrenal gland has been made.8. Abstract

The abstract is 99 pages long and contains the main information necessary for the summary and description of the dissertation.

Dr. Stefan Mihaylov is an assistant and a specialist in pediatric surgery, possessing in-depth theoretical knowledge and excellent practical skills. The proposed dissertation holds scientific, practical, and applied value, and has a confirmatory nature regarding the use of transabdominal laparoscopic access for adrenalectomy as the preferred method in minimally invasive procedures. This provides me with grounds to recommend to the highly respected Scientific Jury that Dr. Stefan Mihaylov be awarded the academic and scientific degree of "DOCTOR."

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Assoc. Prof. Dr. Nikolay Belev, MD, PhD 08/14/2025

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