To the Chairman of the Scientific Jury, determined by Order No. P-109-479/14.12.2022 of the Rector of the Medical University - Varna On your Protocol No. 1/ of 22.12.2022

REVIEW

from

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On the dissertation work of Dr. Inna Gocheva Ivanova, on the topic:

"Robot-assisted partial nephrectomies - functional and oncological results"

for the awarding of a scientific educational degree "Doctor"

The dissertation work for obtaining the scientific educational degree "Doctor" on the topic: "Robot-assisted partial nephrectomies - functional and oncological results" developed by Dr. Inna Ivanova is the result of research and summarization of the experience of the Clinic of Urology at the Medical University of Varna in the field of the surgical treatment of carcinoma of the kidney.

The presented scientific work contains 122 pages and is illustrated with 25 figures and 33 tables. The bibliography includes 151 titles, of which 13 are in Cyrillic and 138 are in Latin.

The structure of the dissertation corresponds to modern requirements and contains all the necessary sections.

The literature overview is detailed in content and in a volume of 33 pages informs us about the main problems related to the diagnosis and treatment of renal cell carcinoma. Issues concerning the emergence and development of robotic-assisted surgery in urology, the staging of the disease and the types of surgical access (transperitoneal and retroperitoneal) in robotic-assisted partial nephrectomy are discussed in detail. This creates a basis for developing the thesis of the scholar's research.

Dr. Inna Ivanova examines in detail the data published in the modern medical literature concerning the frequency, etiological and predisposing factors, the anatomy of the lymphatic system of the kidney, the methods of diagnosis of metastases in renal cell carcinoma, as well as the clinical course of the disease.

Laparoscopic and robot-assisted surgery have a parallel development, which is due to technological innovations in medicine. On the other hand, looking at the development and evolution of robot-assisted systems, their application, and the types of operative interventions in urology, it gives reason to argue the study of the application of robot-assisted surgery in the minimally invasive treatment of renal cell carcinoma. Dr. Ivanova examines the advantages of another minimally invasive surgical method for the treatment of the same disease - laparoscopic partial nephrectomy. In recent years, the scientific literature has asserted that robot-assisted partial nephrectomy has an advantage in terms of ischemic time and renal parenchymal loss, resulting in the preservation of a greater number of nephrons and preservation of renal function.

These discussion questions direct the PhD student towards an attempt to create a more complete understanding of the importance of robotic-assisted partial nephrectomy in the surgical treatment of renal cell carcinoma, thereby supporting the choice of a rational surgical technique and therapeutic behaviour.

The goal set by Dr. Inna Ivanova in developing her dissertation is to prove the importance of robot-assisted partial nephrectomy, to achieve negative surgical margins, preserved renal function and minimal

perioperative complications. The purpose of the dissertation is clear and well-articulated.

For the realization of this goal, Dr. Ivanova sets herself four tasks with which to prove her thesis.

Task I. To establish a relationship between warm ischemia time and postoperative renal function.

Task II. To determine the effect of clear resection lines on recurrence rates.

Task III. To investigate possible intra- and post-operative complications (surgical problems) when performing robot-assisted partial nephrectomy.

Task IV. To study early oncological outcomes after robotic-assisted partial nephrectomy.

The number of tasks set is quite sufficient to substantiate the main thesis of the dissertation work. They are formulated correctly, clearly and accurately.

In the second chapter - experimental clinical trial, Dr. Ivanova presents systematized and summarized clinical-statistical results from the study of 145 patients with renal cell carcinoma. All patients were operated on at the Urology Clinic at the "St. Marina" - Varna from January 2020 to August 2022. The author presents in detail the operative methods used - robot-assisted and laparoscopic partial nephrectomy, as well as the statistical methods used for data processing. The transperitoneal and extraperitoneal access, the positioning of the trocars, the indications for the choice of method are described in detail. Robot-assisted surgery was performed in 72 patients, and laparoscopic surgery was performed in 73 patients. The steps of the operations are covered, illustrated with rich, proprietary photographic material.

The main factors for performing a successful robotic surgical intervention are discussed, namely: a good understanding of the procedure, availability of the necessary surgical skills and training, teamwork, patient positioning and placement of the robotic ports. The correct positioning and placement of the ports for the various accesses is described in detail. The advantages of transperitoneal versus retroperitoneal access depending on individual tumor and patient characteristics, patient history of prior major surgery, dense perirenal inflammation/fibrosis, musculoskeletal limitations

that prevent proper positioning, and surgeon preference are discussed. Their advantages and disadvantages are discussed.

The doctoral student examines step by step each stage of robot-assisted partial nephrectomy, emphasizing the important points and possible difficulties in performing the operation.

Dr. Ivanova describes and discusses various surgical techniques in performing robot-assisted partial nephrectomy in an attempt to reduce warm ischemia time. Renorrhaphy and the use of hemostatic agents were reviewed sequentially.

The third chapter presents the obtained results. At the beginning, the preoperative data, anaesthetic risk, tumor stage of the patients in the two groups: robot-assisted and laparoscopic partial nephrectomy were examined. The number of patients is completely sufficient for statistical processing and obtaining reliable results. Intraoperative and early postoperative outcomes are presented and compared. The longer operative time in the laparoscopic surgery group, the shorter hospital stay in the robot-assisted group is remarkable. A significant, statistically significant difference was observed in mean blood loss in favor of robotic-assisted partial nephrectomy.

The doctoral student presents the results of the obtained complications in the groups: hematoma, pulmonary thromboembolism, urinoma, abscess, positive resection lines. Again, an advantage was observed in the robotic-assisted surgery group.

Another important factor in preserving renal function is that the ischemic time during clamping is up to 20 min. In the group with robot-assisted partial nephrectomy, a shorter ischemic time of about 3 min was achieved, and in one of the patients, surgery was achieved with no clamping or selective clamping of only one artery. An important fact is the successful removal of tumors over 6-7 cm /stage T2/ with robot-assisted surgery.

The next section includes a **summary** and **formulation** of conclusions, which, after the analysis of the obtained results, give in a synthesized form the conclusions regarding the importance of robot-assisted partial nephrectomy, the most important of which are:

- · Reduced blood loss.
- Provided the possibility of easier access to difficult places.

- Fewer complications after surgery.
- Less hospital stay.
- Faster patient recovery.
- Removal of larger tumors while preserving kidney functions.

In the scientific contributions chapter, Dr. Ivanova formulated five scientific contributions of a practical and applied nature. The scientific work is the second in the country after Prof. Kaloyan Davidov's monograph from 2021, examining robot-assisted partial nephrectomy. The most valuable part of the thesis is the demonstration of advantages in several aspects of robot-assisted over laparoscopic partial nephrectomy. Unfortunately, this conclusion was not formulated.

In **conclusion**, I can say that the dissertation work of Dr. Inna Gocheva Ivanova on the topic "**Robot-assisted partial nephrectomies - functional and oncological results**" is properly structured and written in an academically sound style with an emphasized scientifically applied contribution, proving the importance and advantages of robot-assisted partial nephrectomy to achieve negative surgical margins, preserved renal function and minimal perioperative complications The scientific value of the dissertation gives me the reason to recommend to the esteemed scientific jury to award Dr. Inna Gocheva Ivanova the educational and scientific degree "Doctor".

28.01, 2023

Yours sincerely:

Prof. Dr. Nikolay Koley, MD