

## Opinion

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Regarding the dissertation on the topic: "Invasion of the lymphatic and blood vessels in endometrial endometrioid carcinoma - 1st stage by FIGO" with author Assoc. Prof. Elis Hudaim Ismail, MD, PhD.

7.0 Health and sports, professional field 7.1 Medicine;

Obstetrics and Gynaecology 03.01.45

By order No. R-109-237 / 26.07.2019 of the Rector of the Medical University of Varna, pursuant to Part 4, Paragraph 2 of the Law for the Development of the Academic Staff in the Republic of Bulgaria, I was appointed to prepare an opinion on the procedure for obtaining a Scientific Degree "Doctor of Science" with the candidate Assoc. Prof. Elis Ismail, MD, PhD from MU-Varna on the topic: "Invasion of the lymph and blood vessels in endometrial endometrioid carcinoma - stage I by FIGO"

The dissertation presented by Assoc. Prof. Ismail is structured correctly, with the proportions observed between the different sections. It is written on 165 pages, its contents are illustrated with 20 figures and 33 tables. The author cited 211 literary sources, which were cited correctly and as required in the text. The topic of the dissertation is up-to-date. The prognosis and treatment of cancer are dependent on a number of factors, with increasing attention being paid to the biology of the tumor. Endometrial cancer is the most common oncogynecologic localization in both Bulgaria and developed countries. The endometrioid type is more favorable than the non-endometrioid type. In recent years, there has been an increasing interest in tumor factors (histologic factors) that cause recurrence and different survival rates in patients with a favorable prognosis (FIGO stage I endometrioid carcinoma). On the other hand, there are ongoing discussions and controversies about the indications for lymph node dissection, as well as for postoperative therapy in such patients.

One of the factors related to the biology of the tumor is lymphovascular invasion. The literature review analyzes and monitors current state of the art on a number of issues related to tumor biology, indications for lymphatic dissection and postoperative radiotherapy, as well as methods for metastasis. Particular attention is paid to tumor invasion of the blood and lymphatic vessels (lymphovascular invasion) as a prognostic factor.

The review concludes with several conclusions that underpin the clear formulation and goal setting of the thesis: "To determine the prognostic value of tumor invasion in lymphatic and blood vessels in patients with endometrial endometrioid carcinoma stage I according to FIGO."

In order to achieve this goal, Assoc. Prof. Ismail has set herself 10 tasks. The clinical contingent includes 117 patients with stage I endometrial carcinoma under FIGO who underwent surgery at the Gynecology Clinic of the MHAT, St. Anna ” for a period of 6 years (2009 - 2014). The study is retrospective, but with a long enough follow - up period to account for the major oncological parameters:

5 year overall and disease - free survival. The methods used are described in detail, such as: surgical method, radiotherapy, histological examination and data processing. Various statistical methods have been used, and the Kaplan-Mayer method is particularly valuable for assessing overall and disease-free survival. These statistical methods are at the base of the results obtained, which give the author grounds for interpretations and analyzes.

The Results and Discussion section is a step-by-step solution to the ten assignments of the dissertation, brings the contributions of the dissertation and is written on 42 pages. The author found that patients with tumor invasion of the lymphatic and blood vessels had a 28-month lower survival rate than recurrence compared to other patients. On the basis of the obtained results and their discussion, Assoc. Prof. Ismail comes to 14 conclusions and makes 4 recommendations for the practice.

The contributions of the dissertation are 14 and are mainly scientific and practical. Six of the contributions are original in nature, the rest are confirmatory. The scientific articles related to the dissertation are 12, 3 of which have been published abroad and meet the regulatory requirements. The dissident is the first author of 9 and the second - 3 of them.

## Conclusion:

Thesis on the topic: "Invasion of the lymphatic and blood vessels in endometrial endometrioid carcinoma stage I according to FIGO " by Assoc. Prof. Elis Ismail, MD, PhD is a valuable and in-depth scientific development with real scientific contributions. The work answers a number of important scientific questions, contributing to and enriching the concept of an individualized approach in the treatment of oncogynecological diseases, in particular patients with endometrial cancer.

This scientific work is entirely copyrighted and has all the attributes and requirements for the degree of Doctor of Science. Therefore, I recommend that the members of the scientific jury vote positively for the award of the Doctor of Sciences to Assoc. Prof. Dr. Elis Hudaim Ismail, MD, PhD in Obstetrics and Gynecology.

29 - Aug – 2019

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