

OPINION
from
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In reference to the dissertation of **Dr. Girgina Manolova Stoyanova on "Heredity, precancerous lesions and monitoring in patients with colorectal cancer"** for awarding the educational and scientific degree "**Doctor**" in the professional field 7.1 Medicine and Doctoral Program "**Internal Medicine**".

As a member of the scientific panel appointed by order №164/29.03.2021 of Dr. Venelina Atanasova - Executive Director of Acibadem City Clinic MHAT Tokuda EAD and based on the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for its implementation I share the following opinion.

The object of the dissertation work of Dr. Girgina Stoyanova is an important and topical for medical science and gastroenterology problem related to malignant diseases of the colon. These diseases are continually increasing in frequency in certain countries and represent a serious social problem. In countries with established programs for the prevention of colorectal cancer and among first-degree relatives, there is a decrease in its incidence. In Bulgaria, due to the lack of a program for screening and prevention of this disease, there is a tendency to increase the incidence of colorectal cancer. From this point of view, the dissertation of Dr. Stoyanova is extremely relevant and of very important practical importance. It can serve as one of the much-needed studies on the complex causes of the development of colorectal cancer in Bulgarian patients, as well as for their monitoring after the diagnosis of this disease.

PhD thesis presented in 203 pages, distributed as follows: Content and abbreviations - 6 p., Introduction - 1 p., Literature review - 45 p., Purpose and tasks - 1 p. Material and Methods - 3 p., Results - 100 pages, Discussion of results - 15 pages, Conclusions and recommendations - 3 pages, Clinical cases - 5 pages, Conclusion - 2 pages, Contributions - 2 pages, Bibliography - 17 pages. The proportion between the individual sections is complied.

The literature review is contemporary and is systematized in six sections. The first section is devoted to epidemiology, survival and lethality of colorectal cancer. The second section discusses colorectal precancerous, successively describes inflammatory bowel disease, polyps, and adenomas, serrated lesions and serrated polyposis. The third section describes the problems concerning heredity and genetic factors in precancerous lesions and colorectal cancer, reviewing available data on genetic damage, familial adenomatous polyposis and Lynch syndrome. The fourth section is devoted to clinical and morphological features of colorectal

cancer - localization and clinical course, staging and classification and factors for metastasis. The fifth section discusses the methods for diagnosis and monitoring of precancerous lesions and colorectal cancer, incl. tissue biomarkers. The last sixth section describes the epidemiology, risk factors, heredity and clinical and morphological features of early colorectal cancer under 55 years. age. Literature review ends with conclusions that are actually formulated with nine preconditions for the need for this study. It is impressive that such a complex matter is presented in an understandable way, which shows that the author masters the studied matter.

The goal and set five tasks are well defined and are a natural consequence of the literature review and questions unresolved issues.

The studied contingent includes 213 patients who passed through the departments of gastroenterology and abdominal surgery of the Fifth Hospital - Sofia for the period 2012-2019. These patients were divided into four groups - 87 operated patients with colorectal cancer with a subgroup of early-onset colorectal cancer under 55, 45 patients with inflammatory bowel disease, 71 patients with polyps and adenomas and 10 patients with intestinal polyps. The criteria for grouping patients and the physical, biochemical, instrumental and histological methods used and the imaging methods are described in detail. A panel of modern methods for statistical processing of the material was used.

The results are well structured and visualized, as the whole thesis contains 134 figures and 24 tables. They are presented in four sections, according to the logic of the literature review, the set tasks and the division of patients into groups. The examined parameters of the patients in the four groups are presented in detail. Each section has a correct and in-depth analysis of the results obtained and ends with generalizations. At the end of the chapter with the obtained results are summarized data from the observed groups. Relatively rare, but is positive clinical illustration in the thesis of four patient.

The discussion shows that the author has delved into the research problem, as well as that she has in-depth clinical thinking and excellent professional training. It is structured in five sections, which logically follows the set tasks. This section ends with the development of an algorithm for monitoring in patients with precancerous conditions and in patients undergoing surgery for colorectal cancer, which is an adequate result of the overall thinking of the doctoral student.

The eight conclusions are specific, correct, as a logical consequence of the results obtained and fully accurately reflect the summarized data obtained. There are also 12 recommendations for monitoring intestinal precancerous lesions and for patients undergoing surgery for colorectal cancer, which have great practical application.

The contributions are eighteen - at first glance a large number, but with a careful assessment of the results obtained and the significant scope of the methodology used, they adequately reflect the overall idea of the dissertation. Particularly important to note first, second, third, fifth and eleventh offerings, as noted above, very important is the third contribution on the established algorithm.

The publications in connection with the dissertation are 4 and 2 participations in international scientific forums - completely sufficient according to the requirements.

The bibliography cites 257 sources - 10 of them in Cyrillic and 267 in Latin. Over two thirds of them are from the past 10 years. All cited authors have a direct relation to the research problem and are cited where should, according to the purpose and objectives of the dissertation.

In conclusion, based on the above, I consider that the dissertation of Dr. Girgina Manolova Stoyanova on "Heredity, precancerous lesions and monitoring in patients with colorectal cancer" fully meets the requirements for awarding the educational and scientific degree "Doctor".

16.04.2021

Member of the Scientific Jury:

/Assoc. Prof. Vladimir Andonov, MD/

