

REVIEW of the thesis

“Role of CT and MR enterocolonography for diagnosis and follow-up in Crohn's disease”

Dissertation thesis for the award of the educational and scientific degree “Doctor (PhD)”
with supervisor Assoc. Professor Dr. Radoslav Georgiev, PhD

by Dr. Svetomir S. Chakarov,

full-time doctoral student in the Department of “Diagnostic Imaging, Interventional Radiology and Radiation therapy” and doctoral program “Medical radiology and rentgenology (incl. use of radioactive isotopes)”—

Reviewer: Professor Vassil Hadjidekov, MD, PhD

According Medical University of Varna Rector’s Order: № P-109-169/28.02.2023

1. Relevance and appropriateness of the topic.

Crohn's disease is undoubtedly a socially significant disease affecting young people, with a significant frequency, with a chronic-relapsing course, which course can lead to disability. Nowadays, knowledge about the disease is constantly expanding with the development of medical practice, but its complexity leaves a number of unexplained aspects. Imaging methods, with a key role in its diagnosis, contribute significantly to the accurate morphological assessment of the disease and to its monitoring. The development of the technology of imaging methods constantly expands their possibilities and knowledge about diagnostics. This proves the actuality of the chosen topic.

2. Structure of the dissertation

The dissertation is built on 141 pages and includes 9 tables and 49 figures. There is a traditional structure for works of this type: Introduction of 2 pages, Literature review - 47, Purpose and tasks - 1, Research methodology and organization - 11, Results and Discussion - 40, Closure - 3, Conclusions 1, Contributions -1, Publications and participation in scientific forums in connection with the dissertation - 1, Appendices - 18, Literature cited - 28.

3. Knowledge of the problem

The literature review is comprehensive and detailed. The epidemiology, the clinical picture, the laboratory diagnosis of the disease has been examined successively. The methods of diagnostic imaging are extensively presented, showing data on both the conventional methods (standard X-ray with follow-up of the passage with contrast with barium slurry, enteroclysis and irrigography), as well as ultrasound, computer tomography and magnetic resonance. Describing the methods of the ultrasound examination, the contributions of contrast-enhanced ultrasound for the assessment of increased mesenteric blood flow, elastography for the assessment of fibrotic segments and transperineal ultrasound have been noted. The methods and clinical application of computed tomography and magnetic resonance enteroclysis, the role of different methods of contrast enhancement and the application of antiperistaltic agents are reviewed. The literature data on the imaging findings in the various forms of the disease are summarized. Literature data on dynamic contrast enhancement in magnetic resonance, the possibilities of nuclear medicine, are presented. The literature data on the methods of quantitative assessment of the activity and severity of Crohn's disease - the so-called Scores – are presented.

The bibliography includes 190 papers' titles, 4 out of which are in Cyrillic and 186 - in Latin. 91 out of all used sources were published after 2010, which demonstrates the modernity of the summarized data presented.

The literature review presents the author as fundamentally familiar with the issues underlying the dissertation work.

4. Research material and methodology

The material and methods are presented in the chapter "Methodology and organization of the research". There is a retrospective and a prospective analysis in the study. The inclusion and exclusion criteria for the patient material are clearly stated. The total number of examined patients was 194. Computed tomographic enterocolonography was performed in 188, and magnetic resonance enterocolonography in 47 of. In both imaging methods, two types of equipment are used - for Magnetic Resonance Enterocolonography - one with a field strength/intensity of 1.5T and one with 3T.

Study protocols are clearly and thoroughly described and permit reproducibility. Laboratory methods used in hospitalized patients with Crohn's disease are listed too. The methods for quantitative assessment of the severity of the disease - the Lemann index and the Magnetic resonance index for activity (MEGS) - calculated for the each of segments of the intestinal tract - are very comprehensively presented.

The statistical methods used are appropriately chosen and reasoned.

The material and methods allow the fulfillment of the set purpose of the dissertation thesis and the drawing of conclusions from the results of the study.

5. Characterization and evaluation of the dissertation work

The Purpose of the dissertation work is to investigate changes in CTE and MRE in Crohn's disease and to determine their role in the diagnosis and follow-up of the disease. Six tasks are listed that complement the specified objective.

The chapter "Results and discussion" chapter follows the set tasks. The frequency of findings observed in computer tomography and magnetic resonance enterocolonography was determined. The obtained results are compared with the literature data. The frequency of

the imaging findings was compared with histology data indicating disease activity.

Studies comparing Lemann index values and quality of life assessed using a disease-validated questionnaire called the IBDQ are of interest. A statistically significant relationship was established between the values of the Lemann index at year 1 and after year 2. The characteristics of 47 patients with calculated IBDQ were compared with those of 53 patients from literature data. Through a correlation analysis using the Pierson method, an inverse moderate statistically significant relationship between Lemann index and IBDQ was established. A correlation was determined between IBDQ scores and various CT and magnetic resonance enterocolonography findings. The correlation between the some changes found on CT and MR enterocolonography, the Lemann index, the magnetic resonance enterography global score (MEGS) on one side, and on the other - with some widely used paraclinical and laboratory tests in patients with Crohn's disease(C-reactive protein, fecal calprotectin), as well as with the Crohn's disease activity index (CDAI). When assessing the degree of damage to the intestinal tract using the Lemann index, a statistically significant changes in the values at the second year was found in the follow up of 57 patients . The proposed protocols for computed tomography and magnetic resonance enterocolonography are those used in the study.

The closing summary of the work summarizes the results of the study, highlighting the role of the Lemann index in tracking the development of the disease.

Seven conclusions are drawn from the study. They follow the sequence of the tasks and the construction of the study logically to the obtained results.

The proposed dissertation work is multi-layered. It compared the results of two modern imaging methods with multiple laboratory and other paraclinical studies. Methods have been used to characterize the cumulative structural changes of the disease by a quantitative expression, which is a modern trend in medicine. The statistical processing of the results is flawless.

The Inflammatory Bowel Disease Quality of Life Questionnaire used, Information sheets and Informed consent forms for the patients included in the study are presented in the appendices to the paper.

The abstract correctly reflects the content of the dissertation work. The author presents three work-related publications in Bulgarian periodical scientific journals and two participations in national conferences. There are no related publications in foreign editions.

From the attached documents, it is clear that the procedure for the accomplishing doctoral studies was followed according to sections Nos. II, III and IV of the Regulations for the development of the academic staff at the Medical University - Varna.

6. Contributions and significance of the dissertation

I accept the author's assessment of the contributions of the dissertation work. Among them, I will highlight those related to the quantitative indicators of the imaging studies - the Lemann index and the Magnetic resonance enterography global score (MEGS), as well as those with the Crohn's disease activity index (CDAI) - all of them determined for a population of Bulgarian patients.

7. Critical notes

I have no major critical comments on the nature of the study, the results obtained and the conclusions drawn in the peer-reviewed dissertation proposals.

Nevertheless, some minimal editorial and technical notes can be made:

- Some propaedeutic texts in the overview should be avoided.
- Individual paragraphs could have a tighter expression, even the title the thesis
- Bibliographic signs from the used literature under numbers 121 and 122 are identical, and we did not find numbers 34 and 188 cited

These remarks do not in the least detract from the value of the dissertation.

As a recommendation - suggestion to direct the results of the study for publication in an international scientific periodical.

8. Personal author data

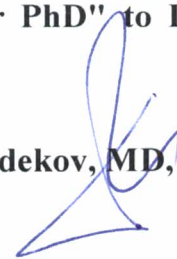
Dr. Svetomir Sevdalinov Chakarov graduated in medicine from the Faculty of Medicine of the Medical University of Varna in 2011. His internship as a radiologist began in October 2011 in the Department of Imaging Diagnostics at "Dr. Atanas Dafovski" Medical Center, Kardzhali, where he worked for a year. Since October 2012, he has been part of the staff of the Diagnostic Imaging Clinic at Sveta Marina University Hospital, Varna.

He graduated as specialist in Diagnostic Imaging in 2018. Starting from January 2020 he is enrolled as a full-time doctoral student at the department of "Diagnostic Imaging, Interventional radiology and Radiation therapy". From September 2021 he is an assistant-professor for the specialty "Radiographers" at the Medical College of the Medical University - Varna, He is member of the Bulgarian Association of Radiology European Society of Radiology (ESR), Bulgarian Medical Union .

9. Conclusions:

The dissertation work "Role of CT and MR enterocolography for diagnosis and follow-up in Crohn's disease" by Dr. Svetomir Sevdalinov Chakarov is a study with a modern structure, covers current imaging methods and clinical practice of a socially significant disease. The work contains scientific and scientific-applied contributions, meets the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and its Regulations, as well as covers the requirements of the Regulations on the terms and conditions for acquiring scientific degrees and occupying academic positions of the Medical University - Varna. I give my positive vote and recommend the Esteemed members of the Scientific Jury to support the awarding of the educational and scientific degree "doctor PhD" to Dr. Svetomir Sevdalinov Chakarov, assistant professor.

Vassil Hadjidekov, MD, PhD



Sofia, April 2023

Professor of Radiology