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"GEORGE EMIL PALADE" UNIVERSITY OF MEDICINE, PHARMACY, SCIENCE, AND TECHNOLOGY OF TÂRGU MUREȘ - SCHOOL OF DOCTORAL STUDIES

Summary of the doctoral thesis:

Pre- and postoperative staging of anorectal carcinoma, prognostic factors of these tumors and surgical treatment of postoperative complications

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Colorectal cancer (CRC) is considered a heterogeneous tumor and is responsible for about 10% of all cancers diagnosed and cancer related deaths worldwide. In terms of frequency of diagnosis, it ranks third in men (after prostate and lung cancer) and second in women (after breast cancer). One third of CRC is located in the rectum, and occurs mainly in men. Anal cancer (AC) is a rare malignancy, accounting for only 1% of CRC and 3% of rectal cancer (RC). A multidisciplinary team is needed to establish the correct diagnosis and treatment.

The aim of this study was to investigate the efficacy of preoperative and postoperative staging in the case of anorectal carcinomas, correlated with classical prognostic factors. In the preoperative phase, it was proposed to demonstrate the prognostic importance of two serum parameters, namely the ratio between neutrophils and lymphocytes (NLR) and the ratio between lymphocytes and monocytes (LMR). Their role in estimating overall survival has also been explored. For postoperative evaluation, we opted to examine the prognostic role of the rate of positive lymph nodes vs. negative lymph nodes (LNR), based on an adequate lymph node resection, correlated with the results of histopathological examinations. Since we highlighted the appearance of incisional hernias, as a postoperative complication, we proposed, as a secondary objective, the complex examination of the surgical aspects related to these hernias. Thus, we focused on the surgical treatment of giant incisional hernias, which appeared as late complications after the classic surgical interventions of anorectal tumors. The main purpose was to adapt the surgical procedure in order to reduce the recurrence rate.

When conducting the first study, we set up a retrospective database that included clinicopathological information on patients who underwent surgery during 2013-2018, following which the excision of the malignant rectal tumor was performed. In this way, an observational study was performed that targeted locally advanced cancers (stages II and III). Cases where only tumor biopsy was performed were excluded and those cases in which patients died in the first

two weeks postoperatively. In this thesis, the first study focused on the prognostic role of LNR, examined postoperatively. It has been shown that in patients diagnosed with RC who have received preoperative chemoradiotherapy (CRT), LNR is an independent prognostic factor.

The second study was performed by retrospective analysis of a large database, which included patients diagnosed with RC, in which malignant tumor resection was performed. In compiling the database, we focused on the systemic inflammatory response, more precisely on the preoperative value of neutrophils, lymphocytes and monocytes. This study focused on the prognostic value of the ratio between neutrophils and lymphocytes (NLR), respectively between lymphocytes and monocytes (LMR). The exclusion criteria targeted tumor biopsies, patients with associated septic conditions, respectively those with autoimmune or hematological diseases and cases where death occurred in the first month postoperatively. The peculiarity of this study consists in the number and origin of patients, because patients from two university clinics, from two countries, were included, these being the National Institute of Oncology in Budapest, Hungary and the Emergency County Clinical Hospital in Târgu Mureș, Romania. In this way the number of examined cases reached 1052 over a period of over 6 years. We also opted to investigate an association between prognostic factors belonging to the systemic inflammatory response and the quality of total mesorectal excision (TME), for which an important value was assigned to histopathological examination and description, in which the quality of TME was evaluated macroscopically (complete, partially complete or incomplete). NLR and LMR have been shown to be independent prognostic parameters. An NLR value ≥ 3.11 may indicate the level of preoperative CRT response but also shows a reduced chance of maintaining the anal sphincter or performing a complete TME.

The third study focused on postoperative complications and focused on giant incisional hernias, often occurring after open surgery performed for resection of malignant tumors. In this way we conducted a prospective study that included patients with giant incisional hernias in which a CT examination was performed preoperatively. With the help of CT, the volume of the incisional hernia, the volume of the total peritoneal cavity, the volume of the remaining abdominal cavity and the size of the parietal defect can be defined. Knowing these parameters, one can define the rate of possibility of developing an abdominal compartment syndrome in the postoperative phase. The surgery consisted of the reconstruction of the abdominal wall, which was performed using a tension-free technique, by placing a Prolene mesh in the retromuscular plane and covering it above and below by using two flaps made of the hernial sac. Intraoperatively and postoperatively the value of intra-abdominal pressure was determined.