

**TITLE: PREOPERATIVE AND POSTOPERATIVE EVALUATION OF LYMPH NODE STATUS,
AS A PROGNOSTIC FACTOR IN COLORECTAL CANCER**

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Colorectal cancer (CRC) is a heterogenous tumor and the third most common type of malignancy worldwide. The screening programs are developed in most countries, but lack of optimization and surveillance by endoscopy lead to diagnosis in advanced stages in many cases in the country. CRC is staged according to the American Joint Committee of Cancer (AJCC) 8th edition using the TNM system. One of the most important prognostic factors in CRC is the lymph node (LN) status – the N stage. The 5-year survival rates decrease drastically from 75-95% in stage I or II to 30-68% in stage III or IV.

Surgical resection combined with chemotherapy/radiotherapy and/or neoadjuvant radiochemotherapy represent the standard treatment guidelines for the management of both colon and rectal cancer. One of the challenges of recent studies is the preoperative identification of LN metastases (LNM). Current guidelines only harvest the regional lymph nodes, in proximity to the tumour. Modern imaging techniques such as computer-tomography (CT) or magnetic resonance imaging (MRI) despite significant development in the recent years, with improvement of the T and M stadialization, the N-stage could benefit from optimization for predicting metastatic LNs.

The theme of this thesis is based on the critical need for better preoperative stadialization using imaging methods to identify and remove the positive LNs that could influence the management of CRC with better overall survival rates and lower recurrences.

The importance of a multidisciplinary team for a better management of the CRC cases is highlighted in this paper, that included Surgery Department, Pathology Department and Radiology Department within Emergency Clinical County Hospital of Târgu Mureș.

The general part presented the state of art regarding epidemiology, physiopathology, anatomy, stadialization, preoperative imaging techniques and current treatment guidelines in CRC.

The personal contribution included three studies and a case presentation that allowed obtaining the proposed objectives.

In the first study, we followed up retrospectively 112 patients diagnosed with CRC that were surgically treated by the surgical team within Emergency Clinical County Hospital of Târgu Mureș. All patients had previous colonoscopy with a positive biopsy for carcinoma. These patients were referred to the Radiology Department for preoperative contrast-enhanced CT imaging. Our contribution was mainly based on integrating a map of nodal stations in the preoperative staging protocol, where suspect LNs were marked using criteria such as dimension, homogeneity, contour and roundness. Three categories of LNs were

established regarding their distance to the tumor, loco-regional - under 5 cm, intermediate - between 5 and 10 cm and central - beyond 10 cm. The contrast-enhancement pattern of the LNs was also analyzed. The imaging criteria were correlated with histological reports and statistically evaluated, with comparison between positive LNs and negative LNs. Risk of LNMs was not correlated with tumor localizations, but was higher in cases with vascular, lymphatic and perineural invasions, as well as high degree of tumor budding present. The sensitivity and specificity obtained were 80% and 69% respectively. Negative predictive value was very high (0,92) suggesting the utility of CT imaging in selecting N0 stage cases. Certain patterns of enhancement were strongly correlated with LNMs (OR 7,84, $p < 0,0001$ for dotted pattern), while others were correlated with negative LNs (OR 1,99, $p: 0,02$ for homogenous type). A novel parameter introduced by our study to evaluate the correlation between suspicious LNs and histologically confirmed metastatic LNs, the SPR parameter (suspicious LNs to positive LNs ratio), with precise values obtained in the distal colon (1,11 and 1,18) and middle rectum cases (1,26). Assessment of this parameter promises to provide further information in future studies. In-house validation of the mapping of the nodal stations affected by CRC might be an important tool in the improvement of preoperative N staging by CT imaging.

The second study focused on synchronous colorectal tumors and their molecular profiles, analyzing the management of different molecular subtypes and gene mutations in these cases, individual evaluation being crucial for a therapeutic decision and response. The study included six patients with two tumors each. The same map of nodal stations was used for identifying the affected LNs on imaging studies, then correlated with histology reports. Imaging studies proved to be very useful, in two of the cases diagnosing the second tumor that was overlooked on colonoscopy due to improper bowel preparation.

A particular case of situs inversus in a patient with CCR was presented for further understanding of anatomic variations and lymphatic drainage in such cases, that could complicate surgical interventions and prognostic of these patients.

The third study included 56 patients diagnosed with rectal cancer in which was analyzed the nodal map correlation using MRI exams, that proved to have a higher sensitivity and specificity for N stage (94% and 73% versus 80% and 69% for CT exams). MRI offers a better tissue contrast providing additional informations such as mesorectal fascia involvement, presence of tumoral deposits or extramural venous invasion. Using the Apparent diffusion coefficient (ADC) values measured on ADC maps could further characterize the status of LNs, which is especially important in LNs localized in intermediate and central stations, sampling of these LNs not being included in the current guidelines. The presence of vascular, lymphatic and perineural invasion, LNMs, as well as tumoral deposits and extramural venous invasion represent independent negative prognostic factors.