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Morphological aspects of the rectal neovascularization in colorectal cancer – anatomical-surgical and imaging implications

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Abstract

Colorectal neoplasia has an increasing incidence among the population, and this fact compels in achieving an early diagnosis and treatment protocols. The extramural vascular invasion (EMVI) score is a method used for staging cancer. It defines the presence of malignant cells in the blood vessels, outside its own vascular tunic. The purpose of the study is to evaluate the extramural vascular invasion, and thus the impact of this determination in diagnosis, treatment and prognosis of colorectal neoplasia. This was done using magnetic resonance images (MRI) of colonoscopic diagnosed patients with colorectal cancer and subsequently comparing these results with the control group of patients without malignancy. The EMVI criteria taken into account were correlated with the images obtained in patients in the study group. In each of the evaluated patients, we found both, arterial and venous blood vessels in 0 stage – EMVI correlated with T2 or T3 stage tumor. In T3 B stages, we could objectify suggestive images for stage 4 EMVI near and distant from the tumor. Blood and lymph vessels have a high density to their origin area and it decreases anteriorly. This distribution is consistent with a predisposition to the formation of a vascular rectal cancer, especially on the posterior wall. In conclusion, anatomical-imaging staging of colorectal cancers using EMVI score is very close to the colonoscopic diagnosis and to the accuracy of the classic cancer staging. Corroborating EMVI score with a vascular radiology reference pattern improves the accuracy for determining an appropriate treatment and assessment of prognosis.

Keywords: colorectal cancer, neovascularization, imaging tests, extramural vascular invasion.

Introduction

Colorectal cancer has become one of the most common forms of malignancy and of these, about a third of cases are localized in the rectum. Rectal cancer has a worse prognosis because it is characterized by a rate of local recurrence and a higher metastasis presence at the moment of diagnosis [1]. The fundamental principle of the curative treatment of these tumors remains surgery, but even that has undergone major changes over time as now is considered to be necessary a multidisciplinary team. The main purpose is individualizing the therapeutic strategy, consistent with patient and tumor characteristics [2, 3]. Both preoperative, but especially postoperative, particular importance has quantitative and qualitative assessment of prognostic factors of patients, and in this respect intra and extramural invasion, the distance between the tumor and the mesorectum edge, the involvement of the lymph nodes, of the blood vessels, the peritoneum and of the sphincter complex, plays a primary role. Weighing all these factors, we have to analyze the best decision regarding the necessity or otherwise of the pre and postoperative neoadjuvant therapy as well as the decision on the appropriate surgical techniques [4–6].

Colorectal neoplasia has an increasing incidence among the population, and this fact compels in achieving an early diagnosis and treatment protocols. High-resolution magnetic resonance brings relevant data on the normal anatomical aspects of the rectum as well as on the possible pathological changes. The magnetic resonance imaging (MRI) investigations, in our study, bring us important information about the location and extent of the tumor, if it affects the mesorectum, its relations with the peritoneum, with surrounding fascia and organs, highlighting the rectal arteries and the neoformation vessels. We evaluated the degree of the extramural invasion of the blood vessels [extramural vascular invasion (EMVI) score] and thus, the impact of this determination in diagnosis, treatment and prognosis of colorectal neoplasia setting.

According to *American Joint Committee on Cancer* (AJCC), the most common method in this respect is the one that takes into account the extent of the tumor, the affecting or not of the lymph nodes and the presence of metastases – TNM staging. The EMVI score is another method used for staging cancer, besides TNM. It defines the presence of malignant cells in the blood vessels, outside its own vascular tunic, near the tumor. This score is long recognized as an independent predictor for local and systemic recurrence as well as for long-term survival [7–9]. Also, this score is used as an indicator for oncological therapy. The accuracy of approximately 52% of the EMVI score can be greatly increased by correlating it to MRI because in the early stages of cancer it is difficult to assess whether a vascular structure is visualized or not. The accuracy increases in advanced stages where vascular structures are invaded, as they have the same native density as the tumor and it captures intramural contrast [10].

Patients and Methods

The study was conducted on a group of 10 patients, colonoscopic diagnosed with rectal cancer, who underwent preoperative contrast MRI to establish tumor localization and resection possibilities. The MRI images acquired on these patients were compared with normal anatomical imaging procured on a control group of 15 patients. Of the 10 patients in the study group, seven were male, aged 46–57 years and three females aged 55–62 years. Of these, five were diagnosed with cancer of the higher portion of the rectum in T2, T3, T4 stages, three were diagnosed with medium rectal tumors in T3 stage and two with lower rectal cancer, T1 and T2 stages.

The MRI sequences obtained are consistent with others found in the literature [11, 12]:

- T2 fast (turbo) spin echo, made from one pelvic wall to the other (transverse);
- Axial, with a wide field throughout the pelvis;
- T2 fine sections in the axial plane – made along its axis, that include rectal tissue with 3 mm thickness;
- Coronal sections with high spatial resolution that allow the visualization of low rectal tumors, the *levator ani* muscle and of the anal mechanism sphincter;
- High resolution sections that go up to 5 mm above the edge of the tumor in order to be able to view a possible a lymphatic tumor invasion in the mesorectum.

The MRI examination was performed using the area antennas after following the protocol: images weighted in T2 FSE (fast spin echo) and T1 SE (spin echo) and ESF (edge-stopping function) in three orthogonal planes – axial, coronal and sagittal – with the following parameters: TR (repetition time) 400 ms, TE (echo time) 130 ms, 400×500 matrix 28 mm FOV (field-of-view) sections of 4 mm exam T1-weighted images natively and FSE after administration of intravenous paramagnetic contrast MIP (maximum intensity projection) and 3D reconstructions followed. For the study, we used a Philips Achieva 1.5T MRI machine. A paramagnetic dye was injected: Magnegita 500 μM/mL solution for injection (Gadopentetate dimeglumine). The MRI dosage used for adults was of 0.5 mL/kg. The injection of the contrast (30 to 40 mL of Gadolinium) was carried out with a MRI specific injector (MEDRAD Spectris®) at a rate of 0.8 mL/s. For the acquisition of bolus MRI angiography, we used sequences followed by successive stages: the EFGRE (enhanced fast gradient-recalled echo) 3D sequence used with the following parameters: 42 cm, matrix 256×192 (reconstructed by interpolation matrix 512×512), TE 1.5 ms, TR 6 ms, TI (inversion time): 25 ms, angle: 25°, section thickness: 4 mm (rebuilt in pieces that overlap 4 mm× 2 mm). The total MRI acquisition time for the angiography was of 95 seconds (five seconds between each step to move the table).

Results

We used the EMVI score correlated with MRI imaging in order to establish the staging of colorectal carcinomas.

The criteria taken into account by the EMVI score were correlated with the images obtained in patients from the study group. In each of the evaluated patients, we found both, arterial and venous blood vessels in 0 stage – EMVI correlated with T2 or T3 stage tumor. In T3 B stages, we could objectify suggestive images for stage 4 EMVI near and distant from the tumor. Thus, T2 in stages (Figure 1), proximal and homolateral of the tumor, we have objectified the vascular paraneoplastic invasion appreciated by the caliber of the blood vessels, the degree of tortuosity, the appearance of their walls (nodule) and heterolateral the vessels appearing to be normal, especially in the early T1 and T2 stages. In T1 stages, on sections made at 3 mm, the paraneoplastic changes of their walls and their content lessen and even disappear at 6 mm maximum, both homo and contralateral of the tumor. In T2 and especially in T3 stages, the vascular paraneoplastic changes seem to interest long vascular portions with an important caliber, going even to the origin vessels (the trunk of the rectal middle artery, the internal iliac artery of the tumor and, especially, the veins of this path – Figure 2).

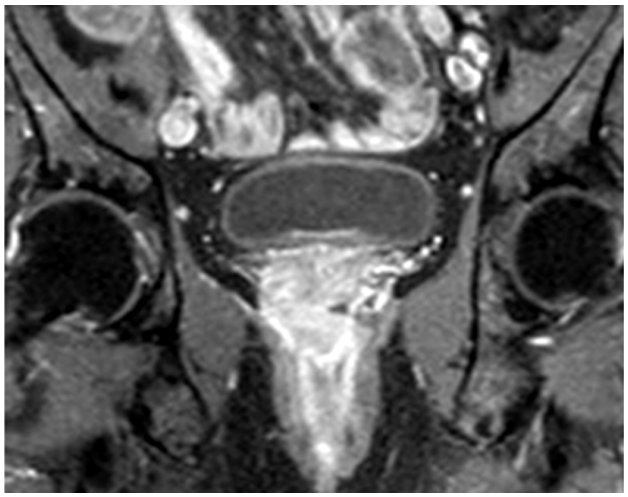

Figure 1 – ***Neoformation vessels in the inferior right rectal artery, in straight angle, with enlarged perivascular lymphadenopathy – stage 2 EMVI.***

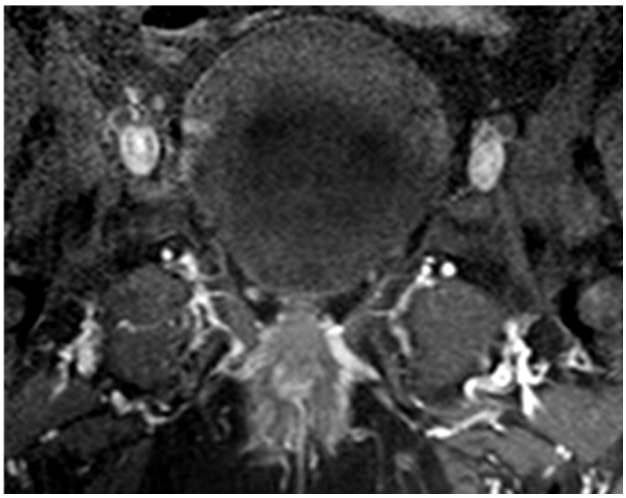

Figure 2 – ***Middle rectal vein in middle rectal cancer, with the equivalent signal outlet to the tumor, specific for stage 4 EMVI.***

The remote damage of the blood vessels (internal iliac vein) is correlated in most cases with secondary determinations of the liver (Figure 3). We believe that the distance paraneoplastic impairment of the vessels (the

trunk of the middle rectal artery) signifies a high probability of microscopic liver determinations.

The aspect of tumor margins shows tumoral invasion in small veins, which goes out of the intestinal lumen and can produce nodules in the venous wall, distinct from desmoplasia (Figure 4). The presence of tumoral signal in the vascular structures is a landmark for tumoral presence (Figure 5). Affected vessels increase their volume and their inside signal is a medium gray.

Extension of tumor inside the vessels causes a smooth, nodular or an irregular appearance of vessels (Figure 6).

In none of the 15 cases of MRI investigated patients who refuted rectal neoplasia could we amend vascular corresponding EMVI score (Figure 7). Moreover, in these patients we have not discovered any benign formations, which can be considered preneoplasic condition, such as polyps, diverticula, or autoimmune diseases.

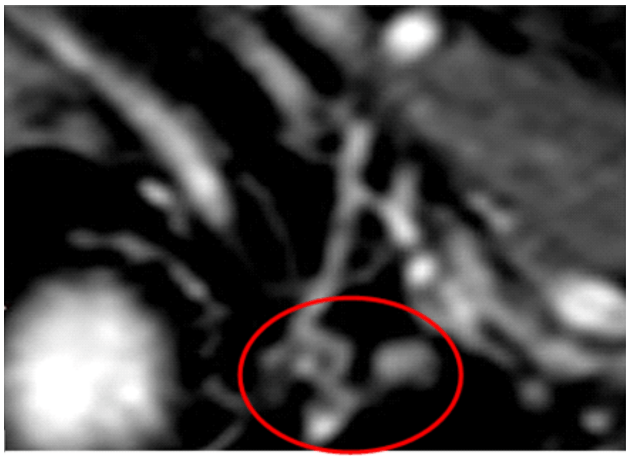

Figure 3 – ***Neovascular degenerative process, on the branches of inferior left rectal veins, with the appearance of a central core and two satellite sanguine cores, typical for arterial paraneoplastic processes – stage 2–3 EMVI.***

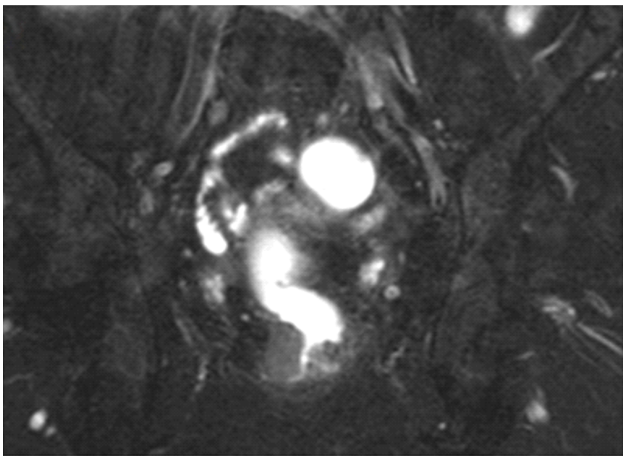

Figure 4 – ***Pseudo-inferior rectal artery stenosis in the left, with similar changes on the contralateral inferior rectal artery, both intramural nodule type, specific to stage 3 EMVI.***

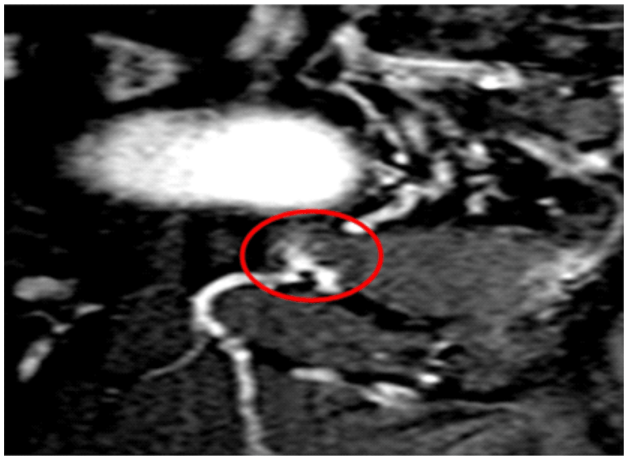

Figure 5 – ***Left middle rectal vein in sagittal section, in a middle rectal cancer with intraparietal invasion – stage 4 EMVI.***

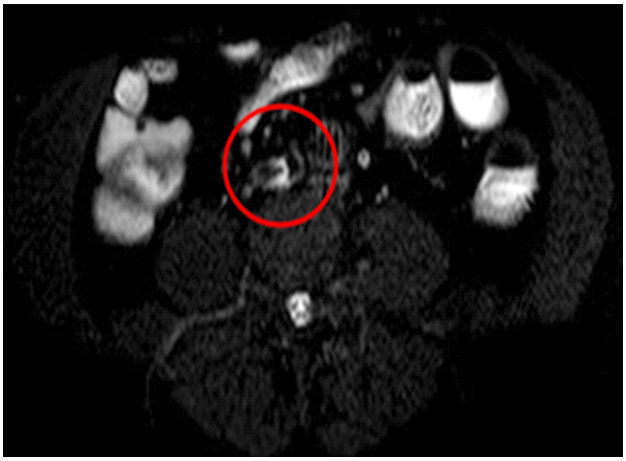

Figure 6 – ***Neoformation vessels on the right inferior rectal artery, in MRI with multicenter condensing processes, characteristic for stage 3 EMVI.***

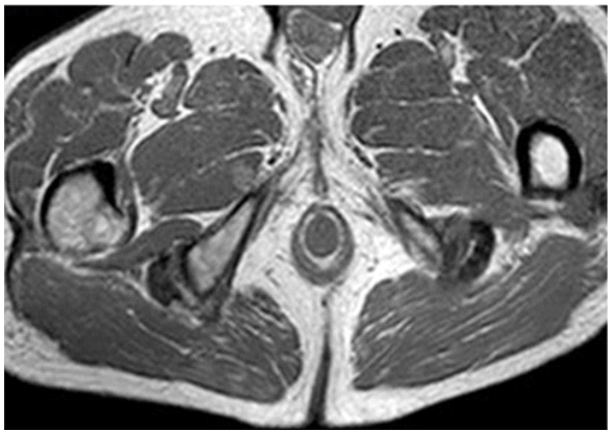

Figure 7 – ***Normal aspect – stage 0 ENVI.***

Of primary importance in determining the localization of the tumor, is the fact that the extramural invasion of the blood vessels in the lower rectal tumors is cranio-caudal and those of the upper and middle rectal tumors are mostly cross bared. This explains the rapid blood-stream metastasis of the lower rectum tumor. In this situation, the medium or large distance vascular invasion is precocious.

Upper and middle rectal neoplasms produce a precocious extramural invasion in proximity.

The most used directions in extramural vascular invasion in various locations suggest the fact that they follow the vascular anastomoses between the three rectum territories.

Given these considerations, it may be proposed an EMVI staging system based on MRI imaging.

Discussion

In T2 transversal section, the radiological anatomy of the rectum shows the rectal lumen followed by *musculara propria* (which is formed sometimes from two distinct layers: internal and longitudinal), then the *tunica submucosa*, with high MRI intensity and *muscularis mucosae*, with low MRI intensity, which delimit the rectal lumen. The muscular layer have irregular grooves steering, but uniform in size, because of the blood and lymphatic vessels which penetrate the rectal wall.

Around the *musculara propria*, with low MRI intensity, we can see an area of high MRI signal intensity, which belongs to perirectal fat. This adipose tissue contains blood vessels with reduced MRI intensity, blood vessels and lymphatic nodes and also conjunctive septa. Finally, we observe another zone with reduced MRI signal, which surround the rectum and the perirectal fat. This is fascia mesorectum. Any changes of these anatomic and radiological issues should be suspected and investigated like presenting paraneoplastic origins.

The blood and lymphatic vessels have a rich density to their home area (posterior and mesorectal), which decrease as we head towards anterior. This distribution is consistent with vascular predisposition of forming a rectal cancer, especially on the rear wall or possibly on the side. Evolution to anterior of a rectal tumor is the second step in neoplastic evolution and is influenced by the anatomy of the pelvis. This occurs because of two aspects:

1. The universal law of bilateral symmetry, which applies for the median unpaired organs;

2. The distance from the center of the tumor, which have been performed various types of sections (3 or 5 mm).

MRI assessment contains a number of protocols which must be individualized according to need of information that are intended to be purchased, to quality of clinical and paraclinical information on the cases, and to local conditions. If high-quality images are needed, about the relationship of tumor to nearby organs, a MRI 2D T2 protocol with sections obtained in sagittal, axial and oblique will be used.

In case of obtaining inconclusive images, to better highlight both the caliber and rectal coating layer it can be used the rectal administration of ultrasound gels or contrast agents. This maneuver allows more accurate delineation of tumor poles, reduce the potential artifacts and allow a better assessment of synchronous tumors [13].

The establishment of a normal vascular pattern of rectum was obtained by comparison of angio-MRI results of patients who do not show degenerative lesions at the level of this organ to those obtained by MRI with contrast in neoplasia and those obtained by arteriography performed on resection pieces.

Major problems arise in a correct preoperative differentiating of a tumoral stage 2 by tumoral stage 3. This is a critical issue because the rectal tumor, starting with stage 3, it requires most often a preoperative radiochemotherapy [14, 15]. However, recent studies [16] question the correctness of the assessment prognostic and therapeutic value of colorectal cancers using only information provided by MRI. For this, a group of researchers [12, 17] developed a local method for staging colorectal cancers corroborating investigations using MRI to determine the extramural venous invasion using the EMVI score, which envisages the histology of the tumor cells in the own vascular endothelium.

The intramural and extramural invasion of blood vessels by a rectal tumor is an important score for prognosis in evaluating patients being correlated with histological demonstration on vascular resection specimen. The extramural vascular invasion corresponding to EMVI score 3, 4 will be stage T3, T4 [10].

Venous invasion of colorectal cancer leads to the presence in blood circulation of tumor cells, which goes in the portal circulation, which results in the appearance of distant metastasis by hematogenous spreading [18, 19].

Conclusions

EMVI score significantly improves the accuracy of determining a proper oncological treatment after surgery. This study raises serious questions over the current staging of colorectal cancers because changes in caliber and trajectory of rectal vessels appear early. Starting with EMVI 2 score, the anatomical radiological changes that occurs seems to be caused by metastatic dissemination processes and not just by the neovasculogenesis. Extramural vascular invasion is depending on the tumor location: superior rectal location has a transversal but also caudal invasion; medium rectal location has a transversal, but also a vertical invasion; inferior rectal location has vertical but also transversal invasion. Atypical invasion directions may suggest the presence of synchronous tumors or one extremely aggressive. Studies are required on extensive groups of patients in order to make the EMVI score a routine method in the diagnosis and prognosis of colorectal neoplasia.

Conflict of interests

The authors declare that they have no conflict of interests.

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