

MORPHOCLINICAL OBSERVATIONS IN COLORECTAL CARCINOMA

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Keywords: colorectal carcinoma, angiogenesis, molecular factors

Abstract: *Introduction: Colorectal cancer is one of the most present neoplastic diseases of the digestive tract and requires constant study of factors that can be influenced to improve patient prognosis. Material and methods: In this study, we focused on selecting the patients who benefited from surgical treatment for colorectal tumour. Beside the clinical trial, we aimed at the immunohistochemical analysis of molecular factor (VEGF), which is involved in stimulating tumour growth. Results: Clinical trial results enrol in the margins presented by other contemporary studies on the biological factors involved and the therapeutic conduct addressed. VEGF positivity in some examined cases can be correlated with subsequent prognosis of the disease. Conclusions: In the treatment of colorectal carcinoma, surgery is extremely important and the diagnosis that involves and determines the molecular factors responsible in tumour development may allow the implementation of a treatment behaviour as accurate as possible.*

Cuvinte cheie: carcinom colorectal, angiogeneza, factori moleculari

Rezumat: *Introducere: Cancerul colorectal, fiind una dintre cele mai prezente afecțiuni neoplazice ale tubului digestiv, impune o permanentă studiere a factorilor care pot fi influențați în vederea îmbunătățirii prognosticului pacientului. Material și metode: În cadrul acestui studiu, m-am orientat în a selecta o parte din pacientura care a beneficiat de tratament chirurgical pentru o tumoră colorectală. În afara unui studiu clinic, m-am orientat și spre o analiză imunohistochimică a unui factor molecular (VEGF), care este implicat în stimularea creșterii tumorale. Rezultate: Rezultatele studiului clinic se înscriu în marjele prezentate și de alte studii contemporane, privind factorii biologi implicați și conduita terapeutică abordată. Pozitivarea VEGF în anumite situații examinate, poate fi pusă în corelație cu prognosticul ulterior al bolii. Concluzii: În tratamentul carcinoamelor colorectale este extrem de importantă intervenția chirurgicală, iar diagnosticul imunohistochimic care implică determinarea factorilor moleculari responsabili în dezvoltarea tumorii, poate permite implementarea unei conduite de tratament cât mai corecte.*

INTRODUCTION

Colorectal neoplasm is one of the most common tumours of the digestive tract and has a high mortality, unfortunately being in a constantly growing. Colorectal neoplasm is on the second rank as mortality after lung cancer in men and breast cancer in women.

Colorectal cancer is considered a true "surgical disease", 92% of patients with colon cancer and 84% of patients with rectal cancer underwent surgery during the progression of the disease.⁽¹⁾

Multidisciplinary approach of this disease and the increased interest of the surgical team have made that in recent years to implement new surgical techniques in colic cancer treatment (laparoscopic surgery) that bring significant benefits to patient recovery and more rapid recovery to a more active social status.

All surgeries were performed to prolong life and improve its quality.

PURPOSE

The purpose of this study is to identify a correlation between many factors involved in surgically approaching this

disease. Among these, we mention: biological factors (age, gender), the nature of the intervention and its character, the type of anaesthesia along with the presence of responsible molecular factors of tumour angiogenesis and prognosis of evolution.

The vascular endothelial growth factor (VEGF) is a hemodimeric glycoprotein, and it is involved in the stimulation of angiogenesis.

OBJECTIVE

The main objective of this paper is to centralize clinical, histological, immunohistochemical and molecular parameters that have a predictive or prognosis role in colorectal carcinoma.

METHODS

We have retrospectively analyzed the casuistry with colorectal cancer operated between 2005 and 2010, the data being taken from the database of the clinical observation sheets and operators protocols. In some of these cases, we followed the immunohistochemical result and its implications in the relation with the tumour staging.

Criteria of inclusion

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Article received on 18.10.2012 and accepted for publication on 20.12.2012
ACTA MEDICA TRANSILVANICA March 2013;2(1):272-274

CLINICAL ASPECTS

The patients who were admitted and operated for colorectal tumour, and to whom the histology result confirmed the malignant nature of the tumour.

Criteria of exclusion

The study did not include the patients diagnosed with colorectal cancer who were admitted to establish the diagnosis (biopsy), or the patients who underwent cancer treatments before surgery (radio-chemotherapy).

Between 2005-2010, within the Surgical Clinic I of Mureş County Hospital, a total of 8940 patients received surgery; we selected those who met the criteria of inclusion.

Thus, 272 cases have been identified who received surgery for a colorectal neoplastic disease, these cases representing 56% of all cancers with digestive location, 486 cases. In 15 of 272 cases, immunohistochemical examination was performed in order to highlight the presence of the molecular factor (VEGF) specific for tumour and neoangiogenesis growth. It was aimed to identify vascular endothelial growth factor (VEGF), which is considered the most active factor in the stimulation of angiogenesis process.

Immunohistochemical study included 15 cases of colorectal carcinoma, selected from among the 272 cases highlighted within the clinical study.

The preparation and examination of samples was made by using modern standards.

The results were interpreted on the basis of the statistical examinations.

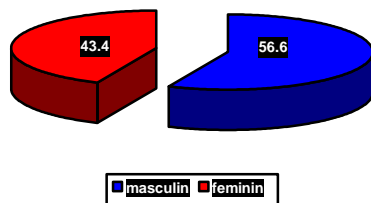
RESULTS

From the total of 272 cases included in the study, 154 were men (56,6%) and 118 were women (43,4 %).

Table no. 1. Distribution of cases according to gender

	Number	Percentages
B	154	56,6
F	118	43,4
Total	272	100.0%

Figure no. 1. Distribution of the investigated cases according to gender



The average age of the entire group was 65.3 years old, the median was 64 years old, the minimum was 25 years old, respectively the maximum was 88 years old. Mann Whitney nonparametric test applied between age values for men and women did not reveal a statistically significant p ($p=0,44$), namely, there is no statistical difference between the age medians of both sexes.

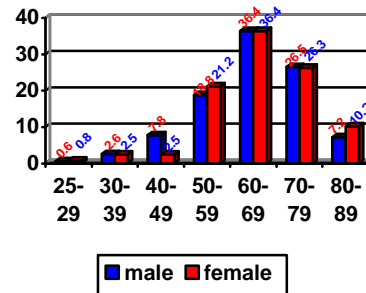
Table no. 2. Descriptive statistics of ages by gender

p=0,44	Masculine	Feminine	Total
No. of cases	154	118	272
Minimum	26,00	25,00	25,00
Median	65,00	64,00	64,00
Maximum	88,00	87,00	88,00

Average	64,82	63,58	65,33
Standard deviation	10,54	10,14	10,88

The most affected age group was the age group of 60-69 years old (36.3%), followed by the age group of 70-79 years old (26.5%). The same can be observed separately by gender, where 36.4% of men and 36.4% of women belonged to the age category of 60-69 years old. ($p=0,74$).

Figure no. 2. Distribution of cases according to gender and age groups



In terms of interventions, most of them were scheduled for surgery (75.3%) and emergency surgery was performed in 24.7%. These rates are valid for each gender separately (no difference by gender: $p=0,8$ on how to conduct the interventions).

Table no. 3. Relation between gender and surgical intervention

p-0,8			SURGERY		Total
			SCHEDULED	EMERGENCY	
Gender	B	number	108	46	154
		%	70,2%	29,8%	100.0%
	F	number	97	21	118
		%	82.2%	17.8%	100.0%
Total		number	205	67	272
		%	75,3%	24,7%	100.0%

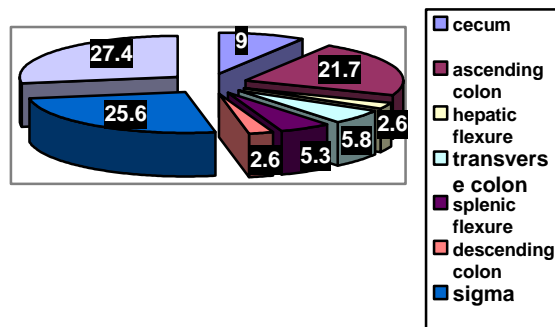
Tumour localizations on segments in emergency operations performed show a predominance of the cecum ascending, sigma and rectum, representing 84%, a comparable percentage value with the reported locations in all colorectal neoplastic pathology, surgically treated at the same time.

Of the total of 67 emergency surgeries, the type of the tumour and localization of complications can be summarized in the below-table:

Table no. 4. Complications type and tumour localization

Localization	Number	%	Complications
Cecum	6	9	5 occlusions, 1 perforation
Ascending colon	14	21,7	10 occlusions, 4 perforations
Hepatic flexure	2	2,6	2 occlusions
Transverse colon	4	5,8	4 occlusions
Splenic flexure	4	5,3	3 occlusions, 1 occlusion + hemorrhage
Descending colon	2	2,6	2 occlusions
Sigma	17	25,6	15 occlusions, 2 perforations
Recto	18	27,4	9 occlusions, 3 perforations, 3 hemorrhages, 3 hemorrhages + perforation

Figure no. 3. Emergency surgeries according to tumour localization



The complication which required emergency surgery in 87.9% of cases was the intestinal occlusion.

The surgeries with radical visa performed in emergency conditions represent approximately 68% of the total, the remaining of 32% having palliative character.

Most interventions in general or by gender were made with radical intent (76%), followed by palliative option (24%). These proportions are observed individually by gender, men-women, so figure no. 4 demonstrates a similar pattern and hence the lack of statistical significance by genders: p=0, 55.

Regarding the type of anaesthesia applied and because the nature of interventions is laborious, the oral-tracheal intubation anaesthesia prevailed by (93.5%), followed by spinal (5.0%). We have not found statistically significant differences by genders, regarding the type of anaesthesia.

All cases were adenocarcinomas with varying degrees of differentiation, 2 being mucinous carcinomas. From the 13 adenocarcinomas without mucinous component, 4 were well differentiated, 7 moderately differentiated, the other 2 cases were poorly differentiated.

Of the 15 cases, 6 were diagnosed in stage pT2 (own muscle invasion), 7 in stage pT3 (subserosal or serosal invasion) the other 2 were diagnosed as stage pT4, exceeding the serosa. As regarding lymphonodular metastases, 7 cases had metastases in at least one regional lymph node, the other 8 cases being non-metastatic tumours.

VEGF-A positivity was detected in 89% of cases. The intensity of VEGF-A expression did not correlate with the degree of tumour differentiation. Most cases were diagnosed with positive VEGF in stages pT3-4N1-2 (80%) compared with pT2-3N0 (20%).

DISCUSSIONS

As far as our study is concerned, colorectal cancer has been diagnosed with a slight weight in males: 154 cases in men (56.6%) and 118 cases in women (43.4%), with no statistically significant difference.

The most affected age group is the age group of 60-69 years old (36.3%), followed by the age group of 70-79 years old (26.5%). The same can be observed separately by genders, where 36.4% of men and 36.4% of women belonged to the age category of 60-69 years old. Similar studies show the same preponderance for this age group.(2,3)

In terms of the nature of the intervention, the study reveals that in young ages, the planned interventions predominate, but with aging, the interventions are increasingly gaining a sense of emergency.

In terms of macroscopic appearance we have centralized tumour types in three categories: polypoid, infiltrative and exulcerated. Our research results showed that the most frequently encountered form is the infiltrative tumour followed by polypoid form and exulcerated form. Similar to

other recent studies (4,5) we have found no significance between macroscopic appearance of colorectal cancer and the gender of patients, or between appearance and age.

High level of VEGF is directly correlated with the formation of metastases and reserved prognosis. The same group of researchers first suggested that VEGF and its receptor flt-1 is a therapeutic target in the treatment of colorectal cancer.(6) Recent studies have shown that patients who were VEGF positive diagnosed, have a poor prognosis compared to the VEGF negative, regardless of the clinical stage in which they were diagnosed.(7)

CONCLUSIONS

In the treatment of colorectal carcinoma, surgery is extremely important, on condition that the disease should be diagnosed at an operable stage. Surgery treatment accompanied by the oncologic one can bring major benefits to the patient.

It is important to implement a behaviour to impose molecular analysis for all patients with colorectal cancer in order to determine the expression of genes associated with the production of metastases.

Acknowledgement:

This paper is developed within the Sectoral Operational Programme Human Resources Development (HRD), financed from the European Social Fund and the Romanian Government by the contract no. POSDRU/89/1.5/S/60782.

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