

Prognosis of colorectal cancer: clinical, pathological and therapeutic correlation

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Abstract

Introduction: Significant progress in the knowledge of carcinogenesis and natural history of colorectal carcinoma (CRC), especially in polyp-cancer sequention and time for transition, are important prerequisites for a new approach to diagnosis. Surgical resection is the mainstay therapy for colorectal cancer, and pathologic assessment of the resected specimen provides data for assessment of outcome and rationale for adjuvant therapy. A pathology report includes TNM stage, tumor type, histologic grade, status of resection margins, and vascular invasion. **Aim:** The purpose of this paper was to highlight the pathological features and their correlations with postoperative evolution and prognosis of this cancer. **Patients and Methods:** Data was collected using the database system of the Emergency County Hospital of Craiova, Romania. A total of 302 patients from January 2003 to December 2005 were included. **Results:** The average survival for the entire group was 44.35 ± 28.94 months, and the D'Agostino-Pearson test for batch distribution showed abnormal distribution with two peaks, separated by a group of five patients who survived between 37 and 8 months. Fifty-one (38.05%) patients presented a median survival of 73.54 ± 10.47 months. **Conclusions:** Factors that contribute to a favorable prognosis in CRC are vegetant gross tumors and papillary microscopic forms, G1 and G2 degree of differentiation and disease diagnosed in stages I and II.

Keywords: colorectal cancer, colonoscopy, adenocarcinoma, prognostic factors.

✉ Introduction

Colorectal cancer was the third most common cancer in the world, with 663 904 new cases per year in men and 571 204 cases in women – representing 10% and 9.4% of all malignancies [1]. New research about colorectal cancer (CRC) are determined by the continuous increase of disease incidence both in developed countries, that already register high levels of prevalence, and in countries where CRC incidence was not regarded as a matter of concern. The increase in incidence of colorectal cancer in Romania and also in Eastern Europe countries could be attributed to lifestyle changes, presumably introduced by westernization, resulting in obesity and physical inactivity [2].

The diagnosis and early detection of CRC is one of the major goals and should become a priority for the health system.

Colorectal cancer recognizes a natural evolution compatible with a long asymptomatic period, generally estimated to last over five years. This period corresponds to early stage of cancer transformation of adenomatous polyps to cancer and invasion beyond the basement membrane. The diagnosis of CRC is most often in advanced stages, when the extent of lesions and their location are determinants of clinical expression and invasion beyond the basal lamina.

General consensus is that flexible colonoscopy is the method of choice for diagnosis. It should be performed

to all subjects belonging to a category of risk. In current practice, the most widely used screening test is fecal occult bleeding, followed by flexible sigmoidoscopy and colonoscopy. More recently, fecal DNA is studied to search for hereditary forms (genetically).

Surgery is the mainstay of therapy. The principles and techniques of surgical treatment were not changed significantly in the last years, but it became more aggressive in complicated cases especially due to progress in intensive care.

The prognosis of CRC patients involves many factors such as histological type of cancer, size, location, degree of tumor invasion, loco-regional metastasis (number of affected nodes) and in other organs [3]. To improve CRC prognosis, fundamental research in genetics and molecular biology, and colorectal screening with the widespread practice of noninvasive techniques (virtual colonoscopy) are some new or relatively new directions to be developed [4]. The most powerful predictors of postoperative outcome in colorectal cancer are the pathologic aspects of the resection specimen. Thus, the pathologic stage and stage-independent prognostic factors should be analyzed: histologic grade, vascular invasion, perineural invasion, and tumor border features. In rectal cancer, the main prognostic factor was the pathologic evaluation of the resection specimen, which serves as an objective indicator for the quality of completeness of total mesorectal excision and is itself predictive of outcome [5].

This study intends to analyze colorectal cancer incidence and mortality trends in the region from 2003 to 2005, to correlate tumor locations, macroscopic and microscopic pathological data with treatment outcomes, results, and to evaluate these findings in the context of changing environmental and social conditions, with possible implications for the health policies.

Patients and Methods

We studied retrospectively a cohort of 302 patients with colorectal cancer hospitalized in the Emergency County Hospital of Craiova (EHC) in all three surgical clinics, from January 2003 until December 2005.

We performed this study in collaboration with the Gastroenterology Clinic, Oncology Clinics and the Pathology Laboratory of the Hospital, in order to identify cases of colorectal cancer, to assess the therapeutic management and establish morphological aspects.

Of the 302 patients hospitalized in EHC, 73 patients were addressed to specialized centers for oncologic surgery, 67 patients had an unresectable tumor and 28 patients were in the end-stages of the disease and surgery was palliative (Figure 1).

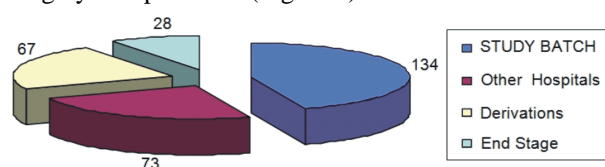


Figure 1 – CRC batch selection, 2003–2005.

The remaining 134 patients represented the group that was studied retrospectively; those cases benefited from tumor resection (which could be pathologically assessed) and adapted oncology treatment.

All 134 patients had a colonoscopy with tumor biopsy or barium enema. Preoperative staging was performed with abdominal ultrasound, chest X-ray and abdominal and/or pulmonary CT-scan to detect metastatic disease. In emergency cases, with obstruction, perforation or bleeding, investigations were limited to abdominal simple X-ray and ultrasound.

Data were collected from the electronic database of the hospital, observation charts and histopathological reports. Data on survival July 1st, 2010 – when the patient follow-up – were from the Registry of Civil Status of Craiova.

The inclusion criteria were: pathology diagnosis of colon or rectal cancer before surgery.

Exclusion criteria were: endoscopic treatment, unresectable cases, adenomatous familial polyposis, Hartmann reversal, colostomies.

After primary selection, patients were studied in groups according to the investigated parameters and endpoints: demography, clinical and staging, aspects of pathology, therapeutic data, prognosis and survival.

Statistical tests were: *chi-square* (χ^2) test to measure the dependence between parameters and significance tests (ANOVA and Student). The main statistical analysis software packages were Microsoft Excel 2003 and Epi Info 2000. Kaplan–Meier curves were obtained for survival prognostic correlations.

The main goals for this study were:

- to examine the correlation between the clinical, pathological and therapeutic aspects, and their influence on the prognosis of colorectal cancer;
- to examine the results of survival at five years after surgery and how it was influenced by pathological aspects.

Results

We noted a global annual increase in number from 87 patients in 2003, 102 patients in 2004, and 113 patients in 2005 (the percentage increase was 29.88%), but when it comes to proportion of resected cases there is a slight decreasing trend, from 61 (2003) to 40 (2004) and 33 patients (2005), with a percentage reduction of 45.91% (Figure 2).

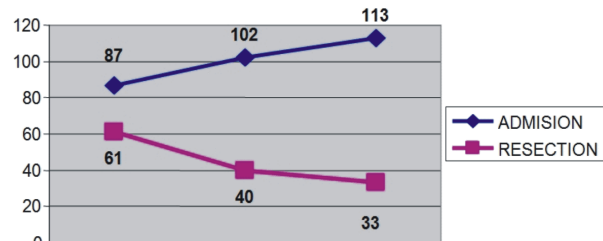


Figure 2 – CRC admissions and resections, 2003–2005.

This could be explained by a greater accessibility of endoscopy that diagnoses cases both in early and in late stage of the disease, with unresectable tumors.

For an effective and comparative analysis of clinical features, treatment and prognosis in CRC, the large bowel was divided based on embryological, anatomical, clinical, pathogenesis and therapy in three segments: right colon (I) until the splenic angle, left colon (II) until the recto-sigmoid junction, and rectum (III) [5]. According to this, the location of CRC was: right colon – 32 cases (23.88%), left colon – 56 cases (41.79%), and rectum – 46 cases (34.32%) (Table 1).

Table 1 – Summary table of the CRC study group

	Patients [#]	Deaths [#/%]	Alive [#/%]	Average survival [months]	Standard deviation	Lower limit [months]	Upper limit [months]
(A) Tumor site							
Right colon	32	18/56.2	14/43.7	53.958	6.054	42.092	65.825
Left colon	56	31/55.3	25/44.6	51.006	4.538	42.112	59.899
Rectum	46	34/73.9	12/26	41.496	4.503	32.67	50.321

	Patients [#]	Deaths [#/%]	Alive [#/%]	Average survival [months]	Standard deviation	Lower limit [months]	Upper limit [months]
(B) Tumor gross aspect							
<i>Ulcerated</i>	52	37/71.1	15/28.8	45.374	4.434	36.684	54.064
<i>Infiltrative</i>	52	30/57.6	22/42.3	47.885	4.79	38.497	57.272
<i>Vegetant</i>	30	16/53.3	14/46.6	55.602	6.108	43.630	67.574
(C) WHO microscopic classification							
<i>Tubular</i>	90	60/66.6	30/33.3	47.926	3.442	41.18	54.672
<i>Mucinous (colloid)</i>	25	14/56	11/44	46.073	7.500	31.372	60.773
<i>Papillary</i>	13	6/46.1	7/53.8	48.231	6.074	36.326	60.136
<i>Particular / rarely</i>	6	3/50	3/50	22.5	2.376	17.843	27.157
(D) Tumor grading							
<i>G1</i>	10	1/10	9/90	81.333	–	–	–
<i>G2</i>	86	51/35.3	35/64.6	55.642	2.963	49.835	61.45
<i>G3</i>	19	12/63.1	7/36.8	36.105	7.321	21.757	50.453
<i>G4</i>	19	19/100	0/0	4.947	0.839	3.302	6.592
(E) TNM stage							
<i>Stage I</i>	18	7/38.8	11/61.1	67.968	5.802	56.596	79.341
<i>Stage II</i>	73	35/48	38/52	62.516	3.182	56.279	68.752
<i>Stage III</i>	3	1/33.3	2/66.6	45.3	–	–	–
<i>Stage IV</i>	40	40/100	0/0	13.375	2.341	8.786	17.964

Gross examination of specimens indicated the following aspects: infiltrative – 34 cases, ulcerative – 18 cases, vegetant – 25 cases, ulcerative and vegetant – 34 cases, infiltrative and ulcerated – 18 cases, infiltrative and vegetant – one case, vegetant-infiltrative-ulcerated

– four cases. For a synthetic analysis we used the classification of colorectal adenocarcinoma in the three macroscopic groups as follows: ulcerated – 52 cases (38.8%), infiltrative – 52 cases (38.8%) and vegetant – 30 cases (22.8%) (Table 1 and Figure 3).

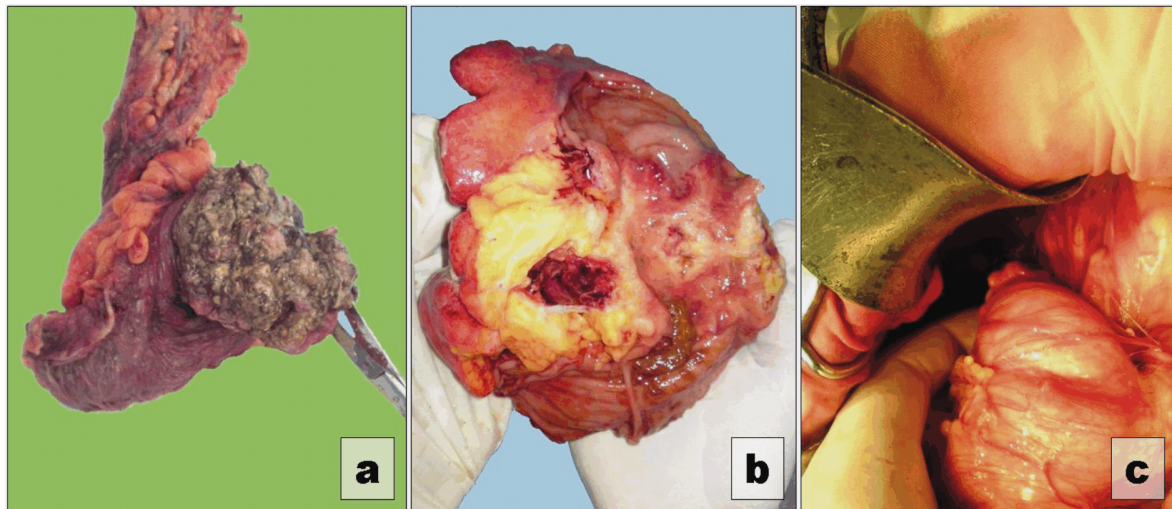


Figure 3 – (a) Vegetant ascending colon cancer. (b) Vegetant and ulcerated: spleen angle colon cancer. (c) Infiltrative transverse colon cancer.

Microscopic evaluation identified a predominance of tubular shapes 90 cases (67.16%), followed by colloid – 14 cases (15.67%), papillary – 13 cases (9.7%) and other particular or rare forms (GIST, etc.) – six cases (7.46%) (Table 1 and Figure 4).

In terms of grading, 10 cases were G1 (7.46%), 86 cases – G2 (64.17%), 19 cases – G3 (14.17%) and 19 cases – G4 (14.17%) (Table 1 and Figure 5).

TMN staging of the study group revealed 18 patients in stage I (13.43%), 73 in stage II (54.47%), three in stage III (2.23%) and 40 cases in stage IV (29.85%) (Table 1 and Figure 6). Positive nodes were identified in 114 patients with stage III and IV, as follows: stage III – N₁ 39 cases and N₂ 35 cases; stage IV – N₁ 33 cases and

N₂ seven cases. Hepatic and peritoneal metastases were identified in all 40 patients in stage IV (Table 2).

All patients were followed postoperatively in oncology and received chemotherapy according to specific protocols.

When analyzing the survival length according to tumor location, we found that survival in colic tumors is higher and statistically significant compared to the rectum – 53.95±6.05 months for right colon, 51±4.53 months for left colon, and 41.49±4.5 months for rectum ($p<0.05$). Kaplan–Meier curves showed significantly higher survival rates for colon compared to rectum (Figure 7).

At macroscopic examination, we found the longest

median survival for vegetant forms (55.6 ± 6.1 months), followed by the infiltrative (47.88 ± 4.79 months) and ulcerative (45.37 ± 4.43 months) types. Analyzing the statistical significance tests and Kaplan–Meier survival curves, we did not find significant differences in survival in terms of macroscopic forms, p -value of \log -rank test 0.351, Wilcoxon test 0.482, both higher than the reference of 0.050.

Concerning the microscopic examination, the highest percentage of patients alive was recorded in papillary forms (53.84%), followed by rare/particular forms (50%), mucinous (44%) and tubular (33.33%). In terms of

number of cases, papillary CRC had the best percentage of five years survival (53.84%) and longest survival (48.23 ± 6.07 months). Tubular forms (90 cases, 67.16%) – the most numerous in our study – had the lowest survival rate (47.92 ± 3.44 months) compared with the mucinous forms (46.07 ± 7.5 months) and papillary forms (48.23 ± 6.07 months). Particular forms had the lowest free-disease period (22.5 ± 2.37 months). However, looking at Kaplan–Meier survival curves at the end of the prospective study we note that there are no significant differences between microscopic forms of CRC in the analyzed group (Figure 8).

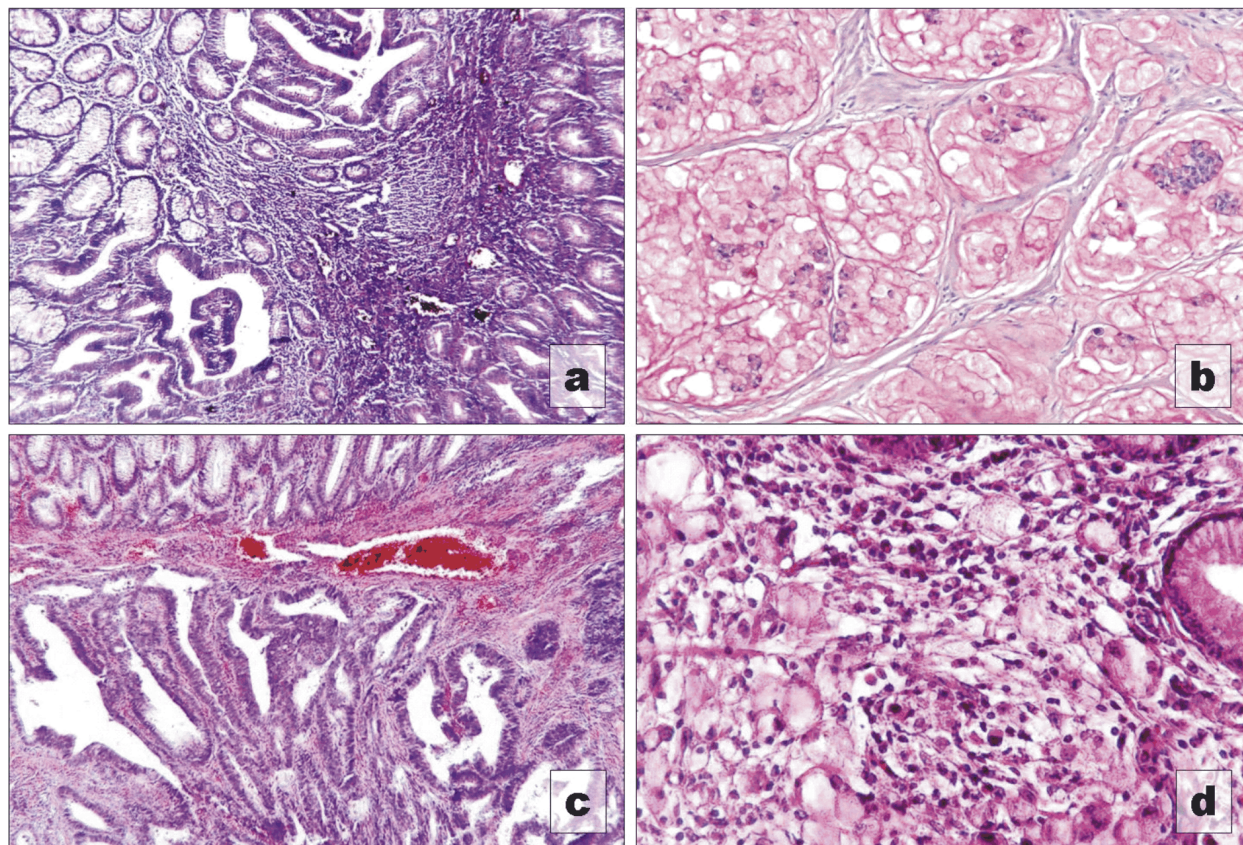


Figure 4 – Histopathologic types of CRC: (a) Tubular type (HE stain, $\times 100$); (b) Mucinous (colloid) type (HE stain, $\times 100$); (c) Papillary type (HE stain, $\times 100$); (d) “Signet ring cell” type (HE stain, $\times 200$).

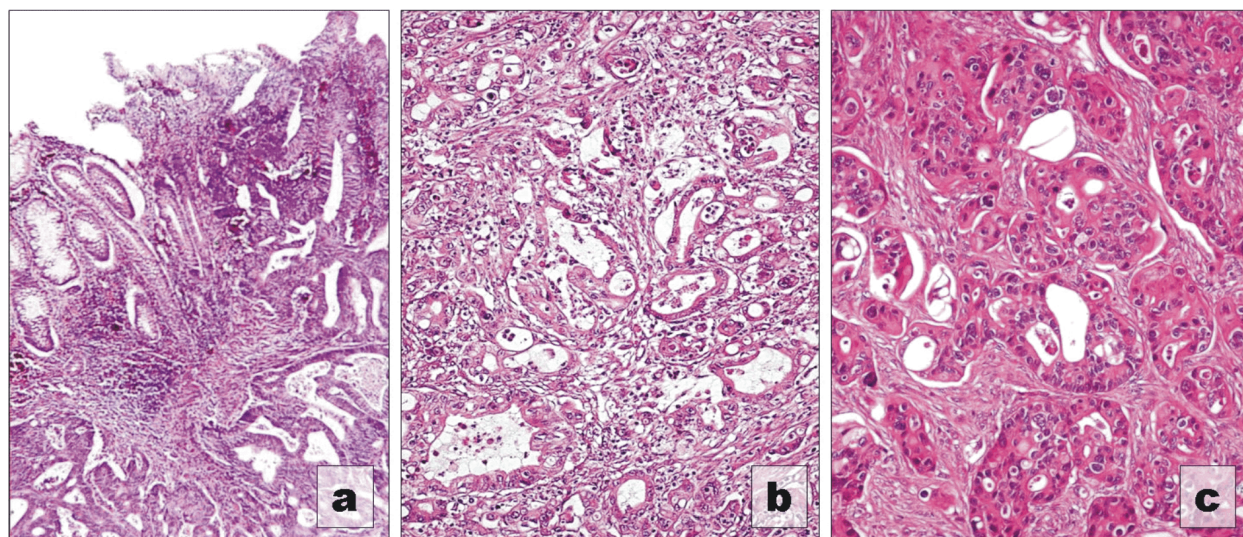


Figure 5 – CRC grading: (a) Well differentiated: G1 (HE stain, $\times 40$); (b) Moderately differentiated: G2 (HE stain, $\times 100$); (c) Poorly differentiated: G3 (HE stain, $\times 100$).

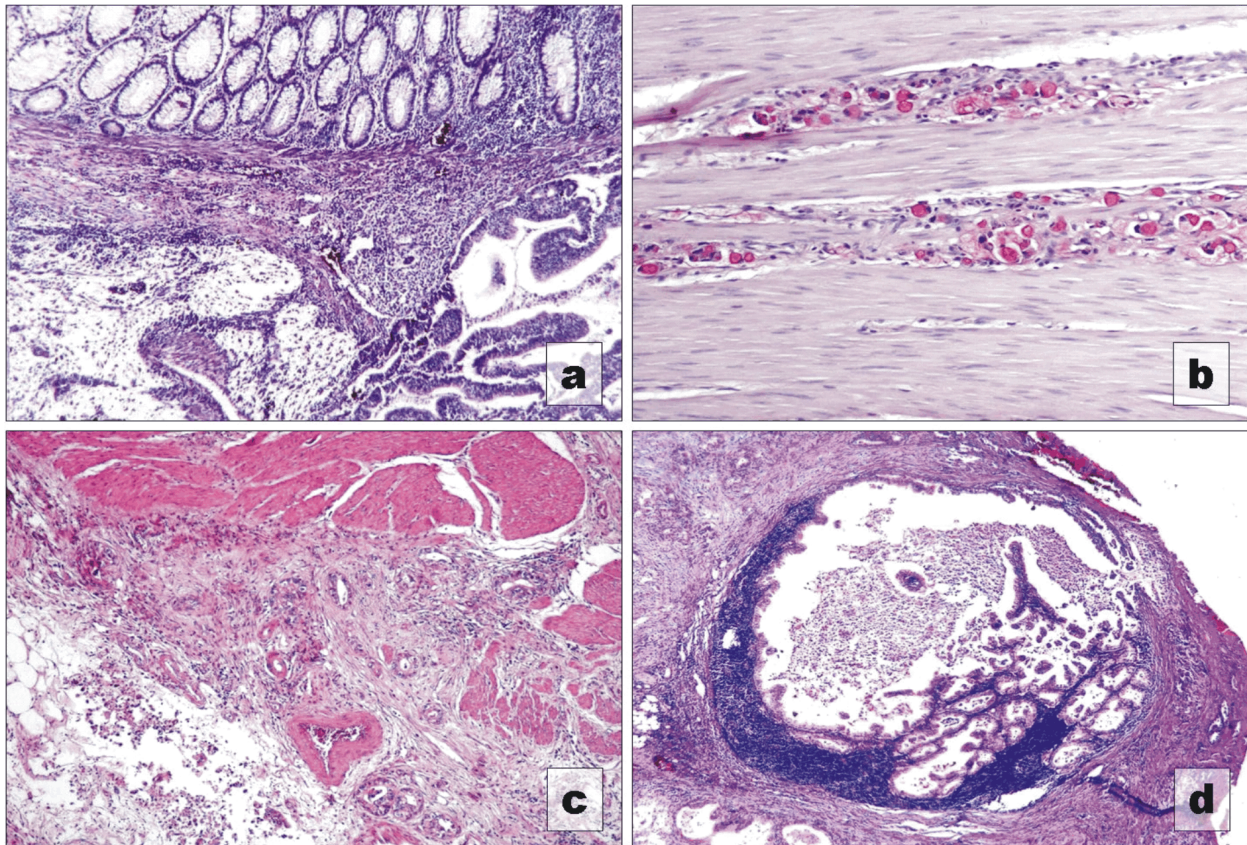


Figure 6 – CRC TNM staging: (a) Tubular adenocarcinoma invading the submucosa – pT1 (HE stain, $\times 100$); (b) “Signet ring cell” carcinoma invading the muscular layer – pT2 (HE stain, $\times 200$); (c) Tubular adenocarcinoma invading the serosa – pT3 (HE stain, $\times 40$); (d) Papillary adenocarcinoma invading a mesenteric lymph node – pN1 (HE stain, $\times 40$).

Table 2 – CRC: TNM staging

Stage	T	N	M	#	#	Stage
0	0	0	0	0	0	0
I	5T ₂	5N ₀	5M ₀	5	5	I
IIA	6T ₃	6N ₀	6M ₀	6	15	II
IIB	9T ₄	9N ₀	9M ₀	9		
IIIA	10T ₂	10N ₁	10M ₀	10	74	III
IIIB	21T ₃ + 8T ₄	29N ₁	29M ₀	29		
IIIC	6T _x + 2T ₂ + 27T ₃	35N ₂	35M ₀	35		
IV	4T _x + 1T ₂ + 18T ₃ + 17T ₄	33N ₁ + 7N ₂	40M ₁	40	40	IV

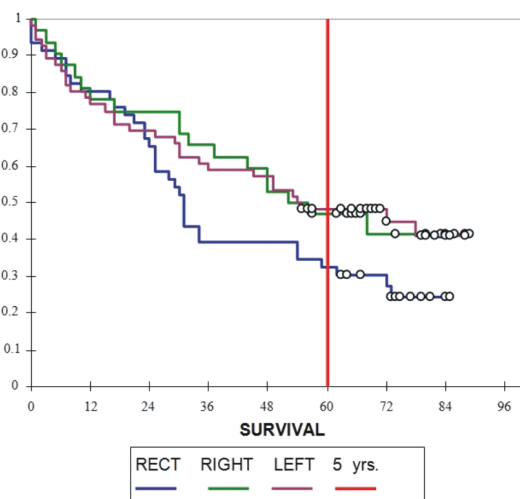


Figure 7 – Kaplan-Meier survival curves and CRC location.

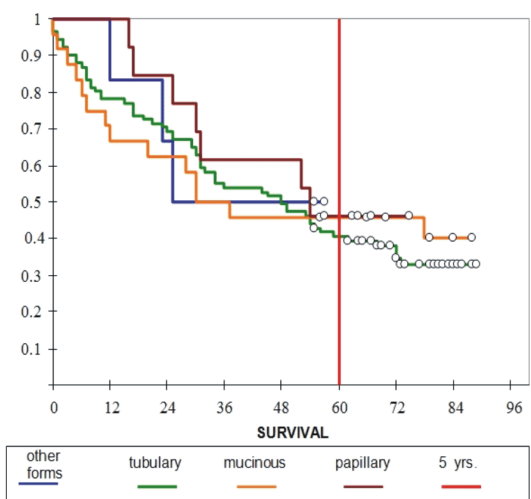


Figure 8 – Kaplan-Meier survival curves and CRC microscopic aspects.

The degree of differentiation of colorectal adenocarcinoma showed a large number of patients alive with G1 (90%), followed by those with G2 (64.62%) and (36.84%). No patient with G4 was alive at the end of the prospective. Patients with G1 had the best survival, on average of 81.33 months, followed by those with G2 with an average of 55.64 ± 2.96 months, G3 (36.10 ± 7.32 months) and G4 (4.94 ± 0.83 months). The differences between survivals according to tumor grade are statistically significant, and this fact is illustrated by the Kaplan–Meier survival curves (Figure 9).

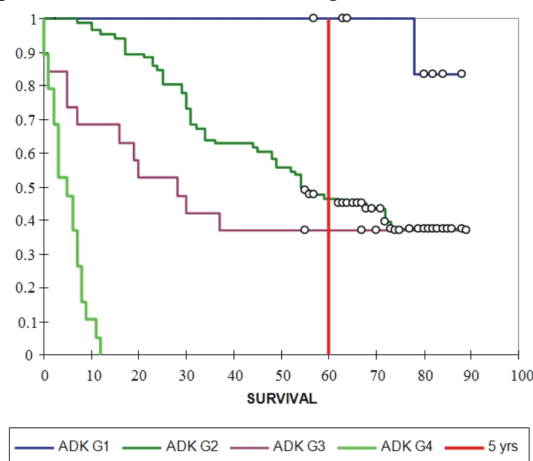


Figure 9 – Kaplan–Meier survival curves according to CRC grading.

Analysis of cases according to disease stage showed higher survival in the early stages compared with advanced ones. TMN staging of all 134 patients with CRC who underwent tumor resection revealed the highest percentage of survivors in stage I (11 patients – 61.1%), followed by those in stage II (38 patients – 52%). Two of the three patients from stage III (66.66%, both with G1 papillary forms) survived at the end of prospects and no patient in stage IV found at July 1st 2010. The average survival in the entire batch of 134 cases was 44.35 ± 29.94 months.

When analyzing tumor (T) stage in the group examined we found no patients with T₁. As expected, the highest percentage of patients still alive was in T₂ stage (44.44%), with a median survival of 57.43 ± 7.06 months. The percentage of T₄ patients (41.17%) is greater than that in T₃ (36.11%). Also, the average survival time of T₃ patients (47.25 ± 4.01 months) is significantly better than that of T₄ patients (43.11 ± 5.15 months) ($p < 0.05$). Patients whose tumor extension could not be assessed (T_x) had a disease-free interval of 44.6 ± 8.02 months.

The adenopathy seen in all 134 cases revealed that 38.01% of N₀ patients and 45.45% of people are alive on July 1st 2010. The number of N₀ cases is much higher than that of N₁, this contributing to the high percentage of patients still alive in the study group. The average survival for N₀ and N₁ patients was approx. 49 months, and for the N₂ patients of 11 ± 6 months, with a highly significant difference ($p < 0.001$).

The study of metastases in patients with CRC revealed that on July 1st 2010 no M₁ patient were alive, their average lifespan being 13.37 ± 2.34 months. M₀

patients survived at a rate of 54.25%, with an average survival of 63.8 ± 2.77 months. Log-rank significance and Wilcoxon tests for patients based on M shows that these differences are highly significant (p -value was below 0.0001, much lower than the α of 0.05). The location of CRC metastases allowed assessments of patient survival. The longest survival after surgery was present seen in one case with resected peritoneal metastases (pT2N1M1), being 42 months, followed by patients with liver and lung metastases (four cases, 0% survival, 19.75 ± 3.68 months), lung (three cases, 0% survival, 17.33 ± 3.18 months) and those with liver metastases (21 cases, 0% survival, 13.71 ± 2.84 months). Patients with peritoneal carcinomatosis survived 4 ± 1.69 months.

According to stage, patients that are still alive had a median survival of 67.96 ± 5.8 months for stage I, 62.51 ± 3.18 months for stage II, 45.3 months for stage III and 13.37 ± 2.34 months for stage IV. Log-rank and Wilcoxon tests showed the same high statistical significance differences between stages, with a p -value of less than 0.0001 (Figure 10).

On July 1st 2010, at five years from the end of the study, 51 patients (38.05%) were alive (Figure 11). In the analyzed group, we not could evaluate the aspects of local and regional recurrence of CRC, because records of these patients could not be made through a local or national cancer registry.

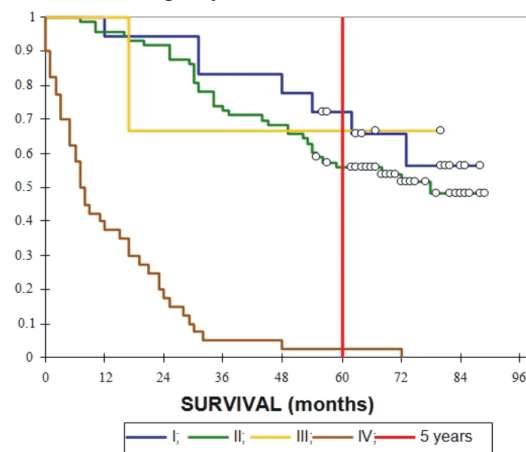


Figure 10 – Survival on July 1st 2010 according to CRC TNM stage.

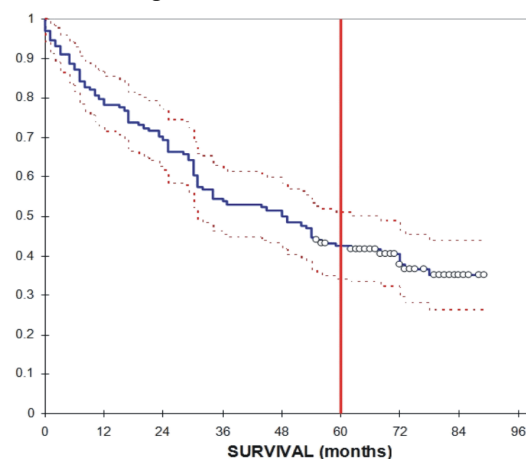


Figure 11 – CRC survival in the studied group at July 1st 2010.

Discussion

In our country, in 2005, the incidence of colon cancer ranked 5th and if cancers of rectosigmoid junction were added, ranked 3rd. Mortality due to colon cancer was on the 4th place among deaths from cancer in 2005. If mortality from rectosigmoid cancer were added, it ranked third [6].

In Romania, the incidence of CRC increased from 7.62/100 000 inhabitants in 2003 to 8.23/100 000 inhabitants in 2005. Separate figures for locations on different colic segments are not available.

Colon cancer is two times more frequent than rectal cancer [7]. CRC mortality in Romania followed a trend of steady increase from 14‰ to 18.3‰ for men and women between 1960 and 1990 to about 22.2‰ in between 1995 and 2003, and decreased slightly to 19.2‰ in 2008, according to EU statistics [8]. CRC incidence and mortality is much higher in urban areas, without a tendency to change from one year to another. Distribution of death rates on different regions of Romania indicates regions with similar levels to Central and Northern Europe – (Arad, Bucharest, Timiș) and areas (Vaslui, Ialomița, etc.) with very low mortality similar to Mediterranean countries (Greece, Albania).

A study by Efremidou EI *et al.* [9] on 143 cases confirmed the increased incidence from left to right for CRC and showed that this change is linked to decreased incidence of colic distal tumors correlated with age. In our study we did not find significant correlations with proximal tumors (17 of 55 cases, 30.9%) in females, but an association with distal colorectal localization in males is obvious (64 of 79 cases, 81.01%).

Proximal colon cancer is more likely to be detected in advanced stages than distal cancer, although there are conflicting communications on independent prognostic significance in relation to tumor location. A study by Zell JA *et al.* examined the survival of patients after colon cancer location using data from cancer registries in California [10]. Patients were analyzed between 1994 and 2004, with their tracking in 2006, dividing neoplasia location in three major segments: proximal/transverse, descending and sigmoid. Specific survival analysis was performed by Kaplan–Meier method and Cox test for risk.

The author has identified 87.586 cases of colon cancer: 54.453 (62%) in the proximal colon, 5.461 (6%) in the descending colon and 27.672 (32%) of the sigmoid. He noted the high number of cases of sigmoid cancer stage I, compared with proximal locations (29.3% vs. 17.3%, $p < 0.0001$). Locations proximal to the sigmoid had a higher percentage of low degree of differentiation (25.9% vs. 14.3%, $p < 0.0001$). After adjusting the group for stage, grading, treatment, number of lymph nodes examined (>12 vs. <12), and other clinically relevant variables, sigmoid cancer specific mortality was lower compared with proximal locations (risk ratio 0.89, 95% CC 0.86 to 0.91%). This analysis shows that large population sigmoid cancer is diagnosed in early stages, with a lower grading, and it has low specific mortality compared with proximal locations [10].

Two thirds of colorectal malignancies are localized

on the left colon and rectum. Recent studies suggest an increasing trend of right colic tumors, which have important implications for screening and surveillance, with total colonoscopy indication in such cases. Cancer incidence showed an overall increase. In Modena (Italy) Cancer Registry, an increase of 33.7% in all colonic segments was shown whereas rectal tumors tended to decrease. TNM staging showed a gradual increase of localized lesions (41.2% in 1984 to 53.3% in 1998), with a proportionate reduction of advanced tumors. Tumor study showed an increased incidence of colon tumors and in all segments, and especially a “migration” to the right. TNM classification showed a downward trend in stages, with an appreciable increase of localized lesions. These findings could be due to wider use of total colonoscopy [11].

The purpose of the study of Manxhuka-Kerliu S *et al.* was to analyze colic cancer concerning all prognostic factors, including histological type and degree of vascular invasion, perineural invasion and limits of tumor resection [12]. Hundred and 49 cases and resection specimens of CRC were investigated. Adenocarcinoma was the most common histological type (85.9% of cases), of which 60.94% and 39.06% in men and women respectively, squamous cell carcinoma was found in 7.38% of cases, of which 63.63% and 36.36% in men and women respectively, mucinous carcinoma in 4.68%, of which 57.15% and 42.85% in men and women respectively, while adenosquamous carcinoma, undifferentiated carcinoma and *in situ* carcinoma represented 0.71% of all cases. Dukes classification was used to define tumor invasion into the wall. Dukes stage B was found in 68.45% of cases, while Dukes stage C was found in 31.54% of cases. Regarding the grading, colic cancer was mostly with moderate differentiation (75.16%) without vascular and perineural invasion, with safe resection limits in all cases. Data indicate that the pathological resection sample is the most powerful predictor for postoperative outcome in colic cancer. Dukes staging and degree of differentiation provided prognostic information independent of colon cancer. However, grading of the tumor should be evaluated as the best prognostic pattern [12]. Concerning histological types, Compton’s study shows that based on current evidence, the only histologic types of colorectal cancer that are prognostically significant are signet-ring cell and small-cell carcinomas (unfavorable prognosis) and medullary carcinoma (favorable prognosis). Mucinous carcinoma, when associated with microsatellite instability, also has favorable prognosis [5]. In our study, papillary and medullary forms have the best prognosis.

Further analysis on a group of 100 patients with CRC assessed the influence of histopathological staging and prognostic factors of surgical treatment on this malignancy. Prognostic factors adversely influencing the outcome of surgery in stage D by Astler–Coller/Dukes or stage IV by TNM classification (T_{1-4} , N_{0-2} , M_1), and poorly differentiated adenocarcinoma, lead to a high statistically significant mortality, during the perioperative period of the disease [13].

In our study, the correlation between the location of CRC and the degree of differentiation revealed no items of significance. The *chi*-square test result is less than 12.592 at 95% significance level, so there is no influence between the two factors. The real *p*-value is 0.586, greater than the limit of $p=0.05$, indicating that there is no significant distribution and statistical difference between carcinoma location and degree of differentiation. Also, we did not find a correlation between the adenocarcinoma subtype, patient age and tumor location.

Tumor differentiation is an important prognostic factor. It is correlated with TNM stage and each of its components. The risk of nodal metastases for each value of T is correlated with tumor grading. The results are important in risk assessment when considering operative procedures or local resection (total mesorectal excision) [14].

Extensive studies of colorectal cancer prognosis assessment differ between Europe and the U.S.A. by location and morphological aspects because they showed a lower survival for colorectal cancer in Europe than in the U.S.A. This analysis suggests that the large survival advantage for colorectal cancer patients in the U.S.A. can only marginally be explained by differences in the distribution of sub-site and morphology. The main explanatory difference is the proportion of adenocarcinoma in polyps [15].

Vertical tumor growth, reflected by T classification, represents the most important prognostic variable in colorectal cancer. Tumor size proved to be an independent prognostic parameter for patients with colorectal cancer. Optimal cut-off values vary among different parts of the large bowel. Whereas prognostic significance is strong within the colon, it appears to be of minor value within the rectum [16]. A retrospective study found that the number of lymph nodes removed in patients with rectal carcinoma (RC) was significantly lower than in the colon carcinoma (CC) ($p<0.001$), while the invaded lymph nodes in the CR group was significantly higher than the CC group ($p<0.001$). Cases with a large number of positive lymph nodes (N+) was higher in CR ($p=0.004$). The number of N+ cases was compared with different subtypes of T (T_1 – T_4), and the results demonstrated the direct association of N with T ($p<0.001$). In addition, the ratio of positive lymph nodes and number of lymph nodes examined in stage III CR group was significantly higher than the CC group ($p<0.001$). Finally, CR appears to be more prone to metastasize in the lymph nodes than CC, which has great clinical importance [17].

While general prognostic factors for colorectal carcinoma have been extensively investigated, the relationship between tumor characteristics and development of liver metastases were not clearly understood. The purpose of a study coordinated by Antić A *et al.* was to determine which histopathologic features of CRC can be associated with subsequent development of liver metastases. They analyzed tumor size, depth of invasion in the intestinal wall, into nearby organs, tumor invasion, vascular and lymphatic invasion,

lymph nodes affected. Statistical analysis revealed significant correlations ($p<0.01$) between tumor size, degree of tumor differentiation, tumor vascular and distant invasion, with subsequent development of liver metastases in both groups [18].

According to the National Cancer Data Base, survival at five years in colon and rectum cancer is shown in Table 3. We can say that our findings are comparable with the literature, mentioning that the number of our patients in early stages of neoplasia is reduced [19].

Table 3 – CRC: survival in CRC (National Cancer Data Base)

Colon cancer			Rectal cancer		
Stage	Distribution [%]	Survival [%]	Stage	Distribution [%]	Survival [%]
I	25.1	70	I	33.9	71.5
II	30.3	60	II	24.8	52.4
III	25.2	44	III	25.9	36.9
IV	19.4	7	IV	15.4	3.6

Results of a European study show that survival at five years in patients with CRC as a whole is especially influenced by stage, and the factors that are directly or indirectly related to the primary tumor. Thus, these prognostic factors that should be considered in assessing the survival and follow-up are: stage, grading and adenopathy [20].

Despite the increasing incidence of CRC, there are several reasons for optimism. Most lesions are currently diagnosed at an early stage, and this is associated with a significant increase in survival. The disease is certainly treated better than in the past; the main challenge for coming years is therefore to achieve a sustained reduction of mortality for colorectal neoplasms [21].

Conclusions

Colorectal cancer tends to increase in terms of incidence and prevalence. Our results are similar to values reported nationwide in terms of incidence, prevalence and mortality in Dolj County. The introduction of new techniques for screening the population, the increasing educational level of the population, the use of recent advances in laparoscopic surgery and oncology management, properly improved the results. The overall survival in our study group was 51 patients (38.05%), indicating that the results were good, even if we had a high percentage of emergency interventions practiced in advanced stages of disease. Factors that contribute to a favorable prognosis in CRC are vegetant and infiltrative gross tumors, papillary microscopic forms, G1 and G2 grading and disease diagnosed in TNM stages I and II.

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