

Histopathological Prognostic Factors for Colic Adenocarcinoma

ANNE-MARIE AL KHATIB¹, ALEX EMILIAN STEPAN²,
CLAUDIU MĂRGĂRITESCU², BIANCA CĂTALINA ANDREIANA²,
MIRELA-MARINELA FLORESCU², CRISTIANA EUGENIA SIMIONESCU²,
RALUCA NICULINA CIUREA²

¹PhD student, Department of Pathology, University of Medicine and Pharmacy of Craiova

²Department of Pathology, University of Medicine and Pharmacy of Craiova

ABSTRACT: The majority of colorectal carcinomas are adenocarcinomas derived from the colic mucosae cell, more frequently moderately differentiated. The purpose of this study was to determine the incidence of CRC and the relationship between histopathological risk factors in patients with colic adenocarcinomas. The study included 144 cases of CRC diagnosed within the Pathology Laboratory of the Clinical County Hospital of Craiova in the year 2017. The biological material consisted in samples from colectomies and hemicolectomies provided from patients admitted within the surgical clinics of the same hospital, then fixed with 10% buffered formalin and afterwards processed using the classic histopathological technique of paraffin inclusion and staining with hematoxylin and eosin. We observed certain histopathological parameters such as: pattern, grading, stage, vascular invasion and neural invasion. The mean age of diagnostic was $68,6 \pm 11,2$, and it was predominantly male patients (64.6%). Most cases presented with mucinous pattern (31.9%) and cribriform comedocarcinoma type (29.9%). The majority were classified as stage III B (34%), being moderately differentiated (64,6%) and associated with vascular invasion (47,2%) and perineural invasion (25,7%). Statistical analysis indicated significant relationships between tumor stage and differentiation grade ($p < 0,01$, X2test), as well as between tumor stage and vascular invasion ($p < 0.05$, X2test), without including perineural invasion ($p < 0.05$, X2test).

KEYWORDS: colic adenocarcinoma, tumoral stage, grading, prognostic

Introduction

Colorectal carcinoma (CRC) originated from the colorectal mucosae, being the third most diagnosed type of cancer and the fourth cause of death worldwide [1]. The mean age of diagnosis is between the ages of 60 to 80, less than 20% of cases are in patients under the age of 50 and even rarer in patients under the age of 40, with the exception of those who present genetic predisposition [2]. In practice, most CRC cases are adenocarcinomas (90%), most frequent being moderately differentiated (70%) [3]. Several studies have demonstrated that the negative prognostic factors are: advanced tumoral stage, positive resection margins, lymphovascular invasion, perineural invasion, other organ invasion, operation type, major morbidity, Dukes' classification, local recurrence, high serum CEA and CA 19-9 levels [4,5]. We observed histopathological parameters as prognostic factors which must be taken into consideration to assess the aggressiveness of CRC.

Objective

Statistical analysis of histopathological parameters of CRC.

Material and methods

The study included 144 cases provided by patients admitted in the Surgical Departments of the Clinical County Hospital of Craiova and diagnosed within the Pathology Department in the year 2017. Biological material consisted of samples of colectomy and hemicolectomy, which were beforehand processed with 10% buffered formalin and processed with the classic histopathological technique of paraffin inclusion and staining with hematoxylin-eosin. Classification by grading and tumor stage was done in concordance with WHO (2016) recommendations [6]. Histopathological data (grading, pattern, tumoral stage, vascular and neural invasion) was analyzed using the IMB SPSS 20 program, after which statistical data was correlated with the help of Chi-square (X²), values lower than 0,005 being considered relevant. The study was approved by the local ethics committee (no. 42/27.03.2018).

Results

For the analyzed CRC, the mean age of diagnosis was of $68,6 \pm 11,2$.

Table 1. Clinical and histological parameters of colorectal cancer

Characteristic	Parameters	Cases (nr.)	Cases %
Age group	31 - 40	3	2.1%
	41 - 50	9	6.2%
	51 - 60	8	5.6%
	61 - 70	48	33.3%
	71 - 80	51	35.4%
	80+	25	17.4%
Sex	F	51	35.4%
	M	93	64.6%
Pattern	cribriform	43	29.9%
	comedo-carcinoma type	7	4.9%
	spindle cell	19	13.2%
	signet ring	7	4.9%
	medullary	8	5.6%
	micropapillary	46	31.9%
	serrated	14	9.7%
Tumor Stage	I	13	9.0%
	IIA	46	31.9%
	IIB	8	5.6%
	IIC	4	2.8%
	IIIA	2	1.4%
	IIIB	49	34.0%
	IIIC	7	4.9%
IV	15	10.4%	
Grading	1	13	9.0%
	2	93	64.6%
	3	38	26.4%
Vascular invasion	yes	68	47.2%
	no	76	52.8%
Perineural invasion	yes	37	25.7%
	no	107	74.3%

The age varied between 34 and 87 years old, of which the majority were within the interval of 71-80 years old (35,4%), and most of the patients were of male gender (64,6%) (Table 1).

On the studied lot, from the histopathological analysis of patterns of the 144 cases resulted the fact that most cases present mucinous pattern (31,9%) and cribriform comedo-carcinoma type (29,9%), the following being represented in a lower percentage: signet ring pattern (13,2%), serrated (9,7%), micropapillary (5,6%), and the spindle cell pattern was put in last place along with medullary type with a representation of 4,9% each (Table 1).

The majority of cases were classified as stage III B (34%) (Table 1), being moderately differentiated tumors (G2) (64,6%), (Table 1) (Fig. 1). The association with vascular invasion (47,2%) (Table 1) (Fig. 1) and neural (25,7%) (Table 1) was representative.

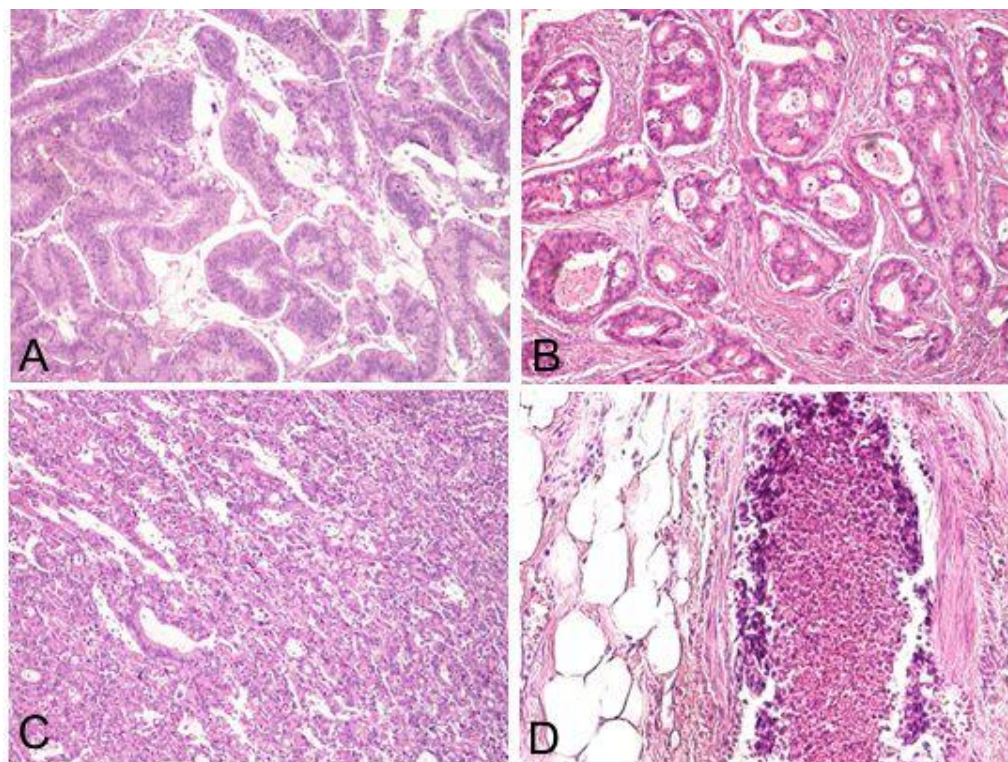


Fig. 1. Histopathological aspects of colic adenocarcinomas. A. Well differentiated colic adenocarcinoma (G1), HE-ob.40x; B. Moderately differentiated colic adenocarcinoma (G2), HE-ob.40x; C. Low differentiated colic adenocarcinoma (G3), HE-ob.40x; D. Vascular invasion-tumoral embolus, HE-ob.10x

We observed significant statistical aspects between tumoral stage and differentiation grade ($p < 0,01$, X2test), as well between tumoral stage and vascular and perineural invasion ($p < 0,05$, X2test). Also, significant statistical

aspects were also found between grading and vascular invasion ($p < 0,05$, X2test), but insignificant in comparison with perineural invasion ($p > 0,05$, X2test) (Fig. 2).

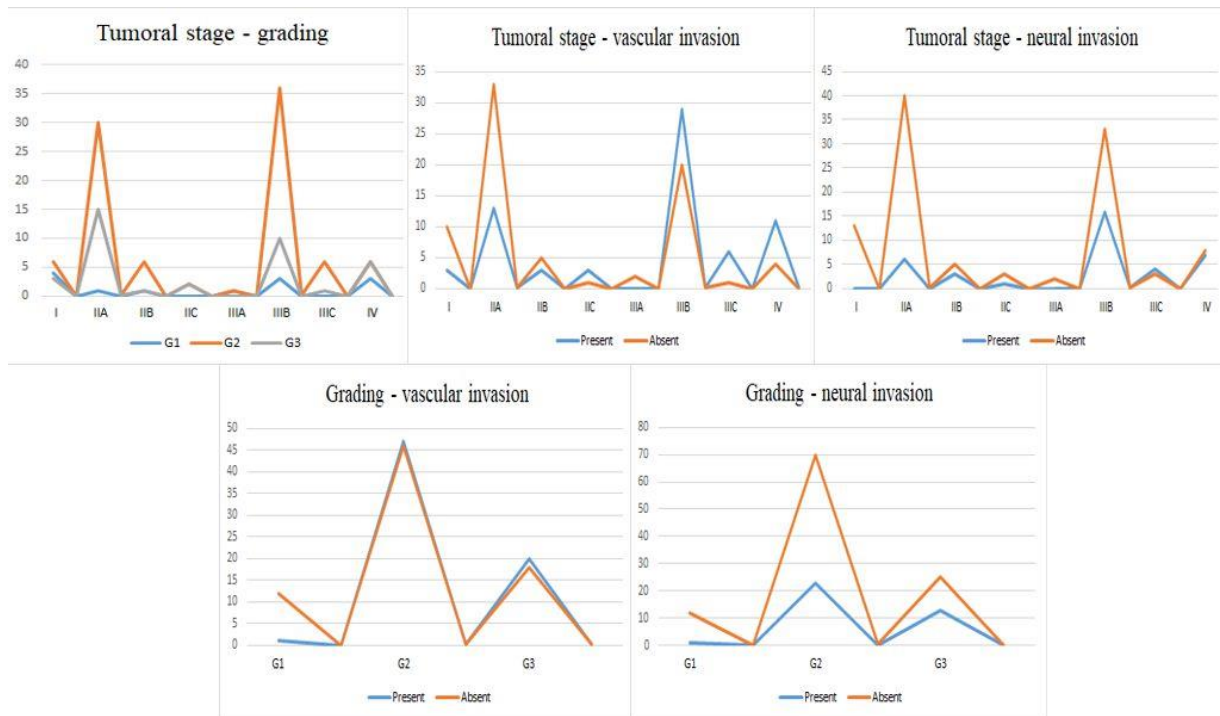


Fig. 2. Association between the analysed parameters

Discussions

CRC is a primary malignant tumor which arises from the colorectal mucosae, being one of the most common types of cancer. Histopathological analysis of the biopsies or surgical resection samples is crucial in the management of the patient as well as his prognostic.

From the age of diagnosis of the studied group, arises the facts that a majority of patients were included within the interval of 71-80 years (35,4%), of which 64.6% were of males. Data described in literature, report that the mean age of diagnosis is with 67-68 years, the majority being males diagnosed between 65 and 84 years [7,8,9].

Histopathological analysis of the 144 cases showed that most presented with a mucinous type pattern (31,9%), stage III B (34%), being moderately differentiated (G2) (64,4%), with the presence of vascular invasion in 47,2% of cases and perineural invasion in 25,7%.

Nitche U et al. have reported similiar data on the frequency for mucinous adenocarcinoma and signet ring cell, resulting statistically significant aspects between tumoral stage and grade of differentiation ($p < 0,01$, X2test) [10]. Similar data was found in a retrospective study on large number of cases in which tumor grading represents an important prognostic factor, correlating significantly with tumor stage ($p < 0,01$). Most cases were classified as stage III and moderately differentiated (G2) [11]. The same statistically significant data was demonstrated between tumor stage and grade of differentiation in several other articles present in literature [12,13].

Tumor stage, vascular and perineural invasion, show a significant statistical aspect ($p < 0,05$, X2test), which indicates an aggressive mechanism of evolution. A study published in 2014 by Fuji et al. which included numerous patients with CRC, shows that the presence of vascular invasion is statistically significant and is an independent prognostic factor in a multivariate analysis [14].

Grade of differentiation, more specifically G2, the most frequent in the present study is also cited in many articles, being statistically significant with vascular invasion ($p < 0,05$, X2test), which shows an unfavorable prognostic independent of tumor stage [15,16].

On the other hand in our study, we could not observe this association with perineural invasion, the statistical aspect being insignificant. In comparison, other studies demonstrate the contrary, resulting in a positive correlation [17,18].

Conclusions

The results of this study underline the importance of histopathological parameters as prognostic factors in colic adenocarcinoma, being useful for stratification of patients in regards of tumor aggressivity of CRC.

References

1. Matthew Fleming, Sreelakshmi Ravula, Sergei F. Tatishchev, Hanlin L. Wang. Colorectal carcinoma: Pathologic aspects. *J Gastrointest Oncol*, 2012, 3(3):153–173.
2. McKay A, Donaleshen J, Helewa RM, Park J, Wirtzfeld D, Hochman D, Singh H, Turner D. Does young age influence the prognosis of colorectal cancer: a population-based analysis. *World J Surg Oncol*, 2014, 2;12:370.
3. Humpath.com-Human Pathology, 2003, Colorectal adenocarcinoma [online]. Available at: <https://www.humpath.com/spip.php?article956> [Accessed 14.05.2018].
4. Caliskan C, Guler N, Karaca C, Makay O, Firat O, Korkut MA. Negative prognostic factors in colorectal carcinoma: An analysis of 448 patients. *The Indian Journal of Surgery*, 2010, 72(3):243-248.
5. Dunlop MG, Tenesa A, Farrington SM, Ballereau S, Brewster DH, Koessler T et al. Cumulative impact of common genetic variants and other risk factors on colorectal cancer risk in 42,103 individuals. *Gut*, 2013, 62:871-881.
6. Bosman FT, Carneiro F, Hruban RH, Theise ND. Tumours of the Colon and Rectum. In: Bosman FT, Carneiro F, Hruban RH, Theise ND (Eds): *WHO Classification of Tumours, 4th Edition, Volume 3 - Pathology and Genetics of Tumours of the Digestive System*, Iarc Press, 2010, Lyon, 105-143.
7. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Contents of the SEER Cancer Statistics Review (CSR), 1975-2016 [online]. Available at: https://seer.cancer.gov/csr/1975_2015/sections.htm [Accessed 04.12.2018].
8. Fante R, Benatti P, di Gregorio C, De Pietri S, Pedroni M, Tamassia MG, Percesepe A, Rossi G, Losi L, Roncucci L, Ponz de Leon M. Colorectal carcinoma in different age groups: a population-based investigation. *Am J Gastroenterol*, 1997, 92(9):1505-1509.
9. Golan T, Urban D, Berger R, Lawrence YR. Changing prognosis of metastatic colorectal adenocarcinoma: Differential improvement by age and tumor location. *Cancer*, 2013, 119(16):3084-3091.
10. Nitsche U, Zimmermann A, Späth C, Müller T, Maak M, Schuster T, Slotta-Huspenina J, Käser SA, Michalski CW, Janssen KP, Friess H, Rosenberg R, Bader FG. Mucinous and signet-ring cell colorectal cancers differ from classical adenocarcinomas in tumor biology and prognosis. *Ann Surg*, 2013, 258(5):775-782.
11. Derwinger K, Kodeda K, Bexe-Lindskog E, Taflin H. Tumour differentiation grade is associated with TNM staging and the risk of node metastasis in colorectal cancer. *Acta Oncol*, 2010, 49(1):57-62.
12. Yang J, Guo R, Kang A, Chen X, Su B, Huang X, Jin Y, Li Z. A novel histological typing and grading-scale system of colorectal cancer. *Nan Fang Yi Ke Da Xue Xue Bao*, 2014, 34(2):169-173.
13. Barresi V, Reggiani Bonetti L, Ieni A, Caruso RA, Tuccari G. Histological grading in colorectal cancer: new insights and perspectives. *Histol Histopathol*, 2015, 30(9):1059-1067.
14. Fujii T, Sutoh T, Morita H, Yajima R, Yamaguchi S, Tsutsumi S, Asao T, Kuwano H. Vascular invasion, but not lymphatic invasion, of the primary tumor is a strong prognostic factor in patients with colorectal cancer. *Anticancer Res*, 2014, 34(6):3147-3151.
15. Gibson KM, Chan C, Chapuis PH, Dent OF, Bokey L. Mural and extramural venous invasion and prognosis in colorectal cancer. *Dis Colon Rectum*, 2014, 57(8):916-926.
16. Harris EI, Lewin DN, Wang HL, Lauwers GY, Srivastava A, Shyr Y, Shakhtour B, Revetta F, Washington MK. Lymphovascular invasion in colorectal cancer: an interobserver variability study. *Am J Surg Pathol*, 2008, 32(12):1816-1821.
17. Liebig C, Ayala G, Wilks J, Verstovsek G, Liu H, Agarwal N, Berger DH, Albo D. Perineural Invasion Is an Independent Predictor of Outcome in Colorectal Cancer. *J Clin Oncol*, 2009, 27(31):5131-5137.
18. Huh JW, Kim HR, Kim YJ. Lymphovascular or perineural invasion may predict lymph node metastasis in patients with T1 and T2 colorectal cancer. *J Gastrointest Surg*, 2010, 14(7):1074-1080.

Corresponding Author: Claudiu Mărgăriteșcu, Department of Pathology, University of Medicine and Pharmacy of Craiova, 66, 1 May Avenue, 200628 Craiova, Romania, e-mail: c_margaritescu2000@yahoo.com