

ARE THERE ANY SPECIFIC MORPHOPATHOLOGICAL FEATURES IN EMERGENCY COLON CANCER SURGERY?

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Abstract

The increased incidence of colon cancer patients requiring emergency surgery should raise more interest in its complete morphopathological characterization. We performed a retrospective analysis of all colon cancer patients admitted through the emergency setting and operated in our Institution during the last 5 years. Special emphasis was put on the morphological features of the cases, such as histopathologic type, grading, TNM staging, tumoral inflammatory infiltrate, perineural and vascular invasion. We identified 104 patients that underwent radical colon cancer surgery in the emergency setting between 2017 and 2021. Most cases were located on the sigmoid colon and were diagnosed as either locally advanced (92%) or metastatic disease (19%). Vascular invasion was identified in 29% of specimens, while perineural invasion was found in 38% of cases. Colon cancer patients undergoing emergency radical surgery display independent risk factors for the postoperative and the overall oncologic outcomes, such as comedo-necrosis, high lymph node involvement, locally advanced or metastatic disease, and perineural and vascular invasion.

Keywords: *emergency surgery, colon cancer, tumor grade, tumor type*

Introduction

The incidence of colorectal cancer has significantly increased over the last half a century in Western societies, accounting nowadays as the third most-commonly diagnosed cancer and the third cause of cancer-related deaths [1-3].

Over the years, the management of colon cancer witnessed multiple improvements, such as better diagnostic procedures, the introduction of minimal invasive surgery and interventional endoscopy as key elements in the modern therapeutic strategy, but also potential indications of radical surgery for the metastatic colorectal disease [4-6]. In face of this onslaught of novel accessories in the fight against

colorectal cancer, the advances in the histopathologic examination may have passed largely unnoticed.

Together with the histopathologic subtype and TNM staging, tumor grading represents one of the most important predictive factors of colon cancer aggressiveness in histopathological common practice [7]. Other equally important factors for the therapeutic outcomes of colon cancer are the perineural and the microvascular invasion, the mitotic rate and the expression of various molecular markers in the tumoral tissue. However, these factors are not yet fully integrated into a well-established clinical algorithm, thus eluding the prospect of an oncologic patient-tailored therapy [8]. A

potential explanation would be that all these variables, which are partially available to the clinician, are too complex and therefore too difficult to use in the clinical practice.

Methods

We performed a retrospective review of all medical records from 2017 to 2021 in order to create a database of patients operated in the emergency setting for a complicated form of colon cancer. Patients that underwent radical procedures with histopathologic specimen evaluation were isolated. The demographic parameters, the types of procedure, and tumor characteristics (topography, staging, histologic subtype, grading) were analyzed.

Inclusion criteria were: radical surgery for colon cancer performed during the emergency admission; the histopathological confirmation of colon cancer.

Exclusion criteria referred to: lack of relevant histopathological data (histologic subtype, perineural invasion, vascular invasion, and lymph node involvement); age less than 18 years; and palliative surgery performed during the primary admission.

The intraoperative staging was based on the American Joint Committee on Cancer (AJCC) staging recommendations [9]. Thus, tumors invading the submucosa were classified as T1, those invading the muscularis propria were classified as T2, while T3 status was allocated to those tumors that penetrate through the muscularis propria into pericolic tissues. Cases were considered as T4a when colon cancer was visible on the visceral peritoneum, or as T4b if it directly invaded or was adherent to the nearby structures. The assessment of the peritumoral inflammatory infiltrate, on a scale ranging from 1 to 3, was based on the Klintrup–Makinen grading system [10], in accordance to the estimations of the pathologist.

Data acquisition was performed by the retrospective analysis of our Hospital electronic clinical database (Hypocrat), followed by individual analysis of each patient's medical file. Relevant data, such as demographics, histologic subtype, TNM staging, tumoral grading, were uploaded in an electronic registry using Microsoft Excel worksheet.

Statistical analysis was performed using Microsoft Excel (Microsoft Office Professional Plus, Microsoft™, Redmond, Washington, US)

Results

After the exclusion criteria were applied, 104 patients were registered to have radical colon cancer surgical procedures performed in the emergency setting in our department during the above-mentioned interval. The clinico-demographic data of the patients is detailed in table 1.

Category	Value	Percentage
Age	69.2 (years)	
<i>Sex distribution</i>		
male	51	49%
female	53	51%
<i>Place of origin</i>		
rural	57	55%
urban	47	45%
<i>Co-morbidities</i>		
cardiac	46	45%
vascular	10	10%
pulmonary	5	5%
renal	11	11%
diabetes	16	16%

Table 1 - The clinico-demographic characteristics of patients with colon cancer undergoing emergency surgery

The mean age of these patients was 69.2 years, with a sex ratio of 0.96 (53 females and 51 males).

The topography of tumors in descending order was sigmoid localization in 33 cases, hepatic flexure in 15 cases, cecum in 14 cases, ascending colon in 13 cases, transverse colon and splenic flexure in 12 cases each, and 5 cases on the descending colon.

The average maximal diameter of the tumors was 4.3 cm, with the average size of the cecum, ascending, transverse, descending, and sigmoid

colon at 5.5 cm, 4.8 cm, 4.1 cm, 3.4cm, and 3.9 cm respectively. Most patients were admitted with locally advanced cancer (92.3% of cases in T3 and T4), while 51% had lymph node involvement (34 cases of N1, 21 cases of N2) and 19% of cases had metastatic disease (liver metastases in 21 patients, carcinomatosis in 4 cases, and pulmonary metastases in 2 cases). From the histopathological perspective, despite the fact that the majority of cases was adenocarcinoma, a significant number of specimens displayed large mucinous component (34% of cases), but with extracellular mucin of

less than 50% of the tumor volume which allowed their classification as adenocarcinoma with mucinous features (mucinous differentiation). We counted 12 cases of mucinous carcinoma (11.5%) and 3 cases of signet ring cell adenocarcinoma (2.8%). Moreover, comedo-type carcinoma was also a rather frequent encounter, in 23.7% of cases, further contributing to the poor outcome of the patients. Vascular invasion was found in 29% of specimens, while perineural invasion was observed in 38.2% of cases (Table 2).

Category	Value	Percent
Localization		
Right colon (including cecum, hepatic flexure)	42	40.3%
Transverse colon	12	11.5%
Descending colon (including splenic flexure)	17	16.3%
Sigmoid	33	31.7%
T		
2	8	7.7%
3	49	47.1%
4	47	45.2%
N		
0	51	49%
1	34	32.7%
2	21	20.2%
M		
0	84	80.8%
1	20	19.2%
Grading		
G1	12	11.5%
G2	72	69.2%
G3	19	18.2%
G4	1	0.9%
Peritumoral inflammatory infiltrate		
1	23	22.1%
2	39	37.5%
3	42	40.3%
Vascular invasion		
	59	56.7%
Perineural invasion		
	49	47.1%

Table 2 - The topographic, morphopathologic and staging characteristics of colon cancer patients in the emergency setting

Discussion

Population aging, poor access to medical resources and education, the nutritional habits, but also the current epidemiologic context

marked by the Covid-19 pandemics, led to an increase in cases of colon cancer admitted in the emergency setting. This new reality offers unforeseen consequences and additional challenges for the medical system in general, and

for the clinician, in particular. Analyzing the current medical context, from its fundamental aspects – such as demographic, clinical and morphological determinants – is therefore of paramount importance.

While most of the colon cancers consist of adenocarcinomas arising from the mucosal cells, the World Health Organization (WHO) provides a much more comprehensive classification. In this regard, colorectal cancer can be divided in a high number of histopathologic subtypes, including mucinous, micropapillary, signet ring cell, medullary, comedo-type cribriform, spindle cell, adenosquamous, and undifferentiated carcinomas, together with the less common variants of colorectal cancer such as leiomyosarcomas, primary lymphomas, carcinoid tumors, gastrointestinal stromal tumors, and melanomas [11]. Up to 10% of all adenocarcinoma are represented by signet ring cell and mucinous adenocarcinoma. The defining histopathologic feature of mucinous subtypes is the high amount extracellular mucin – accounting for > 50% of the tumor mass [12]. In case of signet ring cell subtypes, the intracellular mucin is displacing the nucleus towards the cell periphery. Medullary (MC) and serrated carcinoma (SC) variants of colorectal cancer commonly involve specific molecular pathways, in the way that microsatellite instability is constantly encountered in MC, whereas SC is associated with excess methylation. MCs are predominately found in women as bulky, right colon tumors. MC are expansive tumors consisting of stratified layers of undifferentiated cells with spheroid nuclei, pronounced nucleoli, and frequent Crohn's disease-like reaction. MC is frequently diploid with a fairly good prognosis and low rate of lymph node invasion [13, 14]. Almost 8% of all colorectal cancers and approximately 17.5% of right colon neoplasia are SCs, which are newly acknowledged subtypes defined by specific morphopathological characteristics, with the serrated adenoma being considered as the precursor lesion [15].

Glandular formation is one of the main features of conventional adenocarcinoma. Depending on the degree of gland formation, three degrees of tumor grading can be encountered. Well differentiated tumors (gland formation in more than 95% of the tumor) account for 10% of the total cases of colon

adenocarcinoma, moderately differentiated tumors (gland formation in 50-95% of the tumor), found in most cases (70%) of adenocarcinoma of the colon, and poorly differentiated adenocarcinoma (gland formation in less than 50% of the tumor), diagnosed in 20% of patients. Little effort has been done to assess the incidence and distribution of each of these morphopathological subtypes of colon cancer in the emergency setting, which may vary significantly compared to elective cases. Other histologic aspects that are largely disconsidered in the therapeutic planning, especially during emergency admissions, are the expression of various molecular markers in the tumoral tissue, the microvascular and perineural invasion, as well as the mitotic and apoptotic rate [16-20]. The relevance of these aspects lay in the particularities and the implications for the diagnostic and therapeutic protocol for each of these factors, but also in the variation of intra and postoperative outcomes.

Our study aimed to better evaluate the morphopathological characteristics of colon cancer cases undergoing emergency radical surgery for this pathology. Our results show that most of the patients included in this study presented with locally advanced or metastatic disease, microvascular and perineural invasion, and intense peritumoral inflammatory infiltrate. The high rate of comorbidities further increased the complexity of the surgical management for these cases, partially explaining the unfavorable postoperative results.

Conclusions

Colon cancer patients that are potential candidates for emergency radical surgery associated independent morphopathologic risk factors for the postoperative and the overall oncologic outcomes, such as intense peritumoral inflammation infiltrate, locally advanced or metastatic disease, perineural and vascular invasion.

Conflict of interests: The authors declare no competing interests.

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