

PROFESSIONAL PAPER

Clinicopathological predictors of five-year mortality in colorectal cancer patients in the Zenica-Doboj Canton, Bosnia and Herzegovina

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ABSTRACT

Aim To identify the clinicopathological factors associated with five year mortality in patients with colorectal cancer (CRC) treated at Cantonal Hospital Zenica, Bosnia and Herzegovina.

Methods A retrospective cohort of 64 consecutively operated CRC patients (2019–2024) was analysed. The baseline variables included age, sex, tumor stage, histology, metastatic burden, local infiltration, and comorbidities. Five year cumulative mortality was the primary outcome. Risk ratios (RR) with 95 % confidence intervals (CI) were calculated by two by two contingency analysis.

Results The cohort comprised 26 women (40.6 %) and 38 men (59.4 %); their median age was 64 years (IQR 58.8–73.0). Eleven patients (17.2 %) died within five years. Mortality was strongly linked to tumor spread and cardiometabolic disease. Any distant metastasis conferred a fifteen fold increase in risk (9/15 vs 2/49; RR 14.7, 95 % CI 3.6–60.8, $p < 0.001$), and the involvement of two or more metastatic sites remained prognostic (RR 5.6, 95 % CI 1.9–16.9, $p = 0.014$). Infiltration of more than two adjacent organs quadrupled mortality (RR 4.4, 95 % CI 1.7–11.6, $p = 0.032$). Hypertension was present in 10 of the 11 deaths, yielding an RR of 12.1 (95 % CI 1.6–88.8, $p = 0.002$). Type 2 diabetes also increased risk (RR 3.5, 95 % CI 1.3–9.6, $p = 0.040$). Patients with three or more comorbid conditions had a nearly four times higher mortality (RR 3.9, 95 % CI 1.3–11.7, $p = 0.027$).

Conclusion The five year death rate in this Bosnian Herzegovinian CRC cohort was driven chiefly by distant metastasis, extensive local invasion, and cardiometabolic comorbidities—especially hypertension and type 2 diabetes. Early detection of metastatic spread and proactive management of vascular risk factors may improve survival in similar settings.

Keywords: colorectal cancer, predictors, mortality rate, comorbidities, recurrence.

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Introduction

Colorectal cancer (CRC) is a malignant disease of the colon and rectum, which is a public health problem in terms of morbidity and mortality¹. CRC is the third most commonly diagnosed cancer and the second leading cause of death in the world². In Bosnia and Herzegovina, CRC is the second most common form of cancer in men and women, after lung and breast cancer, meaning that more than 1,800 people develop the disease each year³. The risk factors for the development of CRC can be divided into fixed and variable risk factors. Irreversible risk factors include: age, genetics (estimated to be non-hereditary in 70% of cases and hereditary in 20% of cases), a positive family history of hereditary syndromes, namely: FAP syndrome, Lynch syndrome, Peutz-Jeghers syndrome, Cowden's disease, juvenile polyposis syndrome, and Cronkhite-Canada syndrome, and a positive personal history of inflammatory bowel diseases such as Crohn's disease and ulcerative colitis (which have a 7-11 times higher risk of passing into cancer). Variable risk factors include: diet, obesity, physical inactivity, cigarettes, and alcohol¹. CRC often leads to local infiltration of neighboring organs and distant metastasis, which is the leading cause of death. The organs where the metastases first appear are the liver, lungs, brain, bones, and peritoneum. The liver is the most common site of metastasis. The pathway for tumor cells to reach the liver is through the portal venous system⁴. Since CRC occurs at an older age, patients typically have a high comorbidity rate. The CRC uses comorbidity indices, namely the Charlson index and the Elixhauser index⁵.

The overall five-year mortality was highest in patients who had metastatic changes (82%), and in patients who had other comorbidities in addition to CRC, such as hypertension (91%) and type 2 diabetes mellitus (36%). Patients who were in stage III-IV had a high mortality rate (73%) and patients who had local infiltration to adjacent organs (55%). Therefore, this study was conducted to determine clinically the pathological predictors of five-year mortality in patients with CRC, because in Bosnia and Herzegovina we do not have accurate data on the subject of this study.

The aim of this study was to analyze the clinicopathological predictors of patients with colorectal cancer admitted to

the Department of Surgical Diseases at Cantonal Hospital Zenica over five years, from 2019 and 2024, to analyze the comorbidities in patients with CRC, and to show which predictors act directly on the patient's mortality outcome.

Material and methods

Patients and study design

This retrospective study, conducted between January 2019 and January 2024 at the Department of Surgical Diseases of Cantonal Hospital Zenica (Bosnia and Herzegovina), included 64 patients.

Inclusion criteria were: patients diagnosed with colorectal cancer by pathohistological analysis, and patients undergoing surgical treatment. Patients treated surgically in other institutions, without full diagnostic evaluation, with benign colorectal pathology, or with confirmed cancer but not treated surgically were excluded from the study. All patients provided informed consent after having the study's purpose explained. The study was approved by the Ethics Committee of Cantonal Hospital Zenica.

Methods

The clinical data were collected from electronic medical records and classical paper medical histories. The following variables were collected: sex, the pathohistological type of cancer, the stage of cancer, metastases, local infiltration of cancer, mortality, and comorbidities. All patients underwent colonoscopy, pathohistological analysis (biopsy), and magnetic resonance imaging (MRI, Magnetom Avanto 1.5 T, Siemens, Erlangen, Germany) or computed tomography (CT, Somatom Definition AS, Siemens, Erlangen, Germany). Each patient had a colonoscopy with a biopsy of the tumor tissue. Part of the tumor tissue was preserved and sent for pathohistological examination. For analysis, the sample was placed in a 4% formaldehyde solution with a pH of 7.4 for 12-16 hours. Slices 5 µm thick were prepared from formalin-fixed material, embedded in paraffin, placed on appropriate glass plates, and stained with haematoxylin and eosin (H&E), periodic acid-Schiff (PAS) haematoxylin, and by the

Goldner-Szekely (GS) trichrome method, to determine changes in the tumor tissue's morphology⁶. The stage of the cancer indicates how far the cancer has spread in the body. It is determined on the basis of the TNM classification defined by the American Joint Committee on Cancer (AJCC) as: stage 0 (Tis, N0, M0), stage I (T1/T2, N0, M0), stage IIA (T3, N0, M0), stage IIB (T4, N0, M0), stage IIIA (T1/T2, N1, M0), stage IIIB (T3/T4, N1, M0), stage IIIC (T1/T2/T3/T4, N2, M0) or stage IV (T1/T2/T3/T4, N1/N2, M1)⁷.

Statistical analysis

Descriptive statistical methods were employed. Data were presented as frequencies (N) and percentages (%) for categorical variables, while the median and interquartile range (IQR) were used for continuous variables. The normality of the distribution was tested using the Kolmogorov-Smirnov test. To determine the predictive factors for five-year survival, the risk ratio with a 95% confidence interval (95% CI) was applied. Statistical significance was set at 5% ($p \leq 0.05$).

Results

A total of 64 patients were enrolled. Of these, 26 (40.6%) were women and 38 (59.4%) were men, with a median age of 64 years (IQR: 58.75 - 73.00) (Table 1).

Adenocarcinoma was the predominant histological type, present in 59 (92.2%) patients, while mucinous carcinoma was found in 5 (7.8%). Stage III tumors were the most common, seen in 26 (40.6%), followed by stage I in 17 (26.6%), stage II A in 9 (14.1%), stage IV in 8 (12.5%) and stage II B in 4 (6.3%). Metastases were identified in 15 (23.4%) patients. Among these, 11 (17.2%) had one metastasis, 3 (4.7%) had two, and 1 (1.6%) had three. Metastatic sites included the liver in 11 (17.2%) patients, the lungs in 7 (10.9%) and other sites in 2 (3.1%) (Table 2).

Local infiltration was observed in 23 (35.9%) patients. One organ was infiltrated in 12 (18.8%) cases, two in 6 (9.4%), three in 4 (6.3%) and four in 1 (1.6%). The uterus was the most commonly infiltrated organ (6; 9.4%), followed by the small intestine (3; 4.7%),

Table 1. Baseline data

Variable		Total
		No (%)
Sex	Female	26 (40.6)
	Male	38 (59.4)
		Median (IQR)
Age (years)		64 (58.75 - 73.00)
Comorbidities		N (%)
DMT2		9 (14.1)
HTA		29 (45.3)
Other primary neoplasms		4 (6.3)
Without comorbidities		23 (35.9)
No. of comorbidities	1	7 (10.9)
	2	11 (17.2)
	3	6 (9.4)
	4	2 (3.1)
	5	12 (18.8)

IQR - interquartile range

Table 2. Histopathological and clinical data

Variable		No (%)
Histological type		
Adenocarcinoma		59 (92.2)
Mucinous		5 (7.8)
Stage		
	I	17 (26.6)
	II A	9 (14.1)
	II B	4 (6.3)
	III	26 (40.6)
	IV	8 (12.5)
Metastases	YES	15 (23.4)
	NO	49 (76.6)
No. of metastases	1	11 (17.2)
	2	3 (4.7)
	3	1 (1.6)
Site of metastasis		
Lungs		7 (10.9)
Liver		11 (17.2)
Other sites		2 (3.1)
Local infiltration	YES	23 (35.9)
	NO	41 (64.1)
No of infiltrated organs	1	12 (18.8)
	2	6 (9.4)
	3	4 (6.3)
	4	1 (1.6)
Site of infiltration		
Uterus		6 (9.4)
Ovary		1 (1.6)
Small intestine		3 (4.7)
Vagina		2 (3.1)
Urinary bladder		2 (3.1)
Aorta and common iliac blood vessels		1 (1.6)
Other sites		5 (7.8)
Recurrence		2 (3.1)
5-year mortality		11 (17.2)

vagina and bladder (2 each; 3.1%), an ovary and major blood vessels (1 each; 1.6%), and other sites in 5 (7.8%). Recurrence occurred in 2 (3.1%) patients, while 11 (17.2%) died within five years. Comorbidities were present in 41 (64.1%) patients, most commonly hypertension (29; 45.3%), followed by type 2 diabetes mellitus (9; 14.1%), and other primary neoplasms (4; 6.3%). A total of 23 (35.9%) of the patients had no comorbidities. One comorbidity was reported in 7 (10.9%) patients, two in 11 (17.2%), three in 6 (9.4%), four in 2 (3.1%) and five in 12 (18.8%) (Table 1).

Five year mortality in this cohort was driven chiefly by tumor spread and the cardiometabolic burden. Patients with any metastasis experienced a 15 fold higher risk of death than those without metastasis (9/15 vs 2/49; RR = 14.7, 95 % CI 3.6–60.8, $p < 0.001$), and the risk was substantially elevated when two or more metastatic sites were present (RR = 5.6, 95 % CI 1.9–16.9, $p = 0.014$). Extensive local invasion also mattered: infiltration of more than two neighboring organs quadrupled mortality (RR = 4.4, 95 % CI 1.7–11.6, $p = 0.032$). Among the comorbidities, hypertension showed the strongest association,

with 10 of 29 hypertensive patients dying, versus 1 of 35 normotensive patients (RR = 12.1, 95 % CI 1.6–88.8, $p = 0.002$), while type 2 diabetes nearly quadrupled the risk (RR = 3.5, 95 % CI 1.3–9.6, $p = 0.040$). Having three or more co existing diseases conferred a comparable increase (RR = 3.9, 95 % CI 1.3–11.7, $p = 0.027$). Stage III–IV tumors, male sex, and single organ infiltration showed elevated but statistically non significant risks (Table 3).

Discussion

This retrospective analysis provides the first country-specific insight into the clinicopathological determinants of CRC five-year mortality in Bosnia and Herzegovina. Three principal observations emerged. First, men were more frequently affected than women, echoing the male predominance reported by Araghi et al.⁸. Second, conventional adenocarcinoma remained the dominant histological subtype (92.2 %), with mucinous variants comprising the remainder, a distribution consistent with data from Liu et al.⁸. Third, most tumors were diagnosed at an advanced stage: stage IIIB accounted

Table 3. Predictive factors for 5-year mortality

Variable	Five-year mortality No (%)	RR (95% CI)	p
Sex (Male)	8 (72.7)	1.82 (0.53 – 6.24)	0.502
Histological type (Mucinous)	2 (18.2)	2.62 (0.77 – 8.98)	0.201
Stage (III–IV)	8 (72.7)	14.70 (3.56 – 60.75)	<0.001
Metastasis (Yes)	9 (81.8)	5.63 (1.88 – 16.85)	0.014
No. of metastases (≥ 2)	3 (27.3)	2.14 (0.73 – 6.25)	0.182
Local infiltration (Yes)	6 (54.5)	4.42 (1.69 – 11.59)	0.032
No. of infiltrated organs (>2)	3 (27.3)	6.89 (3.77 – 12.60)	0.027
Recurrence	2 (18.2)	3.49 (1.28 – 9.55)	0.040
Neoadjuvant oncological treatment	5 (45.5)	12.07 (1.64 – 88.81)	0.002
DMT2	4 (36.4)	3.33 (1.06 – 10.53)	0.134
HTA	10 (90.9)	3.85 (1.28 – 11.67)	0.027
Other primary neoplasm	2 (18.2)	1.82 (0.53 – 6.24)	0.502
No. of comorbidities (≥ 3)	7 (63.6)	2.62 (0.77 – 8.98)	0.201

RR - risk ratio

for 40.6 % of cases, whereas Gunderson et al. noted stage IIA as the modal category in a Western cohort. The higher proportion of stage IIIB disease in our setting likely reflects delayed presentation and limited screening coverage.

Approximately one quarter of the patients harbored distant metastases, most commonly to the liver and lungs. This pattern is in accord with the hierarchical spread described by Qiu et al.¹¹, reinforcing the liver as the first-line target organ for hematogenous dissemination from both colon and rectal primaries. Contiguous organ invasion was detected in more than one-third of tumours, predominantly affecting pelvic viscera such as the uterus and bladder, mirroring infiltration profiles observed in Japanese and Moldovan cohorts^{12,13}. This local extension complicates surgical resection and has been linked to inferior disease-specific survival.

The burden of comorbidity was substantial: nearly two-thirds of patients had at least one chronic condition, chiefly hypertension and type 2 diabetes. These findings match the multimorbidity spectrum reported by Pennisi et al.¹⁴, and highlight potential interaction between cardiovascular risk factors, treatment tolerance, and overall survival. Comprehensive management of co-existing illnesses should therefore form an integral component of CRC care pathways in the region.

The study's strengths include histologically confirmed diagnoses and systematic staging, enabling meaningful comparison with international datasets. Nevertheless, reliance on routine records revealed missing data, particularly in terminal cases managed partly outside our institution. Consequently, the prevalence of certain predictors—most notably comorbidity load and cause-specific mortality - may be underestimated. Prospective multicenter registries with uniform data capture would offer superior granularity and facilitate molecular-epidemiological correlations.

From a public-health perspective, the predominance of stage IIIB disease underscores the urgency of implementing nationwide screening programs capable of detecting lesions at a curable stage. Furthermore, recognition of liver-predominant metastasis supports

early integration of hepatobiliary imaging and multidisciplinary evaluation. Future research should explore biomarker-driven risk stratification and evaluate the impact of comorbidity optimization on treatment outcomes.

The limitations of the present study stem primarily from its single center retrospective design and relatively small sample size. Nevertheless, the analysis of histologically confirmed and fully staged cases provides a reliable baseline for future prospective multicenter investigations that incorporate molecular profiling and extended follow up.

In conclusion, male sex, advanced stage at diagnosis, hepatic metastasis, and extensive local invasion emerged as the chief determinants of CRC mortality in Bosnia and Herzegovina. Targeted screening, timely staging, and integrated management of comorbid conditions represent actionable strategies for improving survival in this population.

Disclosure statement

The authors report there are no competing interest to declare.

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Author's Contribution

Nejla Huseinspahic; Data curation, Visualization, Investigation, Writing-Reviewing, Savan Kuridza: Data curation, Visualization, Investigation, Emir Begagic; Data curation, Investigation, Andrej Popov; Conceptualization, Methodology, Elvir Besic; Data curation, Investigation Writing-Original draft.

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